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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.