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Depressive rumination alters cortisol decline in Major Depressive Disorder

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ABSTRACT

Depressive rumination – a central characteristic of Major Depressive Disorder (MDD) – is a maladaptive emotion regulation strategy that prolongs sad mood and depressive episodes. Considerable research demonstrates the emotional and behavioral consequences of depressive rumination, yet few studies investigate its effect on neuroendocrine functioning. The current study examined the effect of an emotion regulation manipulation on the trajectory of cortisol concentrations among individuals with MDD and healthy controls (CTL). Sadness was induced via forced failure. Participants then were randomly assigned to a depressive rumination or distraction emotion regulation induction. MDDs in the rumination condition exhibited less cortisol decline compared to MDDs in the distraction condition and compared to CTLs in either condition. Findings suggest that depressive rumination alters the trajectory of cortisol secretion in MDD and may prolong cortisol production. Results thereby provide important insights into the interaction of biological and psychological factors through which distress contributes to MDD.

1. Introduction

A central feature of Major Depressive Disorder (MDD) is the tendency to respond to sadness with rumination, a maladaptive emotion regulation strategy that has been shown to predict the duration and severity of depressive episodes (McLaughlin & Nolen-Hoeksema, 2011; Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). The response styles theory (Nolen-Hoeksema et al., 2008) defines depressive rumination as a method of processing negative events by repetitively focusing on feelings of distress as well as the potential antecedents or repercussions of these feelings. A substantial body of research has demonstrated negative behavioral and emotional consequences of depressive rumination. Compared to more adaptive emotion regulation strategies, such as distraction, ruminative responses to sad mood diminish problem solving, increase engagement in maladaptive behaviors, and hinder recovery from negative events (Lyubomirsky & Tkach, 2004; Nolen-Hoeksema et al., 2008). Most notably, experimental research has shown that when individuals are in a sad mood state, rumination leads to more self-reported sadness compared to distraction (Feldner, Leen-Feldner, Zvolensky, & Lejuez, 2006). Depressive rumination, therefore, is believed to directly contribute to the pervasive low mood associated with depressive episodes (Morrow & Nolen-Hoeksema, 1990). In contrast to the considerable research examining the emotional and behavioral effects of depressive rumination, relatively little is understood about the consequences of depressive rumination on physical health, and in particular, on neuroendocrine functioning.

Recent theories posit that the maladaptive consequences of some forms of repetitive thought, including stressor-focused and depressive rumination, extend beyond emotional wellbeing to physical wellbeing (Brosschot, Gerin, & Thayer, 2006; see review by Watkins, 2008). Specifically, the continual processing or contemplation of a depressing or stressful event is predicted to alter individuals' biological functioning. The neuroendocrine system plays a primary role in our body's biological functioning (Patchev & Patchev, 2006). A central component of the neuroendocrine system is the hypothalamic-pituitary-adrenal (HPA) axis, a primary index of which is the hormone cortisol. Whereas moderate cortisol fluctuation facilitates adaptive responses to environmental changes, excess cortisol production – often stemming from chronic HPA axis activity – can be detrimental (Dedovic, Duchesne, Andrews, Engert, & Pruessner, 2009; Gold, Drevets, & Charney, 2002; Sephton & Speigel, 2003). Prolonged cortisol secretion leads to neurotoxicity in areas of the brain responsible for regulating emotions and coping effectively with distress (McEwen, 2006). Excessive cortisol

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secretion also has been shown to increase risk for medical conditions, including cancer, diabetes, and arthritis (McEwen, 1998), making it critical to understand factors associated with greater cortisol secretion.

Initial work in nonclinical populations has provided evidence for a connection between stressor-focused rumination and cortisol elevations (see review by Zoccola & Dickerson, 2012). Extending these findings to a sample of depressed adolescence, Stewart, Mazurka, Bond, Wynne-Edwards, (2013) found that trait depressive rumination was associated with elevated cortisol levels during the recovery period, whereas the tendency to use more adaptive emotion regulation strategies (e.g., distraction/problem solving) was associated with faster cortisol decline. The one study to use an experimental manipulation exposed participants to a sad mood induction and then randomly assigned them to a depressive rumination or distraction condition (Kuehner, Huffziger, & Liebsch, 2009). Results showed less cortisol decline in the rumination condition among students with high versus low depression symptoms. The effect of experimentally induced depressive rumination on cortisol levels, however, has never been examined within a clinically depressed sample.

The current study aimed to extend past research by examining the effects of induced depressive rumination versus distraction on cortisol secretion in clinically depressed and healthy control participants. Participants were exposed to a forced-failure paradigm, which was designed to place them in a sad mood state prior to the emotion regulation induction (Hammen, 2005). Participants then were randomly assigned to the depressive rumination or distraction condition. Salivary cortisol was measured when participants entered the lab, and during forced failure, emotion regulation, and post-emotion regulation periods. Overall, we expected cortisol levels to decline across the experiment as participants habituated to the stress of coming into the laboratory (Marceau, Dorn, & Susman, 2012). However, we expected depressive rumination to interrupt this cortisol decline. Specifically, we predicted that both depressed and healthy control participants in the depressive rumination condition would demonstrate less cortisol decline compared to individuals in the distraction condition. In addition, we expected that the effects of depressive rumination would be stronger in the group with clinical depression.

2. Methods and materials

2.1. Participants

Adults 18–60 years of age were recruited via newspaper advertisements and Internet postings. Inclusion and exclusion criteria were determined via an in-person Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 1996). Three clinical psychology graduate students and one post-doctoral fellow completed the SCIDs. All interviewers completed more than 20 h of training in videotapes, live observation, written tests, and group supervision in addition to the formal coursework required by the doctoral program. Inter-rater disagreements or queries were discussed via a biweekly SCID meeting. Inter-rater reliability was excellent, $\kappa = 1.00$. Two groups were included: those who met criteria for current MDD and those who did not meet criteria for any past or current Axis I disorder (Control; CTL). Participants were excluded due to severe head trauma, learning disabilities, bipolar disorder, psychotic symptoms, alcohol or substance abuse within the past 6 months, or health conditions known to interfere with HPA axis activity (including pregnancy and endocrine disorders, per Kudielka, Hellhammer, & Wust, 2009). After excluding one extreme outlier (CTL), whose initial cortisol value was more than 10 *SD*s greater than the mean, there were 46 participants in the MDD group and 51 in the CTL group.

At the time of testing, 16 MDD participants were on medication(s), including psychotropic medication (15) and oral contraceptives (1). Percent of depressed participants who were on medication did not differ across emotion regulation condition, $\chi^2(1, N = 46) = 1.53$, $p = .22$. In addition, 5 CTL participants were on medication(s) at the time of testing, including oral contraceptives (4) and blood pressure medication (1). Percent of control participants who were on medication did not differ across emotion regulation condition, $\chi^2(1, N = 51) = 0.18$, $p = .67$. Within the MDD group, 35 participants met criteria for a comorbid anxiety disorder. Percent with comorbidity did not differ across emotion regulation condition, $\chi^2(1, N = 46) = 1.80$, $p = .18$.

2.2. Forced-failure paradigm

Three forced-failure tasks were used to induce mild sadness. The first was a 15-min facial identification task with false feedback indicating that the participant performed poorly (Tran, Siemer, & Joormann, 2011). Participants were asked to identify the emotional expression (happy, sad, angry) depicted in subliminally presented facial expressions. Participants repeatedly received feedback that they were performing poorly relative to others who had already completed the task, and the experimenter urged participants to try harder. The second task was a 5-min anagram task, in which approximately 30% of the anagrams were unsolvable (van Randenborgh, Hüffmeier, LeMoult, & Joormann, 2010). Participants were given 5 min to solve as many anagrams as possible but were allowed only 30 s to solve each anagram. The third was a serial subtraction task (Kirschbaum, Pirke, & Hellhammer, 1993). Participants were given 5 min to count backward aloud from 2,083 to zero in 13-step sequences as quickly and accurately as possible. If an error was made, the experimenter would say "error, start again at 2,083." No participant reached zero in the time allotted.

2.3. Emotion regulation (ER) induction

Participants were randomly assigned to either a depressive rumination or distraction condition, adapted from the frequently used emotion regulation (ER) induction procedure developed by Nolen-Hoeksema and Morrow (1993). This ER manipulation was selected given its use in prior studies on depressive rumination (see review by Lyubomirsky & Tkach, 2004), its use when examining the relation between depressive rumination and cortisol in a student sample (Kuehner et al., 2009), and its consistency with Nolen-Hoeksema and colleague's definition of depressive rumination (Nolen-Hoeksema, 1991; Nolen-Hoeksema et al., 2008). Regardless of condition, participants viewed seven prompts one-at-a-time on the computer screen. They were asked to think and write about each prompt for 2 min. The prompts differed by condition. Depressive rumination prompts focused participants' attention on thoughts that were emotion or self focused (e.g., "why things turn out the way they do for you."). Distraction prompts focus participants' attention on thoughts that were unrelated to the self (e.g., "the layout of a mall you have been to."). Participants' written statements were later coded by two independent raters who were blind to group and condition. Rumination score ratings, which were based on Hilt and Pollak (2013), were made on a 5-point Likert scale ranging from 1 (*Not at all ruminating*) to 5 (*Completely ruminating*), ICC = .84.

2.4. Measures

2.4.1. Sadness ratings

Self-reported sadness was assessed at 10 points: upon entering the lab, following a 5-min nature video, during the forced-failure paradigm, after the forced-failure paradigm, immediately after the ER induction, and five times during the nature video. Participants utilized an 11-point Likert-scale ranging from 0 (*not at all*) to 10 (*very much*). To test the specific effects of the forced-failure and ER-induction, we focused our analyses on assessments made following the nature video, during the forced-failure paradigm, and immediately after the ER induction. The general pattern of findings does not differ based on whether all 10 samples are used, with the three-way time by group by condition interaction remaining significant at Order 4, $F(1, 91) = 5.85$, $p = .02$, $\eta^2 = .06$.

2.4.2. Questionnaires

Participants completed the Beck Depression Inventory-II (BDI; Beck, Steer, & Brown, 1996), a 21-item measure assessing depressive symptom severity ($\alpha = .97$). Additionally, participants completed the Ruminative Responses Scale of the Response Style Questionnaire (RRS; Nolen-Hoeksema & Morrow, 1991), a 22-item self-report questionnaire assessing individual differences in the tendency to ruminate when sad ($\alpha = .99$).

2.5. Cortisol collection and assay

Cortisol was extracted from saliva collected using salivette swabs (Sarstedt, Numbrecht, Germany). Samples were stored at −20 °C until shipped to a laboratory for cortisol assay. Samples were centrifuged at 3000 rpm for 5 min to produce a clear supernatant of low viscosity. Using a commercially available immunoassay with chemiluminescence detection, 50 μL were removed for cortisol analysis. The lower detection limit of this assay was 0.43 nmol/L. Intra- and interassay coefficients of variation were below 8% for low (3 nmol/L) and high (25 nmol/L) cortisol levels.

2.6. Procedure

The experiment was approved by the Institutional Review Board at the University of Miami, and all experiments were performed in accordance with ascribed guidelines and regulations. In-person SCIDs were conducted by trained interviewers. Participants who met inclusion and exclusion criteria were invited to return for the main study session. We gave participants verbal and written instructions to refrain from eating, drinking other than water, using nicotine, brushing their teeth, and exercising for 2 h prior to the main study session.

The main study session was scheduled between 12 pm and 6 pm to minimize the effects of diurnal fluctuation in cortisol levels. The session consisted of a 5-min nature video, 30-min forced-failure paradigm, 16-min ER induction, and 35-min post-ER period. During the post-ER period participants watched a nature video. Timing of saliva samples was selected to identify changes in cortisol levels as a result of the ER manipulation. Participants provided 11 cortisol samples: immediately upon entering the lab (enter lab), after the 5-min nature video, in the middle of the forced failure induction, at the end of the forced-failure period (30 min after failure onset; post-failure), in the middle of the ER induction, at the end of the ER induction and every 7 min thereafter (post-ER 1–6). Lastly, participants completed the questionnaires. Due to missing data or duplicate information, samples 2, 3, and 5 were not included in the final analyses.

2.7. Statistical analyses

Demographic data, affect ratings, and baseline differences between diagnostic group (MDD, CTL) and ER condition (rumination, distraction) were examined in SPSS 20.0 (SPSS Inc., USA) using analyses of variance (ANOVAs) and chi-square tests. Cortisol data were analyzed using multilevel modeling; a series of growth models were conducted with hierarchical linear modeling software (HLM), Version 6.01 (Raudenbush, Bryk, & Congdon, 2004). Multilevel modeling is ideal for analyzing nested data. Multilevel growth models allow researchers to partition the variance into two levels: Level 1 (within individual) represents intraindividual variability in scores at different measurement occasions, and Level 2 (between individuals) represents the variability between individuals' scores. HLM was specifically selected because it allows for the examination of variably spaced measurement occasions or observations that are unevenly spaced over time (Hruschka, Kohrt, & Worthman, 2005). In our models, the exact time of cortisol collection was allowed to vary by individual, thereby providing a more precise estimation of time for each participant (Singer & Willet, 2003). Diagnostic group, ER condition, and group × condition were examined as predictors at Level 2.

3. Results

3.1. Participant characteristics

Participant characteristics are presented in Table 1. There were no significant differences in age across group, $F(1, 93) = 0.19$, $p = .67$, $\eta^2 = .002$ or condition, $F(1, 93) = 0.01$, $p = .93$, $\eta^2 = .00001$, and the group by condition interaction was not significant, $F(1, 93) = 2.75$, $p = .10$, $\eta^2 = .03$. There was also no significant difference in ethnicity across group, $\chi^2(1, N = 96) = 0.53$, $p = .47$, or condition, $\chi^2(1, N = 96) = 0.04$, $p = .83$. Although there was evidence of differences in proportion who were female across group, $\chi^2(1, N = 97) = 3.67$, $p = .06$, and condition, $\chi^2(1, N = 97) = 3.71$, $p = .05$, the proportion female did not differ across ER condition within the MDD group, $\chi^2(1, N = 46) = 0.81$, $p = .37$. There were, however, slightly fewer females in the rumination condition than the distraction condition within the CTL group, $\chi^2(1, N = 51) = 3.36$, $p = .07$. Thus, gender was included as a covariate when testing the main study hypotheses. As expected, the MDD group obtained significantly higher BDI scores than the CTL group, $F(1, 93) = 235.54$, $p < .001$, $\eta^2 = .72$; however, there was no significant main effect of condition, $F(1, 93) = 1.19$, $p = .28$, $\eta^2 = .01$, or group by condition interaction, $F(1, 93) = 0.15$, $p = .70$, $\eta^2 = .002$. In addition, although the MDD group obtained significantly higher RRS scores than the CTL group, $F(1, 92) = 325.11$, $p < .001$, $\eta^2 = .78$, there was no significant main effect of condition, $F(1, 92) = 0.24$, $p = .63$, $\eta^2 = .003$, or group by condition interaction, $F(1, 92) = 0.03$, $p = .87$, $\eta^2 = .0003$.[1] As expected, the MDD group reported significantly higher baseline sadness scores than the CTL group, $F(1, 91) = 45.68$, $p < .001$, $\eta^2 = .33$; however, sadness scores did not significantly differ by ER condition, $F(1, 91) = 0.32$, $p = .57$, $\eta^2 = .004$, and the group by condition interaction was not significant, $F(1, 91) = 0.42$, $p = .52$, $\eta^2 = .01$.[2] Cortisol levels when participants entered the laboratory did not significantly differ by group, $F(1, 93) = 0.78$, $p = .38$, $\eta^2 = .01$, or condition, $F(1, 93) = .001$, $p = .98$, $\eta^2 = .00001$, and the group by condition interaction was not significant, $F(1, 93) = 1.81$, $p = .18$, $\eta^2 = .02$.

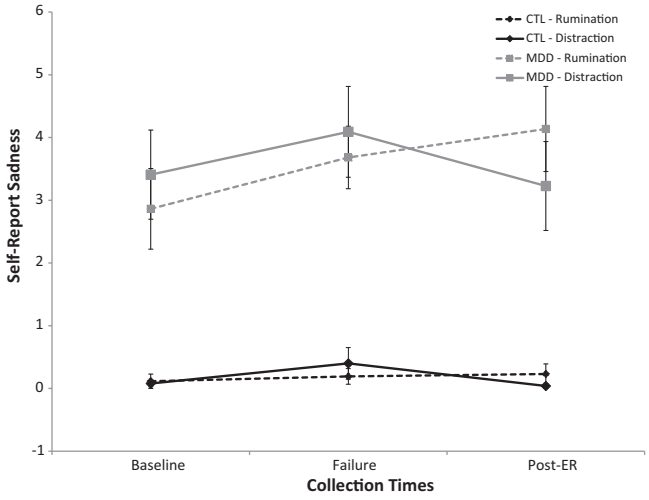

Fig. 1. Self-reported sadness by group (MDD versus CTL) and condition (rumination versus distraction).

3.2. Emotion regulation check

Participants' written responses during the ER induction were coded to determine the amount they were ruminating (see Table 1; rumination score). There was a significant main effect of group, $F(1, 92) = 30.57$, $\eta^2 = .25$, and condition, $F(1, 92) = 58.48$, $\eta^2 = .39$, $ps < .001$. In addition, the group by condition interaction was significant, $F(1, 92) = 11.36$, $p = .001$, $\eta^2 = .11$. Importantly, individuals assigned to the rumination condition ruminated significantly more than those assigned to the distraction condition in both the CTL, $t(48) = 4.57$, and MDD groups, $t(44) = 6.05$, $ps < .001$. Although between-group differences were not found within the distraction condition, $t(45) = 1.83$, $p = .07$, MDDs in the rumination condition ruminated significantly more than CTLs in the rumination condition, $t(47) = 5.56$, $p < .001$.

3.3. Manipulation check

See Fig. 1 for sadness ratings. The repeated-measures ANOVA on sadness scores revealed a main effect of group, $F(1, 91) = 69.63$, $p < .001$, $\eta^2 = .43$, indicating higher self-reported sadness in the MDD versus CTL group. There was also a main effect of time, $F(2, 182) = 4.17$, $p = .02$, $\eta^2 = .04$, which was qualified by a time by ER condition interaction, $F(2, 182) = 4.22$, $p = .02$, $\eta^2 = .04$. No other main or interaction effects were significant, $Fs < 2.05$, $\eta^2 < .03$, $ps > .05$.

Follow-up tests examining the change in sadness from baseline to failure revealed a significant increase in sadness, $t(94) = 3.25$, $p = .002$, which did not significantly differ between the rumination and distraction conditions, $t(93) = 0.26$, $p = .80$. However, the change in sadness from failure to post-ER differed by condition, $t(93) = 2.35$, $p = .02$. Whereas sadness ratings significantly decreased in the distraction group, $t(46) = 2.44$, $p = .02$, sadness ratings did not significantly change in the rumination group, $t(47) = 0.91$, $p = .37$.[3]

[1] One CTL participant (rumination) did not provide ethnicity data or complete the RRS.

[2] Sadness ratings could not be obtained from two MDD participants (one rumination and one distraction).

[3] Exploratory analyses conducted on a negative affect composite score (sad, angry, tense, anxious, irritated, upset, and nervous) revealed an increase in negative affect during the forced-failure induction, $t_{paired}(95) = 4.84$, $p < .001$, and a decrease in negative affect following the forced-failure induction, $t_{paired}(95) = 2.62$, $p < .02$. The increase in negative affect during the forced-failure induction was greater in the MDD versus CTL group, $t(94) = 2.49$, $p < .02$. No other main or interactive effects were significant.

Table 1
Participant demographics.

Variable	CTL ($N = 51$)		MDD ($N = 46$)	
	Rumination	Distraction	Rumination	Distraction
Age, *M* (SD)	34.27 (11.59)	38.48 (11.54)	39.30 (12.25)	35.52 (12.08)
Sex (female:male)	7:19	13:12	12:11	15:8
Caucasian (%)	40	44	35	32
BDI, *M* (SD)	2.81 (4.65)	4.21 (5.18)	28.71 (11.66)	31.23 (11.39)
RRS, *M* (SD)	30.84 (10.16)	31.48 (8.76)	66.22 (8.72)	67.52 (10.98)
Rumination score, *M* (SD)	10.50 (3.50)	7.21 (0.41)	17.35 (5.06)	8.87 (4.42)

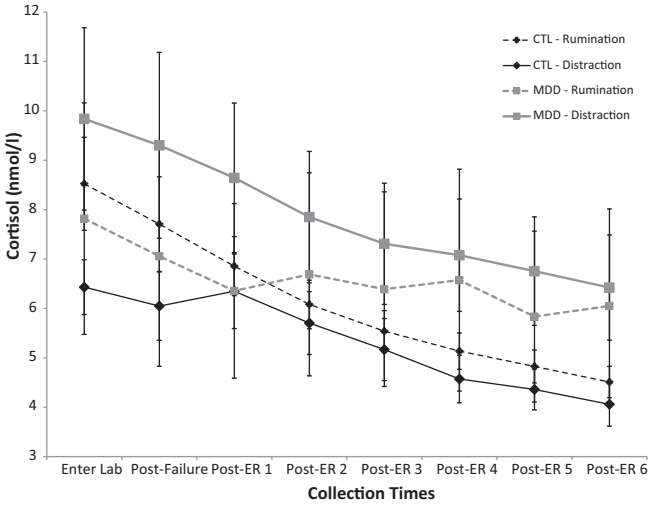

Fig. 2. Cortisol levels by group (MDD versus CTL) and condition (rumination versus distraction).

3.4. Effects of ER condition on salivary cortisol

See Fig. 2 for cortisol data. In line with our study design and previous research (Taylor, Gonzaga, Klein, Hu, Greendale & Seeman, 2006), a two-rate piecewise linear growth model (Raudenbush and Bryk, 2002) was used to simultaneously model linear changes in cortisol before and after the ER induction. The Level 1 function was as follows:

$$\text{Cortisol} = \pi_{0j} + \pi_{1j}(\text{pre-ER}) + \pi_{2j}(\text{post-ER}) + e_{ij}$$

where π_{0j} represents cortisol level when participant *j* entered the laboratory, π_{1j} represents the slope of cortisol prior to the ER induction for participant *j*, and π_{2j} represents the slope of cortisol after the ER induction for participant *j*. Table 2 provides the average intercept, pre-ER, and post-ER coefficients, each of which had sufficient random effects variance, *ps* < .001. Whereas cortisol level did not change prior to the ER induction, there was a significant decline in cortisol level after the ER induction.

At Level 2 we tested the effects of diagnostic group, ER condition, and the group-by-condition interaction predicting Level 1 parameters. Diagnostic group was dummy coded as 0 (CTL) and 1 (MDD). ER condition was dummy coded as 0 (rumination) and 1 (distraction). Gender (also dummy coded with 0 [female] and 1 [male]) was included in all analyses given evidence of differences between groups and conditions in percent female.[4] We specified the following models at Level 2:

$$\text{Intercept:}\quad \pi_{0j} = \beta_{00} + \beta_{01}(\text{gender}) + \beta_{02}(\text{group}) + \beta_{03}(\text{condition}) + \beta_{04}(\text{group} \times \text{condition}) + r_0$$

$$\text{Slope Pre-ER:}\ \pi_{1j} = \beta_{10} + \beta_{11}(\text{gender}) + \beta_{12}(\text{group}) + \beta_{13}(\text{condition}) + \beta_{14}(\text{group} \times \text{condition}) + r_1$$

$$\text{Slope Post-ER:}\ \pi_{2j} = \beta_{20} + \beta_{21}(\text{gender}) + \beta_{22}(\text{group}) + \beta_{23}(\text{condition}) + \beta_{24}(\text{group} \times \text{condition}) + r_2$$

Coefficient estimates and significance tests can be found in Table 2. Cortisol levels when participants entered the lab were influenced by gender, with males displaying higher cortisol levels than females. Cortisol levels when participants entered the lab did not differ by group or condition, and the group by condition interaction was not significant. As expected, change in cortisol prior to the ER induction was not influenced by gender, group, or condition, and the group by condition interaction was not significant. Change in cortisol after the ER induction, however, differed by gender, with males displaying steeper cortisol decline than females. There was a marginally significant main effect of group, suggesting flatter cortisol decline in the MDD versus CTL group, and this was moderated by the expected group × condition interaction.

Additional HLM analyses were run to follow-up on the group × condition interaction predicting change in cortisol after the ER induction. Within the CTL group, cortisol levels declined post-ER in both the rumination, $\beta = -0.04$, $t(48) = 2.74$, $p = .01$, and distraction conditions, $\beta = -0.02$, $t(48) = 2.24$, $p = .03$. Cortisol decline did not differ between the rumination and distraction conditions, $\beta = 0.01$, $t(48) = 0.87$, $p = .39$. In contrast, within the MDD group, cortisol levels declined post-ER for those in the distraction condition, $\beta = -0.03$, $t(43) = 2.34$, $p = .02$, but cortisol levels failed to decline for MDDs in the rumination condition, $\beta = 0.00$, $t(43) = 0.18$, $p = .86$. Moreover, MDDs in the rumination condition experienced less cortisol decline compared to MDDs

Table 2
Hierarchical linear modeling of salivary cortisol.

Predictors	Coefficient	SE	*t*-Value	*p*-Value
Level 1				
Intercept	8.13	0.76	10.72	**<.001**
Pre-ER (linear)	−0.01	0.01	1.14	0.256
Post-ER (linear)	−0.04	0.01	6.19	**<.001**
Level 2				
Intercept	6.03	1.80	3.36	**0.001**
Gender	3.40	1.52	2.24	**0.028**
Group	0.17	2.09	0.08	0.936
Condition	−1.23	2.05	0.60	0.548
Group × condition	3.70	2.93	1.26	0.210
Pre-ER (linear)	−0.03	0.02	1.25	0.214
Gender	0.01	0.02	0.78	0.436
Group	−0.001	0.03	0.04	0.967
Condition	0.02	0.02	0.96	0.338
Group × condition	−0.01	0.04	0.20	0.839
Post-ER (linear)	−0.03	0.01	2.37	**0.020**
Gender	−0.02	0.01	2.12	**0.036**
Group	0.03	0.02	1.93	0.057
Condition	0.01	0.02	0.64	0.522
Group × condition	−0.04	0.02	2.00	**0.048**

Note: Bolded values indicate $p < .05$.

[4] We also examined whether gender moderated the effect of group, condition, or the group by condition interaction. There was no evidence that gender significantly interacted with any of the predictor variables to influence cortisol levels when participants' entered the lab (π_{0j}), slope prior to the ER induction (π_{1j}) or slope following the ER induction (π_{2j}), all *ps* > .05.

in the distraction condition, $\beta = -0.04$, $t(43) = 1.99$, $p = .05$, and compared to CTLs in either condition, $\beta = 0.03$, $t(71) = 2.40$, $p = .02$.

4. Discussion

This study is the first to examine the effect of a depressive rumination versus distraction manipulation on salivary cortisol in clinically depressed and healthy control participants. Results showed that the ER manipulation affected the trajectory of depressed participants' cortisol levels. Prior to the ER induction, cortisol production did not differ by group or condition. Following the ER induction, however, cortisol decline differed by group and condition. MDDs in the rumination condition exhibited less cortisol decline compared to MDDs in the distraction condition and compared to CTLs in either ER condition. In fact, cortisol levels significantly declined for MDDs in the distraction condition, CTLs in the depressive rumination condition, and CTLs in the distraction condition, whereas cortisol levels did not significantly decline for MDDs in the depressive rumination condition.

Although authors have posited that forms of repetitive thought, such as stressor-focused rumination, change salivary cortisol secretion (Brosschot et al., 2006; Watkins, 2008), the effects of depressive rumination on salivary cortisol had never been experimentally investigated in a clinically depressed sample. The majority of past research linking rumination and cortisol has been correlational (e.g., Zoccola, Dickerson, & Zaldivar, 2008), making it difficult to determine whether rumination leads to higher cortisol levels or whether higher cortisol levels lead to rumination. This study demonstrates, for the first time, that experimentally induced depressive rumination alters cortisol decline in MDD. Our findings are in line with an experimental study using a non-clinical sample, in which undergraduates were exposed to a sad mood induction and then randomly assigned to ruminate on their sad mood, distract themselves from it, or mindfully self-focus (e.g., Kuehner et al., 2009). Similar to results from the current study, participants reporting high depression symptoms who were assigned to the depressive rumination condition showed less cortisol decline. Such findings lend support to perseverative cognition models (Brosschot et al., 2006; Watkins, 2008), which suggest that repetitive thought processes – such as depressive rumination – have consequences for both emotional and physical wellbeing.

Results from the current study advance our understanding of MDD in several ways. For one, results have direct relevance for the stress sensitization/kindling model of depression (Hammen, 2005; Post, 1992). This model posits that neurobiological changes during depressive episodes lead to increasing interdependence between negative events and depression. Past research indicates that such neurobiological change can come from chronic cortisol activation, which increases atrophy of brain regions such as the prefrontal cortex and hippocampus, and in turn hinders one's ability to regulate emotional responses to negative events (Gold et al., 2002; McEwen, 1998). With this in mind, our findings suggest that depressive rumination increases the chance that depressed individuals will experience neurobiological changes that sensitize them to future negative events, thereby increasing their chance of experiencing recurrent depressive episodes.

In addition, knowledge elucidated from this study has important implications for our understanding of health and disease in MDD. A diagnosis of depression places individuals at increased risk for poor health outcomes, including faster progression of illness, immunosuppression, and increased risk of cardiac events (e.g., Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002). Past research has demonstrated that chronic cortisol hypersecretion has substantial effects on cardiovascular health and immune functioning (McEwen, 1998, 2008). Results from the current study suggest that depressive rumination may contribute to the cortisol hypersecretion that places depressed individuals at increased risk for health difficulties. This possibility has important implications for clinical interventions for individuals with MDD and comorbid health conditions. For example, interventions that target depressive rumination may be an important addition to behavioral medicine.

Interestingly, healthy controls in the current study did not differ in their cortisol decline based on whether they were assigned to ruminate or distract. Although unexpected, this is in line with a study by Young and Nolen-Hoeksema (2001), in which high and low trait ruminators did not differ in their cortisol response to stress. The authors attributed their null results to a lack of depressive rumination in their non-clinical sample, as determined by a retrospective analysis of participants' thought samples. A similar explanation might apply to the current study given that our manipulation check suggested that the depressive rumination induction was less effective for CTLs than MDDs. However, there is evidence supporting the effectiveness of our emotion regulation induction in both the CTL and MDD groups: In both groups, participants exhibited more rumination when in the depressive rumination compared to distraction condition. In addition, depressive rumination prolonged self-reported sadness in both the CTL and MDD group. Thus, another explanation for our findings might be considered. It is possible that depressive rumination did not affect CTLs' cortisol levels due to effective functioning of their HPA axis. An important component of HPA axis functioning is the ability to down-regulate cortisol production when optimal cortisol levels have been reached. This is accomplished via negative feedback loops; receptors on the hypothalamus, pituitary, and hippocampus identify elevated levels of cortisol and signal the HPA axis to decrease cortisol production (McEwen, 2006). The chronic cortisol elevation often associated with MDD can damage the sensitivity of glucocorticoid receptors, and thus contribute to difficulty down regulating cortisol production (Burke, Davis, Otte, & Mohr, 2005; McEwen, 2008). In contrast, healthy functioning of negative feedback loops helps avoid excess cortisol production and may have protected CTLs against the effects of depressive rumination. Although additional research is needed to explore this possibility, it is in line with results from Kuehner et al. (2009) showing that participants who reported low depressive symptoms did not differ in their cortisol decline based on whether they were in the depressive rumination or distraction condition.

Several limitations of the current study should be mentioned. For one, many participants with depression also met criteria for a comorbid psychiatric diagnosis. However, participants were randomly assigned to either the rumination or distraction condition and there were no systematic differences between the two conditions. Second, several participants were taking medications. Although the sample size in the current study prevented us from examining the effects of specific medication classes on change in cortisol, the percent of individuals on medication did not significantly differ between the rumination and distraction conditions in either group. In addition, the current study did not include an assessment of baseline cortisol. Given that the first cortisol sample was taken almost immediately after participants arrived in the laboratory and there is typically a 10–20 min lag in cortisol response (Dickerson and Kemeny, 2004), there would not have been enough time for cortisol levels to reach baseline. Given that the goal of the current study was to examine change in cortisol as a result of the ER induction, we structured the study procedure to maximize the amount of time and number of cortisol samples after the ER induction. As a result, however, we are unable to answer questions related to baseline cortisol or changes from baseline in this sample. The lack of baseline cortisol sample may explain why we did not see a change in cortisol from when participants entered the laboratory to the end of the forced failure induction. Any potential decline in cortisol due to participants' habituating to the laboratory may have

been offset by potential increases in cortisol due to the forced failure induction. Future research might examine this question more closely.

Despite these limitations, the current study provides important information about how rumination affects cortisol production in MDD. In doing so, this study advances integrated emotional-cognitive-biological models of MDD (Hammen, 2005; Post, 1992; Watkins, 2008). Moreover, keeping in mind the consequences of prolonged cortisol levels on cardiovascular health and immune functioning (McEwen, 1998), rumination may be a key factor that places depressed individuals at increased risk for poor health outcomes, such as increased risk of a cardiac event and faster progression of illness. Thus, identifying rumination as a mechanism underlying excess cortisol production in MDD may have important implications for understanding not only the maintenance and recurrence of depressive episodes but also the comorbid physical health conditions associated with depression (see Watkins, 2008, for a review).

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