

Concordance of mother–daughter diurnal cortisol production: Understanding the intergenerational transmission of risk for depression

Joelle LeMoult^{a,*}, Michael C. Chen^b, Lara C. Foland-Ross^a, Hannah W. Burley^c,
Ian H. Gotlib^a

^a Stanford University, United States

^b Harvard University, United States

^c Boston University, United States

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ABSTRACT

A growing body of research is demonstrating concordance between mother and child diurnal cortisol production. In the context of maternal history of depression, intergenerational concordance of cortisol production could contribute to hypercortisolemia in children of depressed mothers, which has been shown to increase risk for MDD. The current study is the first to examine concordance in diurnal cortisol production between mothers with a history of depression and their never-depressed, but high-risk, children. We collected salivary cortisol across 2 days from mothers with (remitted; RMD) and without (CTL) a history of recurrent episodes of depression and their never-depressed daughters. As expected, RMD mothers and their daughters both exhibited higher cortisol production than did their CTL counterparts. Moreover, both across and within groups, mothers' and daughters' cortisol production were directly coupled. These findings suggest that there is an intergenerational concordance in cortisol dysregulation that may contribute to hypercortisolemia in girls at familial risk for depression.

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In the United States alone, 10–15 million children under the age of 18 live with a depressed parent (England & Sim, 2009); approximately half of these children will develop depression by adulthood (Beardslee, Versage, & Gladstone, 1998; Goodman et al., 2011; Williamson, Birmaher, Axelson, Ryan, & Dahl, 2004). Indeed, parental depression is associated with a three- to five-fold increase in children's risk for developing a depressive episode. Moreover, compared with children of well parents who develop depression, children of depressed parents tend to have an earlier age of depression onset, longer episode duration, and greater functional impairment (Hammen, Shih, Altman, & Brennan, 2003; Keller et al., 1986). Little is known, however, about mechanisms through which risk for major depressive disorder (MDD) is transmitted from parent to child.

Dysregulation of the hypothalamus–pituitary–adrenal (HPA) axis has been found consistently to be related to elevated depressive symptoms and to familial risk for depression across a variety

of ages, making it a potential mechanism underlying the transmission of risk for depression (Chrousos & Gold, 1992; Ehlert, Gaab, & Heinrichs, 2001; Goodman & Gotlib, 1999; Guerry & Hastings, 2011; Holsboer, 2000). Researchers have shown that anomalous diurnal cortisol production is a core neurobiological abnormality in depression. Compared to never-depressed controls, currently and formerly depressed adults exhibit a steeper cortisol awakening response (CAR), higher peak cortisol in the morning, and higher overall cortisol levels across the day (Bhagwagar, Hafizi, & Cowen, 2005; Dienes, Hazel, & Hammen, 2013; Vreeburg et al., 2009; although see Knorr, Vinberg, Kessing, & Wetterslev, 2010, for more equivocal results). Although altered functioning of the HPA axis may be a consequence of depression, a growing body of research is now beginning to document that dysregulation of this system precedes and even contributes to the onset of illness. Indeed, several investigations of children and adolescents at high risk for depression show that increased vulnerability for MDD is associated with heightened diurnal cortisol secretion (Chen, Joormann, Hallmayer, & Gotlib, 2009; Mannie, Harmer, & Cohen, 2007). For example, Mannie et al. (2007) observed risk-related elevations in cortisol levels in the first 30 min after waking. These findings parallel data presented by Halligan, Herbert, Goodyer, and Murray (2004)

* Corresponding author at: Department of Psychology, Jordan Hall, Building 420, Stanford University, Stanford, CA 94305-2130, United States.
E-mail address: jlemoult@stanford.edu (J. LeMoult).

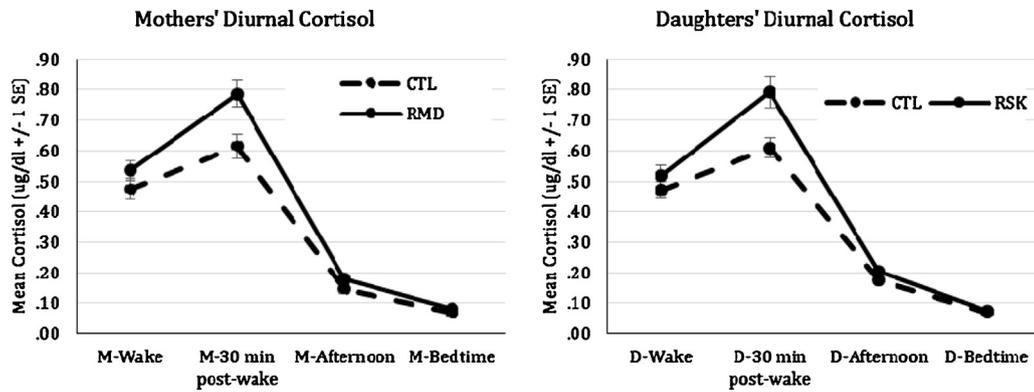


Fig. 1. Diurnal cortisol at waking, 30 min post-waking, mid-afternoon (approximately 3:30pm), and 30 min before bedtime for mothers with (RMD) and without (CTL) a history of depression and their high-risk (RSK) and low-risk (CTL) daughters.

showing that youth at risk for psychopathology exhibit higher morning cortisol secretion than do their low-risk peers. Importantly, in their sample of high-risk youth, Halligan and colleagues also found that hypercortisolemia predicted symptoms of depression 3 years later (Halligan, Herbert, Goodyer, & Murray, 2007; see also Goodyer, Tamplin, Herbert, & Altham, 2000; Harris et al., 2000). This finding was replicated in an unselected sample of older adolescents: those participants who showed a steeper CAR were more likely to develop MDD in the upcoming year (Adam et al., 2010).

Investigators have attempted to understand and predict children's diurnal HPA-axis activity by examining the concordance, or synchrony, between parent and child diurnal cortisol production. In samples of healthy dyads, children's diurnal cortisol patterns have been closely related to their mothers' cortisol production (e.g., Mörelius, Broström, Westrup, Sarman, & Örténstrand, 2012; Stenius et al., 2008). In fact, maternal cortisol level is among the strongest determinants of children's cortisol production (Bright, Granger, & Frick, 2012). Mörelius et al. (2012), for example, examined diurnal cortisol secretion in mothers and their 6-month-old infants and found strong correlations between mother and child cortisol levels in the morning, afternoon, and evening. Although studies of dyadic concordance have typically focused on mothers and their infants (e.g., Laurent, Ablow, & Measelle, 2011), high levels of concordance between mother and child diurnal cortisol production have been reported throughout childhood and adolescence (Papp, Pendry, & Adam, 2009; Young, Vazquez, Jiang, & Pfeffer, 2006).

Concordance between mother and child diurnal cortisol production becomes particularly important in the context of maternal psychopathology, especially in the context of disorders such as depression that are frequently associated with increased cortisol production. In the context of mothers' depression-related hypercortisolemia, intergenerational concordance of cortisol production could potentiate hypercortisolemia in their children, which has been shown to increase individuals' risk for depression (Halligan et al., 2007; Adam et al., 2010). Despite considerable evidence showing intergenerational concordance of cortisol production, it is not yet clear whether the concordance between mother and child cortisol production is equivalent in mothers with and without a history of depression. It is possible that mothers' history of depression will decrease maternal sensitivity and responsiveness, which has been shown to attenuate dyadic concordance of cortisol production (Gunnar, Brodersen, Nachmias, Buss, & Rigatuso, 1996; Tu et al., 2007). Alternatively, higher levels of maternal negative affect have been reported to increase concordance (Papp et al., 2009). Elucidating the nature of concordance between depressed mothers' and

their children's diurnal cortisol production is a critical next step toward understanding mechanisms underlying both hypercortisolemia in children of depressed parents and the intergenerational transmission of risk for depression. Importantly, no study has yet examined the concordance in diurnal cortisol production between formerly depressed mothers and their never-depressed adolescent offspring.

The current study was designed to examine the concordance in diurnal cortisol production between mothers with a history of depression and their never-depressed, but high-risk, children. Given the high rates of depression in daughters of depressed mothers (Gotlib & Colich, 2014; Hops, 1996), we recruited a sample of adolescent daughters at high or low risk for depression based on whether their mothers did or did not experience recurrent episodes of depression during the daughter's lifetime. We first examined whether our sample of high-risk daughters and their mothers exhibited elevated diurnal cortisol production compared to their low-risk counterparts by assessing risk-group differences in CAR, peak morning cortisol, and daytime cortisol production. We then examined the concordance between mother and daughter diurnal cortisol production, and tested whether maternal history of depression moderated the strength of this association. We expected that mothers with a history of recurrent MDD would exhibit greater overall cortisol production than would mothers with no current or past Axis I disorder. Similarly, we expected that daughters who were at high risk for depression based on their mothers' history of the disorder would exhibit greater overall cortisol production than would low-risk daughters. Finally, we expected to find significant intergenerational concordance in cortisol production in both the high- and low-risk groups, a pattern that could contribute to hypercortisolemia in high-risk daughters and, in turn, increase our understanding of the intergenerational transmission of risk for depression.

1. Materials and methods

1.1. Participants

The current sample consisted of 112 mother–daughter dyads. All dyads included daughters who were between the ages of 9 and 15 years and who had no current or past Axis I disorder. Fifty-three daughters had mothers without a current or past Axis I disorder (low-risk daughters; CTL), and 59 daughters had mothers who had a history of recurrent episodes of MDD but whose depression was in full remission, defined as not meeting criteria for depression for the past two months (high-risk daughters; RSK). Mother–daughter dyads were recruited through advertisements posted throughout the community. A telephone screen was used to assess initial inclusion/exclusion criteria; these dyads were invited to the laboratory for a more extensive interview. No participant had any major neurological or metabolic conditions, significant head trauma, or clinically significant learning disorder, and all were fluent in English.

1.2. Assessment of psychopathology

Interviews. All mothers and daughters were administered structured clinical interviews by trained interviewers. Mothers were administered the Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 2002) to assess the presence of at least two distinct episodes of MDD since the birth of their daughter and the absence of a current depressive episode for past two months (remitted; RMD) or the absence of any current or past Axis I disorder (control; CTL). Daughters and mothers (about the daughters) were administered the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS; Kaufman, Birmaher, Brent, Ryan, & Rao, 2000) to assess the absence of any current or past Axis I disorder in the daughters. To assess interrater reliability, an independent rater who was blind to group membership evaluated 10% of SCID and K-SADS interviews. In all cases, diagnoses and group assignment matched those given by the original interviewer, $\kappa = 1.00$.

Questionnaires. Daughters completed the 10-item version of the Children's Depression Inventory (CDI; Kovacs, 1992), a self-report measure of depressive symptomatology for children between 8 and 17 years of age. Pubertal status was assessed via self-report Tanner Staging (Tanner & Whitehouse, 1976). Daughters also completed the Anxiety Sensitivity Index for Children (ASIC; Laurent, Schmidt, Catanzaro, Joiner, & Kelley, 1998), a 16-item self-report measure of anxiety sensitivity in children. Five daughters elected to not provide Tanner stage and one elected to not complete the ASIC. Mothers completed the Beck Depression Inventory-II (BDI; Beck, Steer, & Brown, 1996), a 21-item self-report measure of depressive symptom severity for adults. They also completed the Beck Anxiety Inventory (BAI; Beck & Steer, 1990), a 21-item measure of anxiety symptoms in adults. The ASIC and BAI were included to test as possible covariates.

Diurnal cortisol collection. Within 2 weeks of the diagnostic assessment, mother–daughter dyads were given Salivette kits (Sarstedt, Germany) for at-home cortisol collection. The CTL and RMD groups did not differ with respect to the time between diagnostic assessment and cortisol collection, $t(110) = 1.06, p = .291$. Both members of the dyad provided cortisol samples on 2 consecutive weekdays by providing a saliva sample at the following four time points: immediately upon waking, 30 min post-waking, mid-afternoon (3:30 pm), and 30 min before bedtime. Participants were instructed not to eat, drink, or brush their teeth for 2 h before each sample. For a subset of participants ($n = 58$), smart caps were used to track the time when participants opened the bottle to retrieve the Salivette. Cortisol collection time obtained from the smart caps did not significantly differ from self-reported collection time at any time point for mothers, $ts < 1.60, ps > .05$, or daughters, $ts < 1.80, ps > .05$. After saliva collection, participants stored Salivettes in their home freezer until they could be transferred to the -20°F freezer at Stanford University. Cortisol levels were assayed by luminescence immunoassay reagents using a commercial kit from Immuno-Biological Laboratories, Inc. (Hamburg, Germany), and the assay sensitivity was set at $0.015 \mu\text{g/dl}$. Samples were assayed together in large batches to control for interassay error, and control samples were included to evaluate variability. The intraassay variation on three saliva pools of the low, medium, and high controls was averaged 2.78%, 10.45%, and 4.79%, respectively. The mean values of the low, medium, and high controls were .054, .228, and .863 $\mu\text{g/dL}$, respectively. The interassay coefficients of the variations of the low, medium, and high controls were 10.9%, 10.5%, and 5.5%, respectively.

1.3. Statistical analyses

Given the dependent nature of the primary outcome data (cortisol levels measured within a dyad over the course of the day), we used multilevel modeling as the analytic framework. Within-dyad variation in mother or daughter cortisol over time was modeled at Level 1. We evaluated linear, quadratic, cubic, piecewise, and exponential models, and we selected the model that best fit the data, based on the smallest value of Akaike's Information Criterion (AIC), and that was consistent with our visual inspection of the data. For concordance analyses, mother cortisol was added as a time-varying, within-dyad characteristic at Level 1 (see also Laurent et al., 2011). At Level 2, between-dyad variability in Level 1 parameters was explained by characteristics that varied across mother–daughter dyads, in this case, mothers' history of depression. In all analyses, time was allowed to vary across persons, thereby accounting for each individual's unique cortisol sampling schedule. At Level 1, we assumed an independent and normally distributed error structure, e_{ij} , with mean of 0 and constant variance of σ^2 . At Level 2, we specified a random effect, r_{pi} , with mean of 0 and a 3×3 covariance matrix, T .

We used hierarchical linear modeling (HLM; Raudenbush & Bryk, 2002; Raudenbush, Bryk, & Congdon, 2004) to test a series of models examining the impact of mothers' history of depression on their own and their daughters' diurnal cortisol patterns. This modeling technique allowed us to test the effects of mothers' history of depression not only on the cortisol response trajectories themselves, but also on the concordance of these responses across mother–daughter dyads. Because salivary cortisol data continued to be positively skewed after logarithmic and other transformations, we winsorized cortisol values 2 standard deviations above the mean to the 2-standard deviation value (4% of samples). Dichotomous variables were effect coded and continuous variables were centered. Models were fit using full information maximum likelihood estimates for the purposes of calculating deviance, degrees of freedom, and AIC; and restricted maximum likelihood for estimating model parameters.

Table 1

Demographic data for the low-risk and high-risk participants.

	Mothers	
	CTL	RMD
Age, <i>M</i> (<i>SD</i>)	44.43 (4.30)	42.76 (6.35)
% Caucasian	75.00	77.97
% College education	86.54	75.86
% Psychotropic meds, current	5.66	47.46
% Psychotropic meds, lifetime	5.66	76.27
% Taking oral contraceptives	11.32	5.08
BAI, <i>M</i> (<i>SD</i>)	3.61 (2.82)	9.90 (7.18)
BDI, <i>M</i> (<i>SD</i>)	3.08 (3.86)	13.73 (10.55)
BMI, <i>M</i> (<i>SD</i>)	24.85 (5.16)	25.81 (4.70)
	Daughters	
	CTL	RSK
Age, <i>M</i> (<i>SD</i>)	12.04 (1.53)	12.02 (1.50)
% Caucasian	71.70	67.80
Tanner stage, <i>M</i> (<i>SD</i>)	6.08 (1.90)	6.28 (2.14)
% Post-menarche	46.67	51.92
% Psychotropic meds, current	0.00	0.00
% Psychotropic meds, lifetime	0.00	0.00
% Taking oral contraceptives	0.00	0.00
ASIC, <i>M</i> (<i>SD</i>)	8.08 (5.50)	9.34 (5.83)
CDI, <i>M</i> (<i>SD</i>)	1.08 (1.19)	2.35 (2.40)
BMI, <i>M</i> (<i>SD</i>)	19.46 (2.36)	20.76 (3.30)

Note: Mothers with (RMD) or without (CTL) a history of depression, and their daughters who are at high (RSK) or low (CTL) risk for depression based on mothers' history of the disorder; Meds, medications; CDI, Children's Depression Inventory; BDI, Beck Depression Inventory; BMI, body mass index.

2. Results

2.1. Participant characteristics

Demographic and clinical characteristics of the CTL and RMD mothers and the CTL and RSK daughters are presented in Table 1. There were no significant group differences in mothers' age, $t(110) = 1.61, p = .110$, ethnicity, $\chi^2(N = 111) = 0.14, p = .713$, education, $\chi^2(N = 111) = 2.49, p = .115$, body mass index (BMI), $t(100) = 0.98, p = .328$, or percent taking oral contraceptives, $\chi^2(N = 111) = 1.41, p = .236$. There were also no significant group differences in daughters' age, $t(110) = 0.07, p = .942$, ethnicity, $\chi^2(N = 112) = 0.20, p = .654$, Tanner stage, $t(105) = 0.51, p = .611$, menarche status, $\chi^2(N = 97) = 0.27, p = .606$, or BMI, $t(83) = 1.32, p = .191$. The RMD mothers obtained significantly higher scores on the BAI than did the CTL mothers, $t(110) = 5.97, p < .001$; however, the RSK and CTL daughters did not differ in their scores on the ASIC, $t(109) = 1.17, p = .245$. The RMD mothers obtained significantly higher scores on the BDI than did the CTL mothers, $t(110) = 6.94, p < .001$, and the RSK daughters obtained slightly but significantly higher scores on the CDI than did the CTL daughters, $t(110) = 3.50, p = .001$. Importantly, sample collection times did not differ as a function of group for mothers or daughters at any time point, $ts(110) < 1.98, ps > .05$. Mothers' first and second cortisol samples were taken an average of 30 min earlier than their daughters' samples, $ps < .001$, the timing of mothers' afternoon samples did not significantly differ from their daughters' sampling times, and mothers' evening samples were taken an average of 8 min after her daughters, $p = .041$.

2.2. Baseline models

We first ran baseline models of mothers' and daughters' diurnal cortisol containing no Level 2 predictors in order to describe the average diurnal cortisol patterns and between-dyad variability in these patterns. We then tested linear, quadratic, cubic, piecewise, and exponential models to determine the model that best

captured the pattern of diurnal cortisol production across the day. Cubic and exponential models failed to converge. For both mothers and daughters, the smallest AIC was associated with the piecewise linear growth model (AIC = -191.09 and -191.74 for mothers and daughters, respectively), which estimated the cortisol awakening response (CAR; reflecting the slope from awakening to 30 min post-waking) and daytime slope (slope from 30 min post-waking through evening). Because time was centered at the second cortisol sample, the intercept term represents the level of cortisol 30 min after waking (see Raudenbush & Bryk, 2002, for additional details).

The baseline cortisol model indicated that mothers' average cortisol increased from awakening to 30 min after waking, $\beta = 0.26$, $p < .001$, reached a peak cortisol value that was significantly greater than zero, $\beta = 0.65$, $p < .001$, and then declined throughout the day, $\beta = -0.04$, $p < .001$. Daughters' diurnal cortisol production followed the same pattern, increasing from awakening to 30 min after waking, $\beta = 0.30$, $p < .001$, reaching a peak cortisol value that was significantly greater than zero, $\beta = 0.65$, $p < .001$, and then declining throughout the day, $\beta = -0.05$, $p < .001$. Significant variability in these parameters, however, demonstrates that these patterns differed across dyads and could therefore be explained by Level 2 predictors.

2.3. Potential covariates

A series of variables were tested as potential covariates in relation to mothers' and daughters' cortisol production. For mothers, we tested the following variables: current psychotropic medications, lifetime history of psychotropic medications, oral contraceptive use, treatment, body mass index (BMI), BAI scores, and BDI scores. For daughters, we tested the following variables: ASIC scores, pre- versus post-menarche, Tanner stage, BMI, and CDI scores; given the exclusion criteria for this study, daughters were not taking any psychotropic medication and were not in treatment. None of these variables predicted mothers' or daughters' cortisol response patterns, $ps \geq .05$, and, therefore, were not included as covariates.

2.4. Group differences in mothers' and daughters' diurnal cortisol patterns

For each of the outcomes reported, we tested the effects of mothers' history of depression on each of the Level 1 parameters: CAR, peak cortisol, and daytime slope (see Fig. 1). For mothers, history of depression significantly predicted the CAR, $\beta = 0.09$, $p = .037$, peak cortisol, $\beta = 0.08$, $p = .005$, and daytime slope, $\beta = -0.01$, $p = .006$, and significantly improved model fit, $\chi^2(df = 3) = 7.98$, $p = .046$. Specifically, compared to CTL mothers, RMD had a steeper CAR, higher peak cortisol levels 30 min after waking, and a steeper daytime slope.¹ In parallel for daughters, mothers' history of depression significantly predicted the daughters' CAR, $\beta = 0.13$, $p = .008$, peak cortisol, $\beta = 0.09$, $p = .002$, and daytime slope, $\beta = -0.01$, $p = .001$, and significantly improved model fit, $\chi^2(df = 3) = 11.31$, $p = .010$. Specifically, compared to CTL daughters, RSK daughters had a steeper CAR, higher peak cortisol levels 30 min after waking, and a steeper daytime slope.²

¹ One mother in the RMD group was taking a corticosteroid; findings did not change when this participant was removed from the analyses.

² Given that BMI has been associated with diurnal cortisol production in other studies (e.g., Daniel et al., 2006), we tested BMI as a covariate in the model predicting mothers' and daughters' diurnal cortisol production. BMI did not significantly predict the CAR, peak cortisol, or the daytime slope for mothers or daughters, $ps > .05$; moreover, the main effect of mothers' history of depression on each index of diurnal cortisol remained significant, $ps < .02$, and the addition of BMI did not significantly improve model fit, $\chi^2(3) < 1.80$, $ps > .05$.

Table 2

Correlations between mother–daughter diurnal cortisol across groups and for dyads in which the mother does (RMD) and does not (CTL) have a history of depression.

	Across groups	RMD	CTL
CAR	0.410**	0.332*	0.426*
Peak cortisol	0.486**	0.481**	0.401*
Daytime slope	0.487**	0.485**	0.393*

* $p < .01$.

** $p < .001$.

2.5. Concordance in mother and daughter cortisol

To directly test the concordance of mother and daughter cortisol production, daughter cortisol outcome was modeled as a function of an intercept and her mother's cortisol production, both of which were allowed to vary across dyads. Overall, mother and daughter diurnal cortisol production was significantly concordant, $\beta = 0.84$, $p < .001$. Mothers' history of depression was entered at Level 2 to explain the significant between-dyad variation in concordance. Importantly, mothers' history of depression was not a significant predictor of the concordance between mothers' and daughters' diurnal cortisol production, $\beta = -0.01$, $p = .765$, and did not significantly improve model fit, $\chi^2(df = 2) = 0.86$, $p > .500$. Moreover, when the association between mother and daughter cortisol production was examined separately based on mothers' history of depression, there was evidence of strong intergenerational concordance in diurnal cortisol production for dyads in which mothers did have a history of depression, $rs(59) > .332$, $ps < .010$, and for dyads in which mothers did not, $rs(53) > .393$, $ps < .010$ (see Table 2).

3. Discussion

This is the first study to examine the concordance in diurnal cortisol production between formerly depressed mothers and their never-depressed adolescents who are at risk for depression based on their mothers' history of the disorder. Using multiple indicators of diurnal cortisol, we found that mothers' history of depression predicted both their own and their daughters' cortisol production. As expected, formerly depressed mothers exhibited a steeper CAR, higher peak cortisol 30 min after waking, and steeper afternoon slope than did healthy mothers. Importantly, this pattern of findings was paralleled in their daughters: daughters of formerly depressed mothers exhibited a steeper CAR, higher peak cortisol 30 min after waking, and steeper afternoon slope than did daughters of healthy mothers. We also found consistent and robust concordance between mothers' and daughters' diurnal cortisol production across both groups of participants: in both groups, mothers with higher-than-average diurnal cortisol production at a given time point had daughters with higher-than-average cortisol production at the same time point. Thus, concordance of mothers' and daughters' cortisol production may contribute to the hypercortisolemia observed in high-risk daughters', which has been shown to increase risk for MDD (e.g., Adam et al., 2010; Halligan et al., 2007).

Our finding of hypercortisolemia in formerly depressed mothers adds to previous studies documenting cortisol dysregulation in individuals with a history of depression (e.g., Appelhof et al., 2006; Trestman et al., 1991; Zobel, Nickel, Sonntag, Uhr, Holsboer, & Ising, 2001). Although these findings are consistent with the formulation that HPA-axis dysregulation is a consequence of the depressive episode, it is noteworthy that we also found evidence of cortisol dysregulation in healthy daughters of formerly depressed mothers. Indeed, the high-risk daughters, who themselves had no current or past Axis I disorder, showed evidence of cortisol dysregulation

on every metric of diurnal cortisol activity. Our findings add to a handful of studies demonstrating cortisol dysregulation in children and adolescents at risk for depression (Goodyer et al., 2000; Halligan et al., 2004; Mannie et al., 2007; Young et al., 2006). Thus, hypercortisolemia may be a marker of risk for depression that signals the need for early intervention. This possibility is consistent with several longitudinal studies that found adolescents who exhibit greater diurnal cortisol production to be more susceptible to developing a mood disorder (Adam et al., 2010; Ellenbogen, Hodgins, Linnen, & Ostiguy, 2011). Moreover, researchers have shown that chronic cortisol elevations can increase atrophy of such brain regions as the prefrontal cortex and hippocampus, which in turn can impair individuals' ability to regulate emotional responses to negative events (Gold, Drevets, & Charney, 2002; McEwen, 1998).

It is noteworthy that we documented concordance of HPA-axis functioning between formerly depressed mothers and their at-risk, yet never-depressed, daughters. This finding increases our understanding of hypercortisolemia in children at familial risk for depression (e.g., Mannie et al., 2007; Halligan et al., 2004). Our results are consistent with the broader literature showing concordance between parent and child biological functioning in both unselected and healthy samples (e.g., Bornstein & Suess, 2000; Mörelius et al., 2012; Mörelius, Theodorsson, & Nelson, 2009; Steinius et al., 2008). Moreover, our results support and extend Young et al.'s (2006) finding of concordance between parent and child cortisol in the context of parental depression. It is important to note, however, that approximately half of the children in Young et al.'s study met criteria for an Axis I disorder; moreover, in one-third of the depressed dyads, it was the nondepressed parent, rather than the depressed parent, who provided the cortisol sample. Our study extends Young et al.'s results by documenting significant concordance in diurnal cortisol production between formerly depressed mothers and their at-risk children before any of the children had developed a psychiatric disorder. Our results are also consistent with findings reported by Laurent et al. (2011), who showed that neither current nor past maternal depressive symptoms influenced the degree of concordance between mother and infant cortisol production during a psychosocial stressor. Laurent and colleagues did find, however, that increasing levels of depressive symptoms over time intensified the concordance between mother and infant cortisol production. It will be important in future research to examine whether changes in depressive symptoms also affect concordance in diurnal cortisol production between depressed mothers and their adolescent children.

Theorists have suggested that both genetic and environmental factors contribute to concordance between parent and child cortisol production. Increasing evidence indicates that cortisol production and regulation is heritable. For example, individuals who are homozygous for the short allele in the promoter region of the serotonin transporter gene have been found to produce higher levels of cortisol, both throughout the day (Chen et al., 2009) and in response to a psychosocial stressor (Gotlib, Joormann, Minor, & Hallmayer, 2008). Moreover, data from twin studies suggest heritability estimates of .40 for the CAR (Wüst, Federenko, Hellhammer, & Kirschbaum, 2000). Evidence from twin studies also demonstrates the importance of environmental factors on HPA-axis activity. For example, concordant cortisol production has been found between twins living in the same environment (Custodio et al., 2007; Schreiber et al., 2006) but not between twins living in different environments (Franz et al., 2010). Moreover, instability and stress in individuals' home environments can directly affect cortisol production (de Weerth, Buitelaar, & Beijers, 2013; Repetti, Taylor, & Seeman, 2002). Similarly, evidence from both human and animal models suggests that early environmental stress can have lasting effects on cortisol dysregulation and neural structures that

support HPA-axis activity (Spinelli et al., 2009; Taylor, 2010). It will be important that future studies quantify the relative contributions of genetic and environmental factors in order to gain a better understanding of mechanisms underlying intergenerational concordance in cortisol production.

We should note three limitations of the present study. First, despite the fact that daughters in the high- and low-risk groups did not meet diagnostic criteria for a current or past Axis I disorder, there were nevertheless group differences in CDI scores. It is important to note, however, that CDI scores for both groups of girls were still far below the recommended cutoff score of 8 (Kovacs, 1992). Moreover, we examined CDI scores as a covariate and found no evidence that, within this narrow and low range of CDI scores, girls' depressive symptomatology affected cortisol levels. Second, although this study provides important first evidence of the concordance in patterns of diurnal cortisol between mothers and daughters, the cross-sectional nature of our data limits our ability to make statements about causation. In this context, it is possible that daughters' cortisol level influenced their mothers' cortisol production, or that there is a bidirectional and interactive relation between mother and daughter cortisol production (Saxbe et al., 2013). Third, we did not assess a number of variables known to influence salivary cortisol functioning, including sleep disturbances, history of trauma, and the phase of participants' menstrual cycle. Future research should examine the influence of these variables on the concordance of cortisol production. Similarly, the use of self-report Tanner stage as a proxy for pubertal development is a limitation of this study. Although self-reported measures of physical maturation have been found to be significantly associated with levels of sex hormones, both testosterone and DHEA levels have been shown to influence diurnal cortisol production. Thus, future research should consider directly assessing gonadal hormones. Finally, although hypercortisolemia has been shown consistently to increase susceptibility to depression in both high-risk and unselected samples (Adam et al., 2010; Goodyer et al., 2000; Halligan et al., 2007; Harris et al., 2000), it will be important to follow this sample of girls over time to examine whether high levels of cortisol production predict the subsequent onset of depression.

Overall, the current findings contribute to our understanding of HPA-axis functioning in children of depressed mothers. Although there is considerable evidence demonstrating that children of depressed mothers are at increased risk for depression, the mechanisms underlying this risk are not well understood. Data from this study indicate that daughters of formerly depressed mothers exhibit hypercortisolemia throughout the day. Moreover, there was an intergenerational concordance in cortisol dysregulation that may contribute to hypercortisolemia in girls whose mothers' have a history of depression. Given the consequences of hypercortisolemia for susceptibility to develop depressive episodes (e.g., Halligan et al., 2007) and for neural development and functioning (Gold et al., 2002; McEwen, 1998), elucidating intergenerational concordance in cortisol dysregulation is likely to have important implications for understanding the onset of MDD in girls at familial risk for depression.

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