Rumination and Impaired Cortisol Recovery Following a Social Stressor in Adolescent Depression

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Abstract Response styles theory promotes rumination as a central cognitive construct driving negative mood and depression, and past research suggests that at least part of the mechanism driving rumination’s depressogenic effect is through inhibiting the individual’s ability to shift attentional focus away from negative environmental stimuli. In the current study, we hypothesized that high trait rumination would be associated with impaired recovery of the body’s biological response to psychological stress. In a community sample of depressed (n=31) and non-depressed (n=33) adolescents we assessed rumination and the more adaptive trait of distraction and problem-solving with the Children’s Response Styles Questionnaire (CRSQ; Abela 2000), and diagnostic status was confirmed using the Child and Adolescent Schedule of Affective Disorders and Schizophrenia (K-SADS; Kaufman et al. Journal of the American Academy of Child and Adolescent Psychiatry 36:980–988, 1997). Participants completed the Trier Social Stress Test (TSST; Kirschbaum et al. Neuropsychobiology 28:76–81, 1993), and the focus of our analyses was the change in salivary cortisol concentration between peak cortisol output (25 min post-stressor) and a sample taken during the “Recovery” period 65 minutes post-stressor. Consistent with the predictions of response style theory, among the depressed adolescents only, high trait rumination was associated with delayed post-stressor cortisol recovery, whereas high trait distraction and problem-solving was associated with more rapid recovery. In contrast, response styles were not associated with cortisol recovery in the non-depressed group. These findings implicate impaired post-stress cortisol recovery as a potential mechanism underlying the pathological effect of rumination on the development and maintenance of Major Depressive Disorder (MDD).

Keywords Depression · Adolescence · Response styles · HPA axis dysregulation · Stress

Rumination is a widely studied cognitive construct that has emerged as central to the etiology, maintenance, and exacerbation of Major Depressive Disorder (MDD). According to Response Styles Theory (RST; Nolen-Hoeksema 1991), rumination is defined as a maladaptive cognitive process involving passive, repetitive thinking about the potential causes and consequences of one’s depressive symptoms, and is conceptualized as a stable trait that increases risk for depressed mood. In contrast, distraction is defined as an adaptive alternative response to one’s depressive symptoms and involves thoughts or activities that direct attention away from these symptoms (Nolen-Hoeksema et al. 2008).

RST proposes that the central maladaptive consequences of rumination are a worsening and prolongation of negative mood and depression. Early experimental work with non-depressed college students has shown that laboratory-induced rumination is associated with increases in self-reported dysphoria over time, whereas distraction is associated with decreases in dysphoria (e.g., Lyubomirsky et al. 1998; Lyubomirsky and Nolen-Hoeksema 1993, 1995; Nolen-Hoeksema and Morrow 1993). Further, in both adult and adolescent clinical samples, high levels of rumination prospectively predict new onsets of MDD, and are associated with longer, more severe episodes of the illness (e.g.,

Researchers have proposed that the mechanism through which rumination acts to worsen and prolong depressed mood is by inhibiting the individual’s ability to shift attentional focus away from negative self-referential information in the environment. For example, functional neuroimaging studies have shown that high trait rumination, particularly in the context of depression, is associated with sustained amygdala activity in response to negatively valenced stimuli (Ray et al. 2005; Siegle et al. 2002). Further, Johnson et al. (2009) found that during a laboratory-induced rumination task, participants with depression showed lower activity than controls in areas of the medial prefrontal cortex (mPFC) that are associated with positively valenced thought. Taken together, the above results suggest that dysphoric and depressed individuals with a tendency to ruminate selectively recruit neural regions responsible for processing negative self-relevant information, and inhibit regions responsible for processing positive information.

The above research has important implications for understanding individual differences in recovery following stress. Young and Nolen-Hoeksema (2001) have suggested that a ruminative self-focus in the face of stress may impair the body’s natural recovery process, and lead to amplification and prolongation of the stress response. The biological stress response is regulated by the hypothalamic pituitary adrenal (HPA) axis, which has the glucocorticoid hormone cortisol as its final output. On average, the concentration of circulating cortisol in the bloodstream reaches its peak 20–30 min after the onset of an acute stressor. When individuals are exposed to laboratory stressors that involve uncontrollable, social-evaluative threat, circulating levels of cortisol fall towards baseline (i.e., recover) over the course of up to 60 min following the offset of the stressor through a process of negative feedback (Dickerson and Kemeny 2004). Meta-analytic work in adults has documented a significant prolongation of the biological response to laboratory stress challenge in patients with MDD versus non-depressed controls, as indicated by impaired recovery of cortisol levels post-stressor ($d=1.39$, $SE=0.35$, $n=4$; Burke et al. 2005). Children and adolescents with MDD also show a dysregulated HPA axis response to stress challenge as indexed by higher peak cortisol (Luby et al. 2003; Rao et al. 2008) and higher cortisol levels during recovery (Rao et al. 2008).

Given the research reviewed above relating high trait rumination to deficits in shifting attentional focus from negative information, one would expect those high in rumination to display a prolongation of the biological stress response, as indexed by a slower return to baseline, and generally increased cortisol concentration in the recovery phase. Presumably, this relation of rumination and prolonged HPA axis activation is mediated by increased amygdalar and decreased mPFC activation, given the anatomical link between the HPA axis and these cortico-limbic structures. Indeed, functional evidence suggests that increased amygdalar and decreased mPFC activation is associated with greater cortisol output (Kern et al. 2008; Taylor et al. 2008). However, despite the shared neural correlates of trait rumination and cortisol secretion, empirical evidence for the impact of trait rumination on cortisol secretion in response to stress has been mixed.

Consistent with predictions, Zoccola et al. (2010) found that high trait rumination (measured using the rehearsal subscale of the revised Emotion Control Questionnaire; Roger and Najarian 1989) was associated with heightened cortisol reactivity and delayed recovery following a laboratory stress challenge paradigm. In contrast, an earlier study by the same group and using the same challenge paradigm, found that their sample of high ruminators (assessed with the Response Styles Questionnaire [RSQ; Nolen-Hoeksema and Morrow 1991]) showed a blunted pattern of cortisol response, and it was low ruminators who showed pronounced cortisol reactivity to the stressor (Zoccola et al. 2008). Finally, Young and Nolen-Hoeksema (2001) reported no difference between high and low ruminators, as assessed by the RSQ, in terms of their peak cortisol output or recovery in response to a social stress challenge.

There are likely several methodological factors that could explain the discrepant results reported above. Most importantly, however, all of these studies employed analogue samples of college undergraduates and none examined the individuals most at risk for prolonged negative mood in response to ruminating — those with heightened levels of depression. Given that RST explicitly conceptualizes rumination as a cognitive reaction to depressive symptoms, research to date has not provided an adequate test of the hypothesis that rumination is differentially associated with impaired recovery of the biological stress response among those with and without depression.

The current study is the first to our knowledge to investigate the relation of trait rumination to cortisol recovery from stress in a sample of adolescents diagnosed with a unipolar depressive disorder according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; American Psychiatric Association 2000) criteria. By focusing on individuals at highest risk for the negative effects of rumination, this will provide a more appropriate test of the hypothesis that rumination is related to HPA-axis dysregulation in MDD (Burke et al. 2005; Lopez-Duran et al. 2009). Adolescence is a key developmental period for the onset of depression (e.g., Kessler and Walters 1998) but research on the etiological mechanisms involved in initial onsets of depression in this group is lacking. Establishing a relation between rumination and impaired recovery of the biological stress response in adolescence represents an important first step to implicating rumination in the maintenance of depression over the lifespan.
We will utilize the Trier Social Stress Test (TSST; Kirschbaum et al. 1993), which has distinct advantages in the laboratory assessment of the stress response given its high degree of social evaluative threat and uncontrollability, thereby ensuring biologically relevant responses (Dickerson and Kemeny 2004). The current study is the first to our knowledge using an adolescent sample that examines cortisol recovery from the TSST in a manner that controls for the inter-individual differences in peak cortisol output. Some studies (Rao et al. 2008; Zoccola et al. 2010) have found that groups that show higher cortisol concentration during recovery also have significantly higher peak cortisol values. Our study will address this confound by controlling for peak cortisol concentration, and thus examining the change in cortisol in response to a stressor to index recovery.

Further, the current study is the first to examine the effects of distraction on cortisol recovery following stress (Nolen-Hoeksema 1991). Studies on the neurobiological correlates of employing distraction to reduce negative affect have found patterns of activation that are opposite to those reported in the studies on rumination. For instance, a recent study found that participants displayed decreased amygdalar activation coupled with increased activation in a large area of the mPFC (including the dorsal Anterior Cingulate Cortex) associated with controlling attention to emotional stimuli and for signaling the need for cognitive control, on trials on which they were distracted from a negatively valenced face using an unrelated stimulus (McRae et al. 2010). As was reviewed above, the same neural correlates of rumination (i.e., increased amygdalar and decreased mPFC activation) are associated with greater cortisol secretion in response to stress (Kern et al. 2008; Taylor et al. 2008). In the current context, therefore, individuals with a tendency to distract may have more rapid cortisol recovery in the face of stress. By focusing on both rumination and distraction we will clarify their respective roles in the pathology of depression.

Finally, the current study will extend previous research by also examining the ratio of rumination to distraction, in addition to rumination and distraction separately. This ratio indexes the probability of engaging in rumination over distraction in response to low mood. Using this approach to response styles assumes that both types of response styles exert independent effects on cortisol recovery and that these effects can be combined in a linear fashion. In a sample of children, Abela et al. (2007) demonstrated that the ratio of rumination to distraction scores was more strongly related to change in depressive symptoms over time than was either scale on its own.

For the purposes of this study, we define cortisol recovery as the cortisol concentration 40 min following the offset of the stressor, controlling for the peak cortisol concentration collected immediately following the stressor. Therefore, lower cortisol recovery values indicate a more rapid return of circulating cortisol to baseline, whereas higher cortisol recovery values indicate a slower return of circulating cortisol to baseline. We hypothesize that, among depressed adolescents only, higher self-reported trait rumination will be significantly associated with higher cortisol recovery values (i.e., slower recovery). In contrast, we hypothesize that higher trait distraction and problem-solving will be associated with lower cortisol recovery values (i.e., more rapid recovery). Finally, again among depressed adolescents only, we predict that a higher ratio of rumination to distraction will be associated with higher cortisol recovery values (i.e., slower recovery).

**Method**

**Participants**

The sample consisted of 64 adolescents (47 females) aged 12–18 years ($M=15.30$, $SD=1.89$) recruited from a mid-sized community in southeastern Ontario. These participants are part of a larger ongoing study examining pathological stress processes in adolescent depression, and data including a subset of the current sample ($n=37$) have been published previously (Harkness et al. 2011). Approximately 90% ($n=58$) of participants were of European ancestry, which is consistent with the ethnic diversity of the population in the area. Demographic and clinical characteristics of the sample, stratified by diagnostic status, are presented in Table 1. Among the depressed adolescents, 19 (61.3%) were receiving some form of treatment, and 9 (29.0%) were taking at least one psychotropic medication at the time of the study. Non-psychiatric control participants were recruited from local high schools, as well as community advertisements. Depressed adolescents were referred from mental health practitioners in the community or were self-referred in response to advertisements.

The depressed group all met DSM-IV-TR (American Psychiatric Association 2000) criteria for a current non-bipolar, non-psychotic mood disorder based on a structured diagnostic interview (see below). Participants were excluded if they met criteria for any of the following: a psychotic disorder, bipolar disorder, substance dependence, conduct disorder, a developmental disability, or a medical disorder that could cause depression. Adolescents in the non-psychiatric control group did not meet diagnostic criteria for any current or past psychiatric illness.

Our initial sample included 106 adolescents. Twenty-eight individuals were excluded based on our diagnostic exclusionary criteria. Further, eight participants did not complete the measure of response styles, and six were missing one or more cortisol samples, leaving 64 usable cases. The final sample did not differ from excluded participants in terms of sex, $\chi^2(1, N=106)=0.56$, $p=0.45$, age, $t(104)=1.44$, $p=0.15$, parental occupation status, $t(104)=1.25$, $p=0.21$, or ethnic distribution, $\chi^2 (3, N=105)=1.70$, $p=0.64$.
Measures

Child and Adolescent Schedule of Affective Disorders and Schizophrenia (K-SADS; Kaufman et al. 1997) We evaluated the presence of current and/or past DSM-IV-TR Axis I diagnoses using the full K-SADS. Advanced graduate students in clinical psychology administered all interviews after being trained to gold-standard reliability status by the second author (see Grove et al. 1981). Trainees participated in at least six interviews (three observing a trained interviewer, and three conducting the interview) and coded diagnoses independently of their co-interviewer. Trainees were required to have 100% agreement with their trained co-interviewer on diagnoses prior to conducting solo interviews. Each interviewer was provided with ongoing clinical supervision, and conferenced each case, with the fifth author for the duration of the project.

In our sample, 31 (48%) participants met diagnostic criteria for a current depressive disorder: (1) Major Depressive Disorder (n=18); (2) Dysthymia (n=5); (3) Depressive Disorder Not Otherwise Specified (n=5), and (4) Adjustment Disorder with Depressed Mood (n=3). Of these adolescents, 17 (55%) met criteria for at least one comorbid Axis I disorder. Comorbid disorders included Social Phobia (n=6), Generalized Anxiety Disorder (n=5), Panic Disorder (n=2), Obsessive Compulsive Disorder (n=2), Post-Traumatic Stress Disorder (n=2), Alcohol or Substance Abuse (n=7), Eating Disorder Not Otherwise Specified (n=1), and Oppositional Defiant Disorder (n=2).

Basic demographic information was collected as part of the diagnostic interview. Parental occupation status was subsequently coded by two independent judges on a 1- to 7-point scale based on the Hollingshead Index of Social Position (Hollingshead 1975). Higher scores indicate a lower social position. Any discrepancies between raters were resolved by consensus, and the consensus ratings were ultimately used in analyses.

Beck Depression Inventory (BDI-II; Beck et al. 1996) Depression severity was assessed with the 21-item BDI-II. This measure is widely used in the assessment of depression in adolescents, and showed excellent internal consistence in our sample (α=0.95).

Mood and Anxiety Symptom Questionnaire (MASQ; Watson and Clark 1991) The MASQ is a 90-item self-report questionnaire designed to measure symptoms of depression and anxiety using a five-point Likert scale. The Anxious Arousal (AA) subscale is comprised of 17-items that measure symptoms of somatic tension and hyperarousal that are hypothesized to be specifically associated with anxiety disorders, and not mood disorders. Watson et al. (1995) reported good internal consistency for the AA subscale across five separate samples, with coefficient alpha values ranging from 0.86 to 0.90 for subscale items. We used the AA scale to index symptoms of anxiety in our primary analyses.

Tanner Stages of Pubertal Maturation (Tanner 1962) In the Tanner, participants chose between five illustrations of breast (females only) and pubic hair (males and females) development, as validated against physician assessment (Taylor et al. 2001). Scores on the scales range from 1 to 5, with higher scores indicating later stages of development. None of the girls in the study had ever been pregnant.

Children’s Response Styles Questionnaire (CRSQ; Abela et al. 2000) The CRSQ was adapted from the RSQ (Nolen-Hoeksema and Morrow 1991) and assesses how often individuals employ different cognitive strategies in response to feeling sad. The CRSQ includes two subscales (Abela et al. 2007): a) Ruminaton (CRSQ-RUM) which includes 13 items describing Ruminative Responses (e.g., “When I am sad, I think: ‘I’m ruining everything’”), and b) Distraction and Problem-Solving (CRSQ-DPS), which includes eight items that redirect attention away from one’s mood (e.g., “When I am sad, I do something fun with a friend”) or employ strategies to overcome sadness (“When I am sad, I think of a way to make my problem better”). Regarding validity, previous research has demonstrated that the CRSQ-RUM is positively correlated with depressive symptoms in children and young adolescents, and that the CRSQ-DPS is negatively correlated with depressive symptoms in young adolescents (Abela et al. 2004, 2007). All items are rated on a 4-point scale from 1 (almost never) to 4 (almost always). In the current sample, the internal consistency for the CRSQ-RUM subscale was α=0.93, and for the CRSQ-DPS it was α=0.63. The two subscales were moderately negatively correlated (r=-0.39, p<0.01).

Procedure

The current study was conducted in compliance with our home institution’s Health Sciences Research Ethics Board. Adolescents participated in two 2.5-hour sessions separated by 1 week, with both sessions occurring in the mid-afternoon with the same experimenter to avoid post-awakening elevations in cortisol. During the first session,
written informed consent was obtained from all participants, and from parents or guardians of adolescents younger than 18. At this time, participants were informed that they would be asked to give a brief speech at the second session. Following consent, adolescents received the diagnostic interview and completed the questionnaires.

The second session involved the TSST (Kirschbaum et al. 1993). Adolescents had been instructed not to eat or drink for at least one hour prior to their session. Upon arrival, participants were instructed to rest alone in the testing room for 10 min, after which the experimenter collected the baseline saliva sample (Sample A). Participants were then led to a separate room and introduced to two research assistants who they were told were members of a selection committee from the human resources department of a major department store. The participants were told to prepare a five-minute speech that would serve as a job interview to be presented to the committee. Participants were then brought back to the original testing room and given 10 min to prepare their speech, after which the experimenter collected a second saliva sample (Sample B). The adolescents then delivered their speech to the committee, were asked several follow-up questions, and performed an arithmetic task (i.e., serial subtractions of 13 from 2,083, as quickly as possible without making mistakes). The stress task took approximately 15 min, after which a third sample was collected (Sample C). Thus Sample C was collected 25 min after the onset of the stressor (i.e., being informed that one needs to prepare a speech) and represented peak cortisol output. The experimenter collected a fourth sample (Sample D) 40 min later, and a final sample 40 min after the fourth (Sample E). Following the TSST, participants were fully debriefed about the purpose of the task and the nature of the deception. Participants were compensated $40 for their participation in the study, and any self-referred participants who we identified as suffering from a psychiatric condition were referred for treatment.

Cortisol Collection and Hormone Determinations All saliva samples were collected in 5-ml polypropylene vials (Rose Scientific Ltd, Edmonton, Alberta) by passive drool (Shirtcliff et al. 2001) between 3 pm and 5 pm to minimize the potential for circadian change during the trial (Groschl et al. 2003). Immediately after collection, all samples were placed in a freezer for short-term storage and eventually transported to a secure storage freezer (−20 °C). The resulting supernatant in each sample was assayed for cortisol using the high sensitivity enzyme immunoassay designed for saliva (1–3002; Salimetrics).

<p>| Table 1 Sample demographic and clinical characteristics by diagnostic group |
|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Depressed (n=31)</th>
<th>Non-depressed (n=33)</th>
<th>Statistic (t or χ²)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (Female), n (%)</td>
<td>25 (80.6)</td>
<td>22 (66.7)</td>
<td>1.60</td>
<td>0.21</td>
</tr>
<tr>
<td>Age, M (SD)</td>
<td>16.00 (1.57)</td>
<td>14.64 (1.95)</td>
<td>3.07</td>
<td>0.003</td>
</tr>
<tr>
<td>Tanner, M (SD)</td>
<td>3.73 (3.42)</td>
<td>3.73 (2.43)</td>
<td>0.002</td>
<td>0.998</td>
</tr>
<tr>
<td>Parental Hollingshead Index, M (SD)</td>
<td>3.84 (1.73)</td>
<td>2.85 (1.64)</td>
<td>2.35</td>
<td>0.02</td>
</tr>
<tr>
<td>CRSQ_RUM, M (SD)</td>
<td>36.58 (8.08)</td>
<td>23.39 (8.28)</td>
<td>6.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRSQ_DPS, M (SD)</td>
<td>14.48 (3.19)</td>
<td>18.94 (3.33)</td>
<td>5.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BDI, M (SD)</td>
<td>30.13 (9.67)</td>
<td>6.97 (6.11)</td>
<td>11.53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AA, M (SD)</td>
<td>39.83 (13.49)</td>
<td>24.63 (7.09)</td>
<td>5.59</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age at first onset, M (SD)</td>
<td>14.23 (2.14)</td>
<td>8 (25.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression History (Recurrent), n (%)</td>
<td></td>
<td>8 (25.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Treatment status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medications Alone, n (%)</td>
<td>4 (12.9)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Therapy Alone, n (%)</td>
<td>10 (32.3)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Therapy + Medications, n (%)</td>
<td>5 (16.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Treatment, n (%)</td>
<td>12 (38.7)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Comorbidity (yes), n (%)</td>
<td>17 (54.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Episode duration in months, M (SD)</td>
<td>17.90 (20.53)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortisol* (ug/dL), M (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample A</td>
<td>0.125 (0.011)</td>
<td>0.120 (0.010)</td>
<td>0.23</td>
<td>0.82</td>
</tr>
<tr>
<td>Sample B</td>
<td>0.119 (0.013)</td>
<td>0.132 (0.012)</td>
<td>0.60</td>
<td>0.55</td>
</tr>
<tr>
<td>Sample C</td>
<td>0.142 (0.023)</td>
<td>0.165 (0.022)</td>
<td>1.07</td>
<td>0.29</td>
</tr>
<tr>
<td>Sample D</td>
<td>0.122 (0.017)</td>
<td>0.137 (0.016)</td>
<td>0.70</td>
<td>0.49</td>
</tr>
<tr>
<td>Sample E</td>
<td>0.102 (0.011)</td>
<td>0.102 (0.010)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*Pairwise t-tests were conducted using Toothaker’s (1991) method for combining between- and within-subjects error.
LLC, State College, PA). To ensure that inter-assay variability did not contribute to quantification error, all samples from one individual were placed on the same plate. Each sample was quantified in duplicate at 25 μl, and duplicate high and low controls were distributed across each plate to monitor precision. Following Berg and Wyne-Edwards (2001), samples that had a coefficient of variation of ≥15 % were repeated on another plate. The repeated samples were not used in the analyses, but were only used to reject one of the original duplicates. In all, 32 assay runs, in six batches, were conducted. The high control, measured at 1.071 μg/dL, had an intra-assay coefficient of variation of 3.6 % and an inter-assay coefficient of variation of 5.0 %. The low control, measured at 0.103 μg/dL had an intra-assay coefficient of variation of 6.2 % and an inter-assay coefficient of variation of 9.8 %.

Data Analysis

Given the substantial positive skew for samples B, C and D (Skew=2.29–3.68), all cortisol samples were common logarithm transformed prior to analyses. There were no outliers (i.e., cases +/- 3SD from the mean) within the transformed variables. We first conducted a 5 (time)×2 (group: control, depressed) repeated-measures Analysis of Covariance (RMANCOVA), using the five cortisol samples as the within-subjects factor. CRSQ-RUM, CRSQ-DPS and their interactions with a dummy-coded group variable (non-depressed vs. depressed) were entered as covariates. This omnibus test allowed us to assess differences in the overall stress response curve (i.e., Sample A through Sample D) as a function of group and response styles, and to evaluate whether it was appropriate to conduct follow-up analyses targeting the recovery portion of the overall stress response. Any significant Group X Time X response styles interactions were followed up by examining the two-way interactions within each group, and analyzing the polynomial trend of the stress response at varying levels of the response styles variables. The results of the trend analyses, in conjunction with crude observation of the overall cortisol curves at varying levels of response style, were used to motivate more fine-grained statistical analysis of the recovery period.

Our follow-up analysis consisted of a hierarchical linear regression to examine the effects of diagnostic group, CRSQ-RUM, CRSQ-DPS and their interactions in predicting the recovery portion of the cortisol curve, and specifically the change in participants’ cortisol concentration from peak (Sample C) to Sample D. We focused on Sample D because, on average, cortisol samples collected 41–60 min post-stressor in tasks such as this TSST remain significantly elevated compared to pre-stressor levels, while also being substantially lower than peak levels (Dickerson and Kemeny 2004) — thus, we deemed the change from Sample C to D the best index of cortisol recovery because it was likely to contain the greatest inter-individual variability in cortisol concentration values relatively to peak concentration values. To analyze change in cortisol, we inserted the common logarithm transformed Sample C values in step 1 of our hierarchical regression model. Step 2 included any demographic and/or clinical variables that were significantly associated with the dependent variable. In step 3, we entered the main effects of diagnostic group (0 = non-depressed, 1 = depressed), CRSQ-RUM and CRSQ-DPS. Finally, in step 4 we entered the Group X CRSQ-RUM and Group X CRSQ-DPS interaction effects — both continuous variables were centered at their mean to create the interaction effects. Two-way interaction effects were followed up by computing simple slopes for each diagnostic group (Aiken and West 1991).

Results

Descriptive Statistics

Relevant demographic and clinical characteristics for the sample, stratified by diagnostic status, are presented in Table 1. Adolescents in the depressed and non-depressed groups did not significantly differ in terms of sex or Tanner scores. However, adolescents in the depressed group were significantly older, and had a lower parental occupation status, than controls. Not surprisingly, depressed adolescents also had significantly higher BDI-II, AA, and CRSQ-RUM scores, and lower CRSQ-DPS scores, compared to the non-depressed adolescents.

Further, there was no evidence that CRSQ-RUM or CRSQ-DPS were significantly associated with sex (t(62)=0.92, p=0.36; t(62)=0.15, p=0.88, respectively) or Tanner scores (r=−0.20, p=0.12; r=−0.01, p=0.94, respectively). However, CRSQ-RUM, but not CRSQ-DPS, was significantly correlated with both older age (r=0.40, p=0.001; r=−0.18, p=0.16, respectively) and lower parental occupation status (r=0.29, p=0.02; r=−0.17, p=0.18, respectively). Finally, covarying Sample C, there was no evidence that Sample D values were associated with sex, F(1, 61)=0.11, p=0.74, Tanner scores, partial r=−0.06, p=0.65, medication status, F(1, 61)=0.82, p=0.37, BDI-II scores, partial r=−0.02, p=0.91, or AA scores, partial r=−0.19, p=0.15. However, higher Sample D values were associated with younger age, partial r=−0.24, p=0.06, and lower parental occupation status (lower Hollingshead score), partial r=0.22, p=0.09, at trend levels. Therefore, we included age and parental occupation status in the main models below.

Within Group Cortisol Output over Time

Common logarithm transformed cortisol concentrations (in μg/dL) at each TSST collection point were analyzed using
a 5 (time) × 2 (group: 0 = non-depressed, 1 = depressed) RMANCOVA, covarying the effects of age and parental occupational status, and including the effects of CRSQ-RUM, CRSQ-DPS and their interactions with group. All continuous variables were centered at their means. The 3-way interaction of time, group, and CRSQ-DPS did not reach statistical significance, nor did the 2-way interactions of CRSQ-DPS with either time or group (all ps > 0.07).

However, there was a significant 3-way interaction of time, group, and CRSQ-RUM, \( F(4, 224) = 2.64, p = 0.04, \eta^2_p = 0.05 \). The Time x CRSQ-RUM interaction was not significant for the non-depressed group (\( p = 0.41, \eta^2_p = 0.01 \)). In the depressed group, using an approach similar to simple slopes for moderated regression (Aiken and West 1991), CRSQ-RUM was centered at one standard deviation above and below the mean, and these two new values were then used to create interaction effects with time. We found a significant quadratic effect of time at low levels (−1 SD) of rumination, \( F(1, 56) = 11.36, p = 0.001, \eta^2_p = 0.17 \), and significant linear, \( F(1, 56) = 8.40, p = 0.005, \eta^2_p = 0.13 \), and quartic, \( F(1, 56) = 10.94, p = 0.002, \eta^2_p = 0.16 \), effects at high levels of rumination (+1 SD). As displayed in Fig. 1, these results suggest a difference between depressed high and low ruminators during the recovery portion of the TSST, whereas high ruminators maintained relatively high levels of cortisol while low ruminators recovered more rapidly. In order to statistically test these general trends in a more fine-grained manner, we conducted hierarchical linear regression analyses that targeted the recovery portion of the curve exclusively.

**Between Group Differences in Cortisol Recovery**

**Response Styles** Sample C was entered alone in Step 1 of our model, and accounted for a substantial portion of variance in Sample D, \( R^2 = 0.64, F(1, 62) = 108.96, p < 0.001 \). In Step 2 of our model, age and parental occupation status contributed a significant amount of unique variance to the prediction of Sample D, above the effect of Sample C, \( \Delta R^2 = 0.04, \Delta F(2, 60) = 3.19, p = 0.048 \). The addition of the diagnostic status and the response styles variables in Step 3 did not significantly improve the model prediction (\( p = 0.42 \)), and none of the individual parameter estimates were significant (all ps > 0.12). However, consistent with hypotheses, the addition of the group by response styles interaction effects in Step 4 of the regression model resulted in a significant increment in variance explained by our model, \( \Delta R^2 = 0.05, \Delta F(2, 55) = 5.55, p = 0.006 \) (see Table 2). The Group x CRSQ-RUM interaction effect was significant in the final model, whereas the Group x CRSQ-DPS interaction approached significance. In total, the model accounted for 74% of the variance in Sample D scores.

Figure 2 presents the simple slopes for the Group x CRSQ-RUM interaction using the untransformed Sample D values for clarity of interpretation. Among depressed adolescents, there was a significant positive association between CRSQ-RUM and Sample D, \( B = 0.007, SE = 0.003, t(55) = 2.07, p = 0.04, d = 0.56 \). In contrast, among the non-depressed adolescents, the slope of the relationship between CRSQ-RUM and Sample D was negative and failed to reach significance, \( B = -0.006, SE = 0.003, t(55) = -1.69, p = 0.10, d = 0.46 \).

---

**Fig. 1** Estimated marginal means for untransformed cortisol concentrations at each sample point for the non-depressed group (\( n = 33 \)), the depressed group at high CRSQ-RUM (\( n = 13 \)), and the depressed group at low CRSQ-RUM (\( n = 18 \)). Age, parental occupational status and CRSQ-DPS were centered at their means when calculating the plotted marginal means. CRSQ-RUM trait rumination; CRSQ-DPS trait distraction and problem-solving.
Although the Group x CRSQ-DPS did not meet statistical significance, the relations between the CRSQ-DPS and Sample D in our models followed the opposite pattern reported for the Group x CRSQ-RUM interaction. Among depressed adolescents, there was a significant negative association between CRSQ-DPS and Sample D, $B=-0.022$, $SE=0.009$, $t(55)=2.39$, $p=0.02$, $d=0.64$. In contrast, among the non-depressed adolescents, the slope of the relationship was not statistically significant, $B=0.001$, $SE=0.008$, $t(55)=0.12$, $p=0.91$, $d=0.03$.

### Discussion

The current study is the first to our knowledge to investigate the association of two distinct response styles — depressive rumination and distraction/problem-solving — on biological recovery from stress in a sample of clinically depressed and non-depressed adolescents. Consistent with our hypotheses, among the depressed adolescents, trait rumination was associated with higher post-stressor cortisol concentration, controlling for peak cortisol output, whereas distraction and problem-solving was associated with lower post-stressor cortisol concentration. In the non-depressed group, in contrast, there was no evidence for a relation of either response style to cortisol recovery. Thus, our results implicates HPA axis dysregulation — specifically, impaired cortisol recovery — as a potential neurobiological mechanism that may help to explain why higher levels of rumination over distraction are so toxic for adolescents with depression. These adolescents are exposed to higher levels of cortisol over time, and as a result may suffer more of the cumulative biological wear and tear — or “allostatic load” — associated with chronic exposure to a heightened neuroendocrine stress response (McEwen and Wingfield 2003). Heightened allostatic load, and the changes to neural structure and function that it brings about over time, are associated with depressive illness (McEwen 2003).

Importantly, most of the depressed adolescents in our sample were very early in their course of depression (75% explained by our model, $\Delta R^2=0.04$, $\Delta F(1, 57)=8.32$, $p=0.006$. As displayed in Fig. 3, among depressed adolescents, the simple slope for CRSQ-ratio score was positive and statistically significantly different from zero, $B=0.108$, $SE=0.034$, $t(57)=3.16$ $p=0.003$, $d=0.84$, whereas it failed to reach significance among non-depressed adolescents, $B=-0.067$, $SE=0.049$, $t(57)=-1.37$, $p=0.18$, $d=0.36$.

### Table 2 Final regression model estimating recovery (sample D) from diagnostic group, response styles, and their interactions

<table>
<thead>
<tr>
<th>Variable</th>
<th>B (SE)</th>
<th>t</th>
<th>p</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample C</td>
<td>0.840 (0.074)</td>
<td>11.32</td>
<td>&lt; 0.001</td>
<td>3.05</td>
</tr>
<tr>
<td>Age</td>
<td>0.025 (0.012)</td>
<td>2.10</td>
<td>0.04</td>
<td>0.57</td>
</tr>
<tr>
<td>Parental Hollingshead</td>
<td>-0.017 (0.012)</td>
<td>-1.37</td>
<td>0.18</td>
<td>0.37</td>
</tr>
<tr>
<td>Diagnostic group</td>
<td>-0.059 (0.054)</td>
<td>-1.10</td>
<td>0.28</td>
<td>0.30</td>
</tr>
<tr>
<td>CRSQ-RUM</td>
<td>-0.006 (0.003)</td>
<td>-1.69</td>
<td>0.10</td>
<td>0.46</td>
</tr>
<tr>
<td>CRSQ-DPS</td>
<td>0.001 (0.008)</td>
<td>0.12</td>
<td>0.91</td>
<td>0.03</td>
</tr>
<tr>
<td>Group X CRSQ-RUM</td>
<td>0.013 (0.005)</td>
<td>2.67</td>
<td>0.01</td>
<td>0.72</td>
</tr>
<tr>
<td>Group X CRSQ-DPS</td>
<td>-0.023 (0.013)</td>
<td>-1.74</td>
<td>0.09</td>
<td>0.47</td>
</tr>
</tbody>
</table>

**Note:** CRSQ-RUM trait rumination; CRSQ-DPS trait distraction and problem-solving

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**Fig. 2** Predicted Sample D values from CRSQ-RUM, controlling for Sample C, CRSQ-DPS, age, and parental occupational status computed using simple slopes, for depressed and non-depressed groups. Low = 1 Standard Deviation below the mean; High = 1 Standard Deviation above the mean.
were on their first episode). Therefore, the current results suggest that the relation of rumination to impaired HPA axis recovery from stress may not require long-term, repeated exposure to depressive illness and any resultant consequences (e.g., personality ‘scars’ from depressive episodes; Zeiss and Lewinsohn 1988). Indeed, high trait ruminators may increase vulnerability to impaired HPA axis recovery from stress even prior to the first onset of depression, particularly in the presence of other depression vulnerability markers. For instance, studies have demonstrated an association between maternal depression and disruptions in HPA axis functioning, as indexed by elevated early morning cortisol concentration (Mannie et al. 2007) and dexamethasone non-suppression (Young et al. 2006). Our study provided support for the RST by showing, first, that rumination and distraction and problem-solving were significantly negatively correlated, and, second, that the two constructs were associated with opposite patterns of cortisol recovery following a stressor. Given that disruptions in the HPA axis system are prospectively associated with chronicity (Goodyer et al. 2003) and recurrences (Adam et al. 2010) in adolescent MDD, our results provide corroborative, neurobiological support for the adaptive nature of distraction and problem-solving over rumination, and contributes to clarifying the roles of these response styles in the pathology of depression.

The precise mechanisms mediating the relation of rumination to impaired cortisol recovery following stress were not the focus of the current study. Nevertheless, our results are consistent with neural mechanisms of rumination and distraction. Specifically, high rumination has been associated with a failure to disengage attention from negative stimuli, mediated at least in part by decreased PFC inhibition of amygdala activity (e.g., Siegle et al. 2002; Johnson et al. 2009). Conversely, high trait distraction has been associated with greater PFC inhibition and thus, enhanced ability to shift response styles theory proposes rumination and distraction as adaptive and maladaptive responses to depressed mood, respectively, and proposes that they should have correspondingly opposing relations to depression symptoms (see Bagby and Parker 2001; Nolen-Hoeksema et al. 1994). However, the evidence supporting this conceptualization is mixed, with some studies finding a paradoxical positive correlation between rumination and distraction (e.g., Schmaling et al. 2002), and others showing that distraction is unrelated to depression (e.g., Just and Alloy 1997; Nolen-Hoeksema et al. 1993). Our study provided support for the RST by showing, first, that rumination and distraction and problem-solving were significantly negatively correlated, and, second, that the two constructs were associated with opposite patterns of cortisol recovery following a stressor. Given that disruptions in the HPA axis system are prospectively associated with chronicity (Goodyer et al. 2003) and recurrences (Adam et al. 2010) in adolescent MDD, our results provide corroborative, neurobiological support for the adaptive nature of distraction and problem-solving over rumination, and contributes to clarifying the roles of these response styles in the pathology of depression.

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### Table 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>B (SE)</th>
<th>t</th>
<th>p</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample C</td>
<td>0.844 (0.073)</td>
<td>11.62</td>
<td>&lt;0.001</td>
<td>3.08</td>
</tr>
<tr>
<td>Age</td>
<td>0.022 (0.011)</td>
<td>1.99</td>
<td>0.05</td>
<td>0.53</td>
</tr>
<tr>
<td>Parental Hollingshead</td>
<td>-0.019 (0.012)</td>
<td>-1.60</td>
<td>0.12</td>
<td>0.42</td>
</tr>
<tr>
<td>Diagnostic Group</td>
<td>-0.028 (0.054)</td>
<td>-0.51</td>
<td>0.61</td>
<td>0.14</td>
</tr>
<tr>
<td>CRSQ-ratio</td>
<td>-0.067 (0.049)</td>
<td>-1.37</td>
<td>0.18</td>
<td>0.36</td>
</tr>
<tr>
<td>Group X CRSQ-ratio</td>
<td>0.175 (0.061)</td>
<td>2.88</td>
<td>0.01</td>
<td>0.76</td>
</tr>
</tbody>
</table>

**CRSQ-ratio** the ratio of trait rumination to trait distraction and problem-solving.
away from negative stimuli. For example, when psychiatrically healthy women were instructed to cognitively reappraise a negative emotional experience, activation in several PFC regions (i.e., medial, dorsolateral, and ventrolateral) was associated with subsequent reduction in amygdala activity (Goldin et al. 2008). This corticobulbar circuit has direct implications on functioning of the HPA axis. For example, Taylor et al. (2008) found that activation of the amygdala in response to threatening faces was associated with heightened cortisol reactivity to the TSST, whereas Kern et al. (2008) found that activation of the medial prefrontal cortex was associated with dampened cortisol reactivity to a laboratory stressor. In the context of our study, then, high levels of rumination over distraction may be associated with a failure to disengage from stress, thereby prolonging the cortisol recovery period.

Our study had a number of strengths, including the use of a structured diagnostic interview to rigorously characterize our sample clinically, an ecologically valid stress induction procedure, and a psychometrically strong and relevant measure of rumination and distraction. The RSQ assesses rumination focused on “symptoms of distress and on the possible consequences and causes of these symptoms” (Nolen-Hoeksema et al. 2008, p. 400). Previous studies using college student samples have failed to find a relation between rumination assessed with the RSQ and cortisol recovery following the TSST (Young and Nolen-Hoeksema 2001) or have reported an overall blunted pattern of cortisol secretion in individuals high, versus low, on a measure of trait rumination, in response to an evaluative stressor (Zoccola et al. 2008). In contrast, studies in non-clinical undergraduate samples that focus on stress-focused rumination, using measures such as the Emotion Control Questionnaire (Roper and Najarian 1989), have found support for a relation between rumination and delayed cortisol recovery (Zoccola et al. 2010). These results suggest that symptom-focused versus stress-focused rumination are differentially relevant to stress recovery for individuals high versus low in depressive symptoms, respectively, and that these differences should be taken into consideration when choosing appropriate constructs for study.

The current findings need to be considered in light of the following limitations. First, our study employed a modest sample size and the results should be replicated in a larger sample. However, our interpretations are based on medium to large effects that were consistent with our a priori hypotheses, indicating that these findings are likely robust. Second, consistent with the TSST protocol, cortisol was only assessed at five points. In their meta-analysis, Dickerson and Kemeny (2004) found that individuals’ peak cortisol concentration was found in a range of time between 20 and 40 min post-stressor. Thus, it is possible that high ruminators may have reacted to a later portion of our stressor, leading them to peak later than low ruminators, and at a time that was not captured by our assessment points. Future research can address this issue by assessing cortisol concentration at a higher frequency, both during the reactivity and recovery phases, than the TSST protocol calls for. Third, we did not collect data on non-psychotropic medication use, including the use of oral contraceptive hormones, which may have affected cortisol functioning in our sample. Fourth, we did not confirm self-reported alcohol/substance abuse by using urine screenings for these substances. Finally, the Distraction and Problem-Solving subscale used in our analyses possessed modest internal consistency in this sample. This finding is consistent with Abela and colleagues (2007) and points to the need for further psychometric scrutiny of the CRSQ.

In summary, the current study provides compelling evidence in a clinically diagnosed sample of adolescents that high trait rumination relative to distraction/problem-solving is significantly associated with later cortisol recovery following stress. This relation was only present among adolescents with depression. As such, these results extend previous literature on the relation between response styles and cortisol recovery to a clinical sample. It is hoped that the results of this study will stimulate further research integrating neurobiological and cognitive factors to understanding the etiology of MDD during adolescence — a key developmental period that has been relatively understudied. This may lead to a more fine-grained understanding of how biological and cognitive factors work in concert with developmental factors (e.g., hormones, normative intrapersonal and social stressors) to predict the course of MDD from early adolescence over the lifespan.

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Conflict of Interest The authors declare that they have no conflict of interest.

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prefrontal cortex are associated with HPA axis response to a psychosocial stressor. *Psychoneuroendocrinology*, 33, 517–529.


