Psychoneuroendocrinology (2009) 34, 76—86

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

The relation between early life adversity, cortisol awakening response and diurnal salivary cortisol levels in postpartum women

Andrea Gonzalez [a,d,*], Jennifer M. Jenkins [b], Meir Steiner [c,d,e], Alison S. Fleming [a]

[a] Department of Psychology, University of Toronto, 3359 Mississauga Road N, Mississauga, ON, Canada L5L1C6
[b] Human Development & Applied Psychology, University of Toronto, 252 Bloor St. West, 9th Floor, Toronto, ON, Canada M5S1V6
[c] Women's Health Concerns Clinic, St. Joseph's Healthcare, 50 Charlton Avenue East, Hamilton, ON, Canada L8N 4A6
[d] Department of Psychiatry & Behavioural Neurosciences, McMaster University, Hamilton, ON, Canada
[e] Department of Obstetrics and Gynecology, McMaster University, Canada

Received 6 April 2008; received in revised form 11 August 2008; accepted 12 August 2008

KEYWORDS
Diurnal cortisol;
Awakening response;
Early adversity;
Postpartum mothers

Summary Early life adversity has been associated with hypothalamic—pituitary—adrenal (HPA) axis dysfunction in both children and adults. However, in adulthood, most studies have focused on the effects of early adversity on HPA axis stress reactivity rather than the cortisol awakening response or diurnal cortisol profiles. The goal of this study was to examine the cumulative effects of early life adversity on the cortisol awakening response (CAR) and diurnal cortisol profiles in a sample of postpartum women. Ninety women between 2 and 6 months postpartum completed two retrospective reports assessing adverse early life experiences (maltreatment and consistency of care). Eighteen women reported having experienced both parental loss and some form of childhood maltreatment and 36 women reported having experienced one type of early life adversity, either parental loss or maltreatment. HPA axis function was assessed through salivary cortisol collections over two consecutive days for measurement of the cortisol awakening response ($n = 61$) and diurnal cortisol rhythm ($n = 90$). Women who reported experiencing adverse early life experiences exhibited a tendency towards higher levels of awakening cortisol compared to women who reported no adverse early life experiences ($p = .07$). These higher awakening cortisol levels were sustained throughout the morning in the groups who experienced early adversity, with all groups exhibiting the typical diurnal decline in the afternoon and evening ($p < .05$). Women reporting early adversity exhibited more heterogeneity in their diurnal cortisol levels across the two collection days ($p < .01$). Our findings suggest that in a community sample of postpartum women, early

* Corresponding author. Tel.: +1 905 521 2100x74458; fax: +1 905 569 4326.
E-mail addresses: gonzal@mcmaster.ca (A. Gonzalez), jenny.jenkins@utoronto.ca (J.M. Jenkins), mst@mcmaster.ca (M. Steiner), afleming@utoronto.ca (A.S. Fleming).

doi:10.1016/j.psyneuen.2008.08.012

adversity is associated with current HPA axis function. These findings may have implications for the nature of mother—infant interactions.

1. Introduction

Converging evidence from animal and human studies demonstrates that adverse early life experiences, such as maltreatment, family conflict and parental loss can have enduring effects on psychological and physical health (Felitti et al., 1998; Meaney, 2001; Sanchez et al., 2001; Repetti et al., 2002; Tarullo and Gunnar, 2006). Many studies focus on linking early adversity to physical problems and psychopathology via biological mechanisms and in most of these the hypothalamic—pituitary—adrenal axis (HPA) is strongly implicated (see Heim and Nemeroff, 2001; Sanchez et al., 2001; Vermetten and Bremner, 2002). The HPA axis is one of the main physiological systems mediating the neuroendocrine response to stress (Chrousos, 1998; López et al., 1999). Basal activity of the HPA axis follows a circadian rhythm such that in humans the peak of cortisol secretion occurs 20—30 min after awakening (cortisol awakening response) followed by a gradual decline throughout the day to its nadir 2—3 h after sleep onset (Doman et al., 1986). Disruptions in diurnal rhythm often reflect physiological or psychological disturbance (Young, 2004). Individual differences in stress reactivity, diurnal cortisol and the cortisol awakening response all serve as potential markers for HPA axis dysregulation (Pruessner et al., 1999; Sanchez et al., 2001; Clow et al., 2004). The purpose of this study was to examine the impact of early adversity (maltreatment and inconsistent care) on parameters of HPA axis functioning including diurnal cortisol profile and the cortisol awakening response in a population of healthy postpartum women.

Animal studies provide direct evidence that early experience alters HPA axis activity and regulation. In rodents, variations in the quality of early life experiences (prolonged periods of maternal separation and exposure to low-licking/grooming (LG) mothers) result in a number of neuroendocrine and structural changes (Plotsky and Meaney, 1993; Ladd et al., 2000; Liu et al., 2000; Rees et al., 2006; Diorio and Meaney, 2007). Similarly, maternal separations in non-human primates during infancy produce altered diurnal rhythms characterized by low early morning cortisol levels and a flattened diurnal profile (Boyce et al., 1995; Sánchez et al., 2005).

Diurnal salivary cortisol changes have also been associated with early adversity in children. Consistent with non-human primate work, Romanian orphan-reared toddlers exhibited low early morning cortisol levels and blunted diurnal cortisol patterns (Carlson and Earls, 1997). Similar profiles have been found in children in foster care, with 38% of foster children showing patterns of low cortisol production and 18% exhibiting high patterns compared to children who were never in foster care (Dozier et al., 2006). In contrast, when Romanian orphans were examined 6.5-years post-adoption, those adopted after 8 months or more of institutionalization exhibited high levels of cortisol across the day (Gunnar et al., 2001).

Maltreatment has also been associated with disturbances in diurnal salivary cortisol profiles in children. Decreased free salivary cortisol levels in the morning and lack of diurnal cortisol decline has been reported in maltreated children with depression (Kaufman, 1991; Hart et al., 1996) and post-traumatic stress disorder (PTSD) (Carrion et al., 2002). In contrast, De Bellis et al. (1999) found even after several years of experiencing neglect and maltreatment, children with PTSD had higher concentrations of 24-h urinary free cortisol compared to controls. Cicchetti and Rogosch (2001) demonstrated that maltreated children who experienced a combination of abuse had higher morning and afternoon cortisol levels.

Retrospective studies of early adversity in adults have typically focused on stress reactivity and pharmacological stimulation, demonstrating that adversity is related to HPA axis dysregulation (changes in total plasma cortisol levels) (Heim et al., 2000a,b, 2001, 2002). In adulthood, early loss has been associated with increased salivary cortisol reactivity to a psychological stressor (Luecken, 2000; Luecken and Appelhans, 2006). This effect was moderated by the presence of early abuse and family conflict, such that if the relationship with the surviving parent was characterized by high abuse and/or conflict, early parental separation was associated with greater cortisol reactivity (Luecken, 2000; Luecken and Appelhans, 2006). In addition, early loss has been associated with a reduced salivary cortisol awakening response (Meinlschmidt and Heim, 2005) and higher levels of salivary diurnal cortisol (Nicolson, 2004).

Despite accumulating evidence that early life adversity affects HPA axis stress reactivity, diurnal and awakening cortisol, the effects of early adversity remain largely unexplored in a normative population of women, in particular during the postpartum. The postpartum period is characterized by a number of transitions, including hormonal changes (Corter and Fleming, 2002), relational changes (Belsky and Pensky, 1988), and increased vulnerability to anxiety and depression (Beck, 2001), yet few studies have specifically targeted a postpartum population. At 2-year postpartum, lower morning salivary cortisol levels and flatter diurnal slopes were associated with a greater number of children in the home and a greater number of hours of employment outside the home (Adam and Gunnar, 2001). Moreover, higher morning values were associated with more positive relationship functions (Adam and Gunnar, 2001).

Exploring diurnal cortisol profiles earlier in the postpartum period, Tu et al. (2006) found that primiparous mothers had greater diurnal salivary cortisol secretion compared to multiparous mothers (Tu et al., 2006). However, when feeding choice (breast versus bottle) was considered, there was no diurnal difference in primiparous mothers, whereas multiparous bottle feeding mothers had higher cortisol levels at awakening and later in the afternoon. Interestingly, there were no differences in the cortisol awakening response based on feeding choice (Tu et al., 2005) or parity (Tu et al., 2005; Federenko et al., 2006).

Numerous forms of early adversity occur in the context of the family unit (Felitti et al., 1998; Repetti et al., 2002; Heim et al., 2003; Dong et al., 2004; Luecken and Lemery, 2004;

Gunnar and Quevedo, 2007). Heim and colleagues propose that the two most salient forms of early life adversity in humans are sexual, physical and emotional maltreatment (abuse or neglect), as well as parental loss (death or separation) (Heim et al., 2003, 2004). Therefore, the goals of the present study were to assess the relation between cumulative early life experiences (ELE; retrospective reports of inconsistent care and maltreatment) and cortisol awakening response (CAR), and diurnal cortisol rhythm in a sample of postpartum mothers We examined the cumulative effect of early life experiences because numerous studies have demonstrated a positive relationship between the number of risk factors during childhood with psychosocial adjustment problems (Rutter, 1979; Forehand et al., 1998) and physical health problems (Anda et al., 2006). Recently, this graded relationship between multiple early adversities and health outcomes has been theoretically linked to cumulative exposure on the developing stress system (Anda et al., 2006).

Given that diurnal cortisol profiles vary in both children (Kaufman, 1991; Hart et al., 1996; Cicchetti and Rogosch, 2001; Carrion et al., 2002) and adults (Heim et al., 2001, 2002) with the presence of affective psychopathology, we included depression and anxiety as potential covariates in our analyses. Previous research has demonstrated that several factors may impact on diurnal cortisol profiles, such as age (Kirschbaum and Hellhammer, 1994) and awakening time (Hucklebridge et al., 2005). In addition, socioeconomic status (SES) and education has also been associated with individual differences in adults' cortisol function (Cohen et al., 2006). Therefore, in addition to our other potential covariates (anxiety, depression, parity and feeding status), we also included these factors (age, education level, SES and awakening time) as potential covariates in our analyses.

2. Methods

2.1. Participants

Postpartum mothers were recruited through three primary sources: (1) Ontario Early Years Centres (OEYC) in Halton, Mississauga, Cambridge, Kitchener and Hamilton, (2) the maternity ward at St. Joseph's Healthcare, Hamilton, Ontario, and (3) a promotional show, 'Baby Time,' for new and expecting mothers held in Toronto, Ontario. The study was approved by the Research Ethics Board of St. Joseph's Healthcare and the University of Toronto and written informed consent was obtained from each participant. At total of 90 women aged 24—42 years (M = 31.8, S.D. = 4.1), participated in the study. The women ranged from 2 to 6 months postpartum at the time of testing (M = 4.0, S.D. = 1.4). 71.1% of the women were first-time mothers and 52% of the women had female infants. The majority of mothers had completed some form of post-secondary education; 16.7% had completed graduate studies, 61.1% had finished college or university, 13.3% had completed some college or technical training, and 7.8% had completed high school. Family income ranged from $20,000 to over $100,000 with 7.8% reporting family incomes less than $50,000, 35.6% of the mothers reporting incomes less than $70,000, and 56.6% of the other reporting family incomes greater than $70,000. On average, the sample was well educated and moderately well off.

2.2. Measures

Early life experiences were assessed using an amended version of the Life History Calendar (Caspi et al., 1996) and the Childhood Trauma Questionnaire (CTQ) (Bernstein and Fink, 1998; Bernstein et al., 1994, 2003). The LHC provides a visual representation of every year of the person's childhood, from birth to age 16 and the mother was asked who was living in the home. Parental separation was coded if both parents were not in the home from the mother's birth until she was 16 years old. The CTQ is a 28-item self-report questionnaire which retrospectively assesses the frequency and severity of different types of childhood abuse experiences among adolescents and adults. The CTQ demonstrates test—retest reliability with values ranging from 0.79 to 0.86 over a period of 2—4 months, suggesting it may be resistant to reporting biases due to transient mood states (Bernstein et al., 1994, 1997; Bernstein and Fink, 1998; Paivio and Cramer, 2004), and convergent validity with a clinician-rated interview of childhood abuse and therapists' ratings of abuse (Bernstein and Fink, 1998). To control for the impact of symptoms of depression and anxiety on HPA axis function, we administered the Edinburgh postnatal depression scale (EPDS; Cox et al., 1987), the Montgomery-Asberg depression rating scale (MADRS; Montgomery and Åsberg, 1979) and the Hamilton anxiety scale (HAM-A; Hamilton, 1959); all instruments have been shown to have good reliability and to be valid measures of maternal depression and anxiety. Information was also obtained using a daily diary on smoking habits and use of medication to control for possible confounds. To examine demographic variables as potential covariates in our analyses, we added the following variables as dummy variables, (a) parity (i.e., primiparous versus multiparous) and (b) feeding status (i.e., breast feeding versus bottle feeding). In addition, basic demographic information was obtained on maternal age, education level (ranging from 'did not complete high school' to 'post-secondary degree'), and household income. To obtain an indicator of SES, family income was divided into seven categories ranging in increments from the lowest (i.e. less than $10,000) to the highest (i.e. $100,000 or more) income categories.

2.3. Salivary cortisol sampling

To establish the cortisol awakening response, maternal salivary cortisol samples were obtained at awakening and 30-min after awakening over two consecutive days. Two awakening samples were chosen to minimize the burden on mothers since subjects were explicitly instructed to refrain from feeding their infants during this time period. A third collection at 60-min would have been problematic with infant feeding restrictions. Previous research has demonstrated that the net cortisol awakening increase between time of awakening and 30-min after awakening is sensitive to group differences (Pruessner et al., 1999; Meinlschmidt and Heim, 2005). Sample values of awakening cortisol were excluded if the reported collection time was greater than 10-min from waking.

To measure the diurnal cortisol rhythm, a series of samples were collected after awakening at 0800 h, 0830 h, 1000 h, 1600 h, 1800 h, and 2100 h. Samples were collected over two

consecutive days using salivettes during the course of the subjects' normal daytime activity. All subjects were provided with detailed verbal explanations of the procedure for sample collections. They were given a study pack that consisted of full standardized written instructions with a schedule and 16 saliva sampling tubes with labels (salivettes, Sarstedt Canada, Inc., St. Laurent, Quebec). Given that numerous substances affect cortisol (Kirschbaum and Hellhammer, 1989, 1994), subjects were asked to refrain from brushing their teeth, smoking, eating, and drinking 60-min before taking each sample. In addition, previous research has demonstrated that salivary cortisol levels decrease within 15 min after an acute breastfeeding bout (Amico et al., 1994); thus, all women were instructed to collect their samples either before breastfeeding their infant or to wait 1 h after feeding before collecting the sample. Those that did not comply with the protocol were not included in subsequent analyses.

2.4. Cortisol assay

Samples were stored in the subject's home freezer until they were transferred to the laboratory and frozen at −20 °C until assayed. On the day of the assay, salivettes were centrifuged for 10 min, at 3000 rpm at 4 °C. All samples were assayed in duplicate using a high sensitivity salivary cortisol enzyme immunoassay kit (Salimetrics, State College, PA) for quantitative measurement of salivary cortisol. Samples from each participant were assayed in the same batch. The interassay variability was 10.6%; the intra-assay variation was 8.3%, for low values, 6.9% for samples with high values.

2.5. Statistical analysis

To assess the cumulative impact of adverse early life experiences (ELE) on HPA axis function, three groups were created. Using the standard cut-offs in the CTQ manual (none-minimal = 0, low-extreme = 1) and the inconsistent care measure on the LHC (consistent care = 0, inconsistent care = 1), women were stratified into one of three groups of early life adversity. Women were classified as having experienced both maltreatment and inconsistent care (n = 18), as either having experienced one form of early adversity or the other (n = 36), or has having experienced neither adversity (n = 36). Demographic data and scores on the mood measures were compared between ELE groups using one-way analyses of variance (ANOVA; maternal and infant age, EPDS, MADRS, HAM-A) and Chi-square tests (parity, breastfeeding status, education and household income).

Using raw cortisol values, the means and standard deviations were calculated for each of the cortisol samples, and data were excluded if values were greater than three standard deviations from the mean. Both log and square-root transformations were applied to correct the positive skew in the cortisol data; we present the square-root transformed data as this transformation provided the best correction. As mentioned above, there are various approaches to statistically examine the pattern of HPA axis activity and its relations to maternal reports of early life experience. Analyses are divided into two components: (1) cortisol awakening response, which constitutes the first two samples taken (awakening, 30-min after awakening) and (2) the diurnal cortisol pattern, six samples taken at specific time points between 0800 h and 2100 h across 2 days.

In preliminary analyses, the ten potential covariates (EPDS, MADRS, HAM-A, parity, feeding status, household income, education, waking time, baby's age and subject's age) were entered into repeated-measures ANOVAs for separate analyses, with cortisol sampling time (cortisol awakening response, diurnal cortisol on day 1 and day 2) as the within-subjects factor and ELE group as the between-subjects factor. In the primary analyses, differences between the ELE groups on the cortisol awakening response were analyzed using a repeated-measures ANOVA, with the awakening values as the within-subject factor and the mother's early life events (none, one, both) as the between-subject factor. Diurnal cortisol was examined in two ways, (a) using repeated-measure ANCOVAs for each day with sample time (0800—2100) as the within-subject factor and ELE as the between-subject factor and wake time as a covariate, and (b) calculation of area under the curve with respect to ground (AUC_G) of diurnal cortisol secretion using the mean of the 2 days of sampling, wake time as a covariate. The AUC provides information about overall levels of cortisol and was calculated using the trapezoidal method (see Pruessner et al., 2003). To account for variability in awakening times, wake time was covaried from the AUC values for each day and the residual was used in the analyses. MANOVAs were used to compare the CAR and AUC_G between the three ELE groups. For relevant analyses, significant interactions were analyzed further using Tukey's post hoc comparisons. All significant ($p < .05$) and near significant ($p < .10$) results are reported to allow for a comprehensive review of patterns in the data.

3. Results

3.1. Early life experience, demographics and psychological variables

Table 1 illustrates the percent of women endorsing exposure to different maltreatment types and severity of abuse using the standard cut-offs in the CTQ manual (see Bernstein et al., 1994). The majority of women did not experience any type of maltreatment, with over 70% reporting 'none-minimal' across the five subscales.

With respect to the Life History Calendar, 66.7% of participants reported consistent care, living with both biological parents throughout childhood and adolescence.

There were no significant differences between the three stratified ELE groups with respect to age, parity, breastfeeding status, education, household income, depression (EPDS, MADRS) or anxiety (HAM-A), see Table 2. The means for the mood measures were all within the normal range.

Potential covariates were entered into an initial series of repeated-measures ANOVAs but as none were significant except for wake time on diurnal days 1 and 2, only wake time was retained in subsequent analyses of diurnal cortisol rhythms. Wake time was not a significant covariate for the CAR analysis and therefore was not retained.

Table 1 Percent of women experiencing various subtypes of maltreatment by severity

	None	Low—moderate	Moderate—severe	Severe—extreme
Emotional abuse	72.2	14.4	5.6	7.8
Physical abuse	86.7	4.4	3.3	5.6
Sexual abuse	78.9	4.4	5.6	11.1
Emotional neglect	71.1	15.6	8.9	4.4
Physical neglect	82.2	10.0	5.6	2.2

3.2. Cortisol awakening response

Twenty-nine of the ninety subjects (32.2%) were missing cortisol awakening and 30-min after awakening samples. During the initial phase of the study women were not instructed to collect awakening samples, therefore eighteen subjects did not collect the awakening samples. A total of 11 participants were excluded due to aberrant collection on both days. For the remaining participants, values from one compliant day was used or the mean of two compliant days was calculated (n = 61). Using a repeated-measures ANOVA, 3 (ELE group) $\times$ 2 (awakening, 30-min after awakening cortisol values), we found a tendency towards an ELE group difference, (F (2, 57) = 2.77, p = .07), with both early life adversity groups exhibiting higher cortisol values at both awakening and 30-min after awakening (see Fig. 1). There was a tendency for a main effect for time (F (1, 57) = 3.36, p = .07), with all groups showing an increase between awakening and 30-min after awakening.

3.3. Diurnal cortisol

Each of the 2 days of sampling were analyzed separately, comparing the 3 ELE groups using a repeated-measures ANCOVA for each day with wake time as a covariate. As shown in Fig. 2a, on day 1 there is a main effect for time (F (1, 86) = 5.98, $p < .05$) and early life experience (F (2, 86) = 3.15, $p < .05$). As shown in Fig. 2b, on day 2 there is a significant main effect for time (F (1, 86) = 5.51, $p < .05$); the time $\times$ group interaction approached significance (F (2, 86) = 2.77, p = .07). On day 2, there was no significant main effect for ELE group. All women showed a typical diurnal decline over the course of the day. Abstracting from both figures, there appears to be a tendency for women with one or both types of ELE to remain higher in the morning with all groups converging in the evening. A posteriori analyses

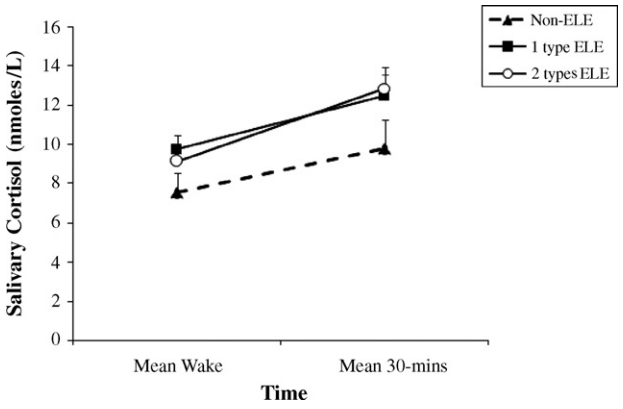

Figure 1 Cortisol awakening response (mean + S.E.M.) at 0 and 30 min after awakening in women with no adverse early life experience (non-ELE; N = 25), with one type of adverse early life experience (1 type ELE; N = 23) and 2 types of adverse early life experiences (2 types ELE; N = 16), p = .07.

revealed that the ELE group with both types of early adversity differed significantly from the ELE group experiencing one type of early adversity and the non-ELE group for the 0830 h and 1000 h samples on day 1 and from the non-ELE group at the 1600 h sample. On day 2, the two ELE groups differed significantly from the non-ELE group for the 0830 sample ($p < .05$, Tukey's post hoc comparison). When comparing the 2 days, as illustrated in Fig. 2a—b, there is consistency of salivary cortisol levels over the diurnal cycle in all groups of women. However, examining the figures visually, it appears that women in the ELE group experiencing both types of early adversity exhibit more variation across the days, especially in the morning.

Total hormonal output (AUC_G) for diurnal cortisol profile was calculated separately for days 1 and 2 with wake time as a covariate for each day. The mean of both days was also computed. Univariate tests revealed a significant main effect of ELE on day 1 (F (2, 89) = 3.30, $p < .05$), but not on day 2, (F (2, 89) = 1.64, p = .20), with the combined early adversity group demonstrating greater AUC_G on day 1 and slightly lower AUC_G on day 2 when compared to the single ELE group. There was no significant main effect on the mean AUC_G between ELE groups, although there was a trend towards higher AUC_G in the ELE group with both types of adversity.

Based on the diurnal cortisol profile findings across days 1 and 2, and the AUC_G findings, it appeared that ELE groups exhibit different patterns of cortisol secretion across the 2

Table 2 Description of demographics and psychological characteristics of all subjects and subgroups stratified by early life experience

Demographics mean (S.D.)	All subjects (N = 90)	No ELE (N = 36)	One type of ELE (N = 36)	Both types of ELE (N = 18)	Statistics
Maternal age	31.8 (4.1)	31.7 (3.8)	32.4 (4.6)	30.9 (3.3)	NS
% Married/common-law	98.9%	100%	100%	83.3%	NS
% Primiparous	71.1%	75%	66.75	72.2%	NS
% Breastfeeding	80.0%	77.8%	75.0%	94.4%	NS
EPDS score	5.83 (3.90)	5.56 (4.24)	6.28 (3.38)	5.50 (3.29)	NS
MADRS score	3.84 (4.16)	3.64 (4.30)	4.19 (4.88)	3.56 (3.53)	NS
HAM-A score	4.18 (3.29)	3.78 (2.89)	4.64 (3.90)	4.06 (2.76)	NS

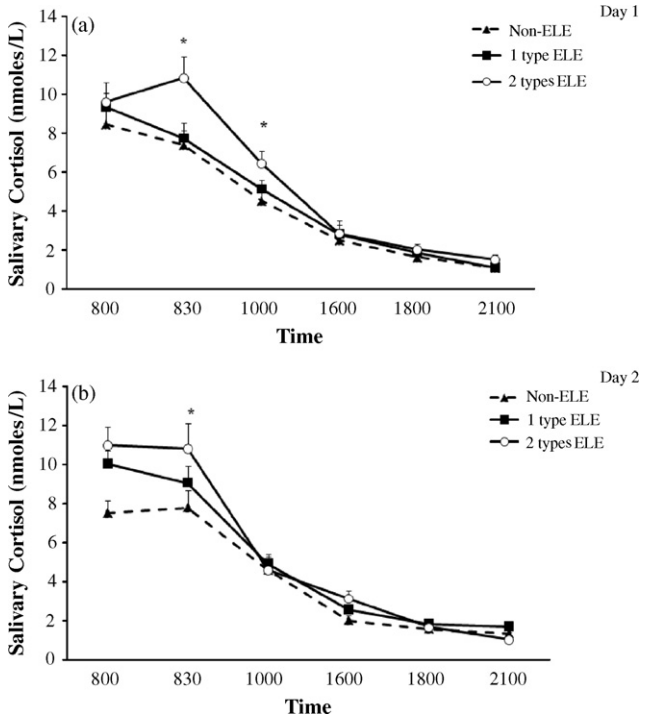

Figure 2 (a) Diurnal cortisol concentrations on Day 1 in women with no adverse early life experience (non-ELE; $N = 36$), with one type of adverse early life experience (1 type ELE; $N = 36$) and 2 types of adverse early life experiences (2 types ELE; N = 18). *$p < .05$, 2 types ELE > 1 type ELE and non-ELE. (b) Diurnal cortisol concentrations on Day 2 in women with no adverse early life experience (non-ELE; $N = 36$), with one type of adverse early life experience (1 type ELE; $N = 36$) and 2 types of adverse early life experiences (2 types ELE; $N = 18$). *$p < .05$, 2 and 1 type ELE > non-ELE.

days whereas the non-ELE group maintain a fairly consistent profile across the two sampling days.

To evaluate the heterogeneity of cortisol secretion across the 2 days between ELE groups, we compared the AUC_G of days 1 and 2 between groups with wake time controlled for, using a repeated-measures ANOVA. This analysis revealed

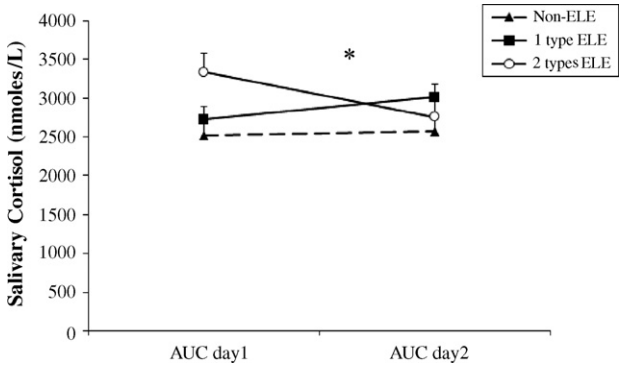

Figure 3 Diurnal cortisol secretion, area under the curve (AUC) on days 1 and 2 in women with no adverse early life experience (non-ELE; $N = 36$), with one type of adverse early life experience (1 type ELE; $N = 36$) and 2 types of adverse early life experiences (2 types ELE; $N = 18$). *Time × ELE group, $p < .01$.

a significant time x group interaction (F (2, 87) = 5.27, $p < .01$) (Fig. 3). Women with no early adversity exhibited stable and consistent AUCs across both days, whereas women experiencing both types of early adversity or one type of adversity exhibited either a decline (2 ELE group) or increase (1 ELE group) in AUC values across the 2 days. This suggests heterogeneity in diurnal cortisol patterns amongst women with some form of early adversity.

4. Discussion

To our knowledge, this is the first study to support the hypothesis that early life experiences (inconsistent care and history of childhood maltreatment) are associated with the awakening cortisol response and diurnal cortisol profile in a community sample of postpartum women. Overall, early life adversity was associated with higher levels of awakening cortisol and sustained, elevated levels of cortisol in the morning. Women who reported experiencing a combination of inconsistent care and maltreatment exhibited higher levels of diurnal cortisol in the morning compared to subjects who experienced one form of early adversity or who reported no early adversity. The discrepancy in morning samples between early adversity groups is most evident on the first day of sampling; whereas on the second day both early adversity groups exhibit higher levels of morning cortisol compared to women who reported no early adversity. This suggests that there may be more variability in diurnal cortisol values in women who experienced some form of early adversity. This hypothesis is partially supported when we examined total hormonal output (area under the curve) across both days. Women who did not experience early adversity were consistent across both days, whereas women with one type or combined adversity exhibited variability across 2 days. At this point it is difficult to ascertain the source of variability between days in the early adversity groups although it is possible that it reflects a hyperresponsive HPA axis to daily stressors and events. Nonetheless, these findings imply that early adversity may be associated with variations in HPA axis function.

Studies examining the relation of early adversity and diurnal cortisol in non-human primates and in maltreated children have demonstrated inconsistent results (Kaufman, 1991; Boyce et al., 1995; Hart et al., 1996; Carlson and Earls, 1997; De Bellis et al., 1999; Cicchetti and Rogosch, 2001; Gunnar et al., 2001; Sánchez et al., 2005; Dozier et al., 2006). Our findings are in accordance with studies suggesting that early adversity may be associated with a hypercortisolism profile in adult postpartum women. Presently we do not know whether the relation between early adversity and diurnal cortisol are unique to the postpartum period. However, a study in adult men suggests that these findings may not be exclusive to the postpartum period. Nicolson (2004) found that men who experienced parental loss during childhood had significant elevations in salivary cortisol throughout the day, with the most notable difference evident in the morning. Further research is required to examine these relations later in the postpartum period and in a sample of non-postpartum women.

In a recent meta-analysis Miller et al. (2007) investigated the relation between chronic stress and HPA axis function,

finding the most common profile associated with chronic stress resembles a hypocortisolemic profile (Miller et al., 2007). Interestingly, the pattern of HPA axis activation depends on a number of features related to the stressor and the individual experiencing the stress (Miller et al., 2007). For example, high levels of cortisol were related to the continued presence of the chronic stressor in the environment and stressors posing a threat to the social self (i.e. divorce) (Miller et al., 2007). Similarly, the presence of daily life stressors have been associated with increased diurnal cortisol levels when accompanied by increased negative affect and agitation (Smyth et al., 1997; Jacobs et al., 2007). Ongoing stressors tend to have larger effects on cortisol than stressors that have recently been terminated (van Eck et al., 1996; Smyth et al., 1997). It is possible that women who experienced early adversity may be more susceptible to daily stressors, increasing negative affect and fluctuations in diurnal cortisol levels. Caring for an infant may be construed as stressful at times and mothers who perceive daily hassles negatively may show elevated cortisol levels in response to pressures around infant care. Unfortunately, daily hassles or affect fluctuations on cortisol sampling days were not assessed in this study.

The mechanisms through which early adverse experiences exert their effects on HPA axis function are not yet fully elucidated. Heim et al. (2000a,b) proposed a model to account for the phenomenon of hypocortisolism in relation to trauma and early adversity (Heim et al., 2000a,b). They suggest that dysregulation can occur at several levels of the HPA axis (see Heim et al., 2000a,b). This model cannot account for our findings given that early life adversity was associated with a profile suggestive of hypercortisolism. This hypersecretion of morning cortisol may instead be related to reduced negative feedback regulation due to impaired glucocorticoid receptor function (van Haarst et al., 1996; Young, 2004). Support for this hypothesis is derived from animal research. In rats, offspring of low-licking/grooming mothers exhibited increased levels of corticosterone and ACTH during the circadian peak in adulthood, mimicking a hypercortisolism profile (Diorio and Meaney, 2007). A similar enhancement of corticosterone during the circadian peak was demonstrated after GR receptor blockade for 3—4 days, presumably via increased adrenocortical sensitivity to ACTH (van Haarst et al., 1996). Although highly speculative in nature, it is possible that differences in diurnal cortisol in relation to early adversity may be due to alterations in glucocorticoid receptors and reduced negative feedback thus resulting in elevated morning levels of cortisol.

In a smaller subset of the sample we found associations between higher awakening and 30-min after awakening values and early adversity. Despite the slightly higher levels of both awakening measures, differences between groups did not reach statistical significance. These findings are in line with a study of Romanian orphans (Gunnar et al., 2001). In contrast to our findings, the only other study examining the relation between early adversity and CAR in adults demonstrated lower levels amongst individuals who had experienced loss of a relative and parental divorce or separation (Meinlschmidt and Heim, 2005). This effect was most pronounced in those who experienced a combination of losses; those who experienced only parental separation or divorce were not significantly different from the group that experienced no early adversity. Presently, it is difficult to ascertain the reason for the different profiles in awakening associated with early loss and adversity. Potential factors may include the nature, duration and severity of early adversity. We did not assess the source of parental inconsistency in our sample; therefore, it is unknown whether the loss was due to parental death or from parental separation/divorce. Future studies need to address a spectrum of factors related to early adversity in relation to HPA axis functioning.

High levels of awakening cortisol have been associated with persistent anxiety problems in children (Greaves-Lord et al., 2007), high levels of perceived stress (Pruessner et al., 1999), feelings of loneliness, sadness, and lack of control the day prior to sampling (Adam et al., 2006), and burnout (Grossi et al., 2006) in adults. Levels of depression and anxiety were unrelated to awakening cortisol values in our sample; however, as highlighted above, women with early adversity may be more susceptible to fluctuations in daily stressors, fatigue and feelings of isolation. These factors are sometimes reported in mothers during the postpartum period, especially in women with postpartum mood disorders (Ross et al., 2004; Ross and McLean, 2006; Lonstein, 2007; Meltzer and Mindell, 2007) and may represent possible risk factors for mothers during the postpartum period. The majority of mothers in our sample did not meet the clinical cut-off for postpartum mood disorders. Symptoms associated with postpartum depression typically emerge within the first 3 months postpartum and decrease over the course of the first year. While we recruited women from 2 to 6 months postpartum, most participants were 4—6 months postpartum; therefore we may have assessed women when symptoms were no longer present or they were occurring below the clinical threshold.

A secondary aim of the study was to examine feeding status and parity in relation to HPA axis functioning. Not surprisingly, there were no differences in parity or feeding choice associated with early life adversity. In accordance with other research (Tu et al., 2005; Federenko et al., 2006), we did not find any parity or feeding status differences in awakening cortisol values. In contrast to previous work (Tu et al., 2006), we did not find any parity or feeding status differences in diurnal cortisol. In this study, primiparous and multiparous mothers exhibited a similar diurnal cortisol profile. Discrepant findings may be due to measurement procedures; cortisol samples were collected at different times of day across studies. Moreover, a significant proportion of our subjects were primiparous mothers (71%) and breast feeding (80%) and a non-postpartum group comparison group was not included.

There are several potential limitations associated with the current study. First, retrospective reporting of early life experiences are plagued with various concerns and qualifiers. Retrospective reports are subject to memory inaccuracies and biases (Hardt and Rutter, 2004; Widom et al., 2004), although there is little evidence to support the claim that recall of childhood experiences is altered by psychopathology (Brewin et al., 1993). Retrospective reports are more susceptible to false negative reports, with estimates around 30%, and false positive reports are fairly rare in the literature (Hardt and Rutter, 2004). In this study, we have no direct means of corroborating reports of early life experiences. However, we included two well-established measures of early experience. Our estimates of the prevalence of childhood

maltreatment across all abuse categories are comparable to, or slightly lower than, estimates from other Ontario and Canadian community samples (MacMillan et al., 2000; Trocmé et al., 2003; Paivio and Cramer, 2004). This suggests that prevalence of maltreatment in our sample may be more likely to reflect biases of under-reporting rather than over-reporting. In addition, our measures of early adversity were limited and did not include specific details of adversity.

A second limitation is our reliance on participants collecting salivary samples at set times in their homes. Prior research has noted poor compliance with salivary collection protocols (Kudielka et al., 2003). In order to improve protocol adherence, we provided participants with a set of instructions and requested participants to record the exact collection time. In addition, participants who were unable to adhere to the protocol were excluded from the study. Nevertheless, we must recognize that variability in diurnal levels may be due to deviations from the protocol. A third limitation was the collection of only two awakening samples for the cortisol awakening response. We were attempting to minimize the burden of samples on the participants but two samples does not allow for full CAR analyses. Future studies should incorporate multiple awakening samples.

Finally, we did not control for menstrual cycle or sleep characteristics (quality and length of sleep and number of disruptions) on sampling days. Previous studies have not found differences in awakening cortisol between follicular and luteal phases and only small, if any, differences in cortisol diurnal profiles between the two menstrual phases (Kirschbaum et al., 1999; Stewart et al., 1993). Moreover, no differences have been found between follicular or luteal phases on the mean cortisol values or acrophase of the cortisol rhythm (Shibui et al., 2000). Findings in the literature have been inconsistent with respect to the effect of sleep characteristics on morning cortisol values. Some studies have found that quality of sleep (Wust et al., 2000) and interrupted sleep through repeated nightly forced waking (Dettenborn et al., 2007) does not affect morning cortisol values. In contrast, another study demonstrated that subjective reports of lower sleep quality and a higher frequency of nightly waking were correlated with lower cortisol awakening values (Backhaus et al., 2004). To our knowledge, no studies have examined the relation of sleep characteristics on diurnal cortisol in a healthy sample of females.

The relationship between early life adversity and HPA axis activity is complex, with many contradictory findings. Overall, the association between early adversity and HPA axis regulation is not well understood and controversial. Most studies in adulthood focus on experimental manipulations and stress reactivity, with only a limited number examining diurnal patterns. Our study demonstrates that in a sample of postpartum women, early childhood adversity may be associated with higher levels of awakening cortisol which are sustained throughout the morning and then decrease with the expected diurnal decline over the course of the afternoon and evening. Although these findings require confirmation, this suggests that childhood adversity may have a long-lasting impact on HPA axis function even in the absence of psychopathology. Further research needs to be conducted to determine whether these findings are applicable in higher risk populations of women who experienced more severe early life adversity.

In a broader context, it is not known if high levels of glucocorticoids impact the mother—infant dyad or how they may influence maternal behavior in humans. In infants, higher cortisol levels have been associated with less sensitive caregiving in the context of daycare (Dettling et al., 2000) and with insecure attachment (Gunnar et al., 1996; Spangler and Schieche, 1998). Animal models illustrate the causal relation between maternal HPA axis function, maternal caregiving and subsequent development in the offspring (Meaney, 2001; Fleming et al., 2002). Further research is needed to identify the impact of maternal HPA axis dysregulation on mother—infant interactions and infant development.

Role of funding source

Funding for this study was provided by the Canadian Institutes of Health Research (CIHR) to A.S. Fleming (PI) and J.M. Jenkins and M. Steiner (co-PIs); CIHR had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

Conflict of interest

Dr. Steiner is a consultant for GlaxoSmithKline, Wyeth Pharmaceuticals, Bayer Shering Pharmaceuticals, Astra-Zeneca, and Azevan Pharmaceuticals; receives honorarium from Azevan Pharmaceuticals, and Ortho-McNeil and currently receives grant support from Wyeth, GlaxoSmithKline, and AstraZeneca. There are no conflicts of interest for the other authors.

Acknowledgments

We would like to thank Jennifer Giardino for her assistance with recruitment and testing, as well as Margaret Coote for her assistance and technical support with the salivary cortisol assay.

References

Adam, E.K., Gunnar, M.R., 2001. Relationship functioning and home and work demands predict individual differences in diurnal cortisol patterns in women. Psychoneuroendocrinology 26, 189—208.

Adam, E.K., Hawkley, L.C., Kudielka, B.M., Cacioppo, J.T., 2006. Day-to-day dynamics of experience—cortisol associations in a population-based sample of older adults. Proc. Natl. Acad. Sci. 103, 17058—17063.

Amico, J.A., Johnston, J.M., Vagnucci, A.H., 1994. Suckling-induced attenuation of plasma cortisol concentrations in postpartum lactating women. Endocr. Res. 20, 79—87.

Anda, R.F., Felitti, V.J., Bremner, J.D., Walker, J.D., Whitfield, C., Perry, B.D., Dube, S.R., Giles, W.H., 2006. The enduring effects of abuse and related adverse experiences in childhood. A convergence of evidence from neurobiology and epidemiology. Eur. Arch. Psychiatry Clin. Neurosci. 256, 174—186.

Backhaus, J., Junganns, K., Hoghagen, F., 2004. Sleep disturbances are correlated with decreased morning awakening salivary cortisol. Psychoneuroendocrinology 29, 1184—1191.

Beck, C.T., 2001. Predictors of postpartum depression: an update. Nurs. Res. 50, 275—285.

Belsky, J., Pensky, E., 1988. Marital change across the transition to parenthood. Marriage Fam. Rev. 12, 133—156.

Bernstein, D.P., Fink, L., Handelsman, L., Foote, J., Lovejoy, M., Wenzel, K., Sapareto, E., Ruggiero, J., 1994. Initial reliability and validity of a new retrospective measure of child abuse and neglect. Am. J. Psychiatry 151, 1132—1136.

Bernstein, D.P., Ahluvalia, T., Pogge, D., Handelsman, L., 1997. Validity of the Childhood Trauma Questionnaire in an adolescent psychiatric population. J. Am. Acad. Child Adolesc. Psychiatry 36, 340—348.

Bernstein, D., Fink, L., 1998. Manual for the Childhood Trauma Questionnaire. The Psychological Corporation, New York.

Bernstein, D.P., Stein, J.A., Newcomb, M.D., Walker, E., Pogge, D., Ahluvalia, T., Stokes, J., Handelsman, L., Medrano, M., Desmond, D., Zule, W., 2003. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse Negl. 27, 169—190.

Boyce, W.T., Champoux, M., Suomi, S.J., Gunnar, M.R., 1995. Salivary cortisol in nursery-reared rhesus monkeys: reactivity to peer interactions and altered circadian activity. Dev. Psychobiol. 28, 257—267.

Brewin, C.R., Andrews, B., Gotlib, I.H., 1993. Psychopathology and early experience: a reappraisal of retrospective reports. Psychol. Bull. 113, 82—98.

Carlson, M., Earls, F., 1997. Psychological and neuroendocrinological sequelae of early social deprivation in institutionalized children in Romania. Ann. N. Y. Acad. Sci. 807, 419—428.

Carrion, V.G., Weems, C.F., Ray, R.D., Glaser, B., Hessl, D., Reiss, A.L., 2002. Diurnal salivary cortisol in pediatric posttraumatic stress disorder. Biol. Psychiatry 51, 575—582.

Caspi, A., Moffitt, T.E., Thorton, A., Freedman, D., Amell, J.W., Harrington, H., Smeijers, J., Silva, P.A., 1996. The Life History Calendar: a research and clinical assessment method for collecting retrospective event-history data. Int. J. Methods Psychiatry Res. 6, 101—114.

Chrousos, G.P., 1998. Stressors, stress, and neuroendocrine integration of the adaptive response. The 1997 Hans Selye Memorial Lecture. Ann. N. Y. Acad. Sci 851, 311—335.

Cicchetti, D., Rogosch, F.A., 2001. Diverse patterns of neuroendocrine activity in maltreated children. Dev. Psychopathol. 13, 677—693.

Clow, A., Thorn, L., Evans, P., Hucklebridge, F., 2004. The awakening cortisol response: methodological issues and significance. Stress 7, 29—37.

Cohen, S., Doyle, W.J., Baum, A., 2006. Socioeconomic status is associated with stress hormones. Psychosom. Med. 68, 414—420.

Corter, C.M., Fleming, A.S., 2002. Psychobiology of maternal behavior in human beings. In: Bornstein, M.H. (Ed.), Handbook of Parenting: Biology and Ecology of Parenting, vol. 2. Lawrence Erlbaum Associates, New Jersey, pp. 141—185.

Cox, J.L., Holden, J.M., Sagovsky, R., 1987. Detection of postnatal depression: development of the 10-item Edinburgh Postnatal Depression Scale. Br. J. Psychiatry 150, 782—786.

De Bellis, M.D., Baum, A.S., Birmaher, B., Keshavan, M.S., Eccard, C.H., Boring, A.M., Jenkins, F.J., Ryan, N.D., 1999. Developmental traumatology. Part I: Biological stress systems. Biol. Psychiatry 45, 1259—1270.

Dettling, A.C., Parker, S.W., Lane, S., Sebanc, A., Gunnar, M.R., 2000. Quality of care and temperament determine changes in cortisol concentrations over the day for young children in childcare. Psychoneuroendocrinology 25, 819—836.

Dettenborn, L., Rosenloecher, F., Kirschbaum, C., 2007. No effects of repeated forced waking during three consecutive nights on morning cortisol awakening response (CAR): a preliminary study. Psychoneuroendocrinology 32, 915—921.

Diorio, J., Meaney, M.J., 2007. Maternal programming of defensive responses through sustained effects on gene expression. J. Psychiatry Neurosci. 32, 275—284.

Doman, J., Thompson, S., Grochocinksi, V., Jarrett, D., Kupfer, D.J., 1986. A computer algorithm to determine the nadir and rise time in nocturnal cortisol secretion. Psychoneuroendocrinology 11, 359—366.

Dong, M., Anda, R.F., Felitti, V.J., Dube, S.R., Williamson, D.F., Thompson, T.J., Loo, C.M., Giles, W.H., 2004. The interrelatedness of multiple forms of childhood abuse, neglect, and household dysfunction. Child Abuse Negl. 28, 771—784.

Dozier, M., Manni, M., Gordon, M.K., Peloso, E., Gunnar, M.R., Stovall-McClough, K.C., Eldreth, D., Levine, S., 2006. Foster children's diurnal production of cortisol: an exploratory study. Child Maltreat. 11, 189—197.

Federenko, I.S., Wolf, J.M., Wüst, S., Schlotz, W., Hellhammer, J., Kudielka, B.M., Kirschbaum, C., Hellhammer, D.H., Wadhwa, P.D., 2006. Parity does not alter baseline or stimulated activity of the hypothalamus—pituitary—adrenal axis in women. Dev. Psychobiol. 48, 703—711.

Felitti, V.J., Anda, R.F., Nordenberg, D., Williamson, D.F., Spitz, A.M., Edwards, V., Koss, M.P., Marks, J.S., 1998. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. Am. J. Prev. Med. 14, 245—258.

Fleming, A.S., Kraemer, G.W., Gonzalez, A., Lovic, V., Rees, S., Melo, A., 2002. Mothering begets mothering: the transmission of behavior and its neurobiology across generations. Pharmacol. Biochem. Behav. 73, 61—75.

Forehand, R., Biggar, H., Kotchick, B.A., 1998. Cumulative risk across family stressors: short- and long-term effects for adolescents. J. Abnorm. Child Psychol. 26, 119—128.

Greaves-Lord, K., Ferdinand, R.F., Oldehinkel, A.J., Sondeijker, F.E., Ormel, J., Verhulst, F.C., 2007. Higher cortisol awakening response in young adolescents with persistent anxiety problems. Acta Psychiatry Scand. 116, 137—144.

Grossi, G., Perski, A., Ekstedt, M., Johansson, T., Lindström, M., Holm, K., 2006. The morning salivary cortisol response in burnout. J. Psychosom. Res. 59, 103—111.

Gunnar, M.R., Brodersen, L., Nachimas, M., Buss, K., Rigatuso, J., 1996. Stress reactivity and attachment security. Dev. Psychobiol. 29, 191—204.

Gunnar, M.R., Morison, S.J., Chisholm, K., Schuder, M., 2001. Salivary cortisol levels in children adopted from Romanian orphanages. Dev. Psychopathol. 13, 611—628.

Gunnar, M., Quevedo, K., 2007. The neurobiology of stress and development. Annu. Rev. Psychol. 58, 145—173.

Hamilton, M.C., 1959. The assessment of anxiety states by rating. Br. J. Med. Psychol. 32, 50—55.

Hardt, J., Rutter, M., 2004. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. J. Child Psychol. Psychiatry 45, 260—273.

Hart, J., Gunnar, M.R., Cicchetti, D., 1996. Altered neuroendocrine activity in maltreated children related to symptoms of depression. Dev. Psychopathol. 8, 201—214.

Heim, C., Ehlert, U., Hellhammer, D.H., 2000a. The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. Psychoneuroendocrinology 25, 1—35.

Heim, C., Newport, D.J., Heit, S., Graham, Y.P., Wilcox, M., Bonsall, R., Miller, A.H., Nemeroff, C.B., 2000b. Pituitary—adrenal and autonomic responses to stress in women after sexual and physical abuse in childhood. JAMA 284, 592—597.

Heim, C., Nemeroff, C.B., 2001. The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. Biol. Psychiatry 49, 1023—1039.

Heim, C., Newport, D.J., Bonsall, R., Miller, A.H., Nemeroff, C.B., 2001. Altered pituitary—adrenal axis responses to provocative challenge tests in adult survivors of childhood abuse. Am. J. Psychiatry 158, 575—581.

Heim, C., Newport, D.J., Wagner, D., Wilcox, M.M., Miller, A.H., Nemeroff, C.B., 2002. The role of early adverse experience and adulthood stress in the prediction of neuroendocrine stress reac-

tivity in women: a multiple regression analysis. Depress. Anxiety 15, 117—125.
Heim, C., Meinlschmidt, G., Nemeroff, C.B., 2003. Neurobiology of early-life stress. Psych. Ann. 33, 1—10.
Heim, C., Plotsky, P.M., Nemeroff, C.B., 2004. Importance of studying the contributions of early adverse experience to neurobiological findings in depression. Neuropsychopharmacology 29, 641—648.
Hucklebridge, F., Hussain, T., Evans, P., Clow, A., 2005. The diurnal patterns of the adrenal steroids cortisol and dehydroepiandrosterone (DHEA) in relation to awakening. Psychoneuroendocrinology 30, 51—57.
Jacobs, N., Myin-Germeys, I., Derom, C., Delespaul, P., van Os, J., Nicolson, N.A., 2007. A momentary assessment study of the relationship between affective and adrenocortical stress responses in daily life. Biol. Psychol. 74, 60—66.
Kaufman, J., 1991. Depressive disorders in maltreated children. J. Am. Acad. Child Adolesc. Psychiatry 30, 257—265.
Kirschbaum, C., Hellhammer, D.H., 1994. Salivary cortisol in neuroendocrine research: recent development and applications. Psychoneuroendocrinology 19, 313—333.
Kirschbaum, C., Hellhammer, D.H., 1989. Salivary cortisol in psychobiological research: an overview. Neuropsychobiology 22, 150—169.
Kirschbaum, C., Kudielka, B.M., Gaab, J., Schommer, N., Hellhammer, D.H., 1999. Impact of gender, menstrual cycle phase, and oral contraceptives on the activity of the hypothalamus—pituitary—adrenal axis. Psychosom. Med. 61, 154—162.
Kudielka, B.M., Broderick, J.E., Kirschbaum, C., 2003. Compliance with saliva sampling protocols: electronic monitoring reveals invalid cortisol daytime profiles in noncompliant subjects. Psychosom. Med. 65, 313—319.
Ladd, C.O., Huot, R.L., Thrivikraman, K.V., Nemeroff, C.B., Meaney, M.J., Plotsky, P.M., 2000. Long-term behavioral and neuroendocrine adaptations to adverse early experience. Prog. Brain Res. 122, 81—103.
Liu, D., Caldji, C., Sharma, S., Plotsky, P.M., Meaney, M.J., 2000. Influence of neonatal rearing conditions on stress-induced adrenocorticotropin responses and norepinepherine release in the hypothalamic paraventricular nucleus. J. Neuroendocrinol. 12, 5—12.
Lonstein, J.S., 2007. Regulation of anxiety during the postpartum period. Front. Neuroendocrinol. 28, 115—141.
López, J.F., Akil, H., Watson, S.J., 1999. Neural circuits mediating stress. Biol. Psychiatry 46, 1461—1471.
Luecken, L.J., 2000. Attachment and loss experiences during childhood are associated with adult hostility, depression, and social support. J. Psychosom. Res. 49, 85—91.
Luecken, L.J., Lemery, K.S., 2004. Early caregiving and physiological stress response. Clin. Psychol. Rev. 24, 171—191.
Luecken, L.J., Appelhans, B.M., 2006. Early parental loss and salivary cortisol in young adulthood: the moderating role of family environment. Dev. Psychopathol. 18, 295—308.
MacMillan, H., Canadian Task force on Preventive Healthcare, 2000. Update: prevention of child maltreatment. CMAJ 163, 1451—1458.
Meaney, M.J., 2001. Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. Annu. Rev. Neurosci. 24, 1161—1192.
Meinlschmidt, G., Heim, C., 2005. Decreased cortisol awakening response after early loss experience. Psychoneuroendocrinology 30, 568—576.
Meltzer, L.J., Mindell, J.A., 2007. Relationship between child sleep disturbances and maternal sleep, mood, and parenting stress: a pilot study. J. Fam. Psychol. 21, 67—73.
Miller, G.E., Chen, E., Zhou, E., 2007. If it goes up, must it come down? Chronic stress and the hypothalamic—pituitary—adrenocortical axis in humans. Psychol. Bull. 133, 25—45.
Montgomery, S.A., Åsberg, M., 1979. A new depression scale designed to be sensitive to change. Br. J. Psychiatry 134, 382—389.
Nicolson, N.A., 2004. Childhood parental loss and cortisol levels in adult men. Psychoneuroendocrinology 29, 1012—1018.
Paivio, S.C., Cramer, K.M., 2004. Factor structure and reliability of the Childhood Trauma Questionnaire in a Canadian undergraduate student sample. Child Abuse Negl. 28, 889—904.
Plotsky, P.M., Meaney, M.J., 1993. Early, postnatal experience alters hypothalamic corticotropin-releasing factor (CRF) mRNA, median eminence CRF content and stress-induced release in adult rats. Brain Res. Mol. Brain Res. 18, 195—200.
Pruessner, J.C., Hellhammer, D.H., Kirschbaum, C., 1999. Burnout, perceived stress, and cortisol responses to awakening. Psychosom. Med. 61, 197—204.
Pruessner, J.C., Kirschbaum, C., Meinlschmidt, G., Hellhammer, D.H., 2003. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology 28, 916—931.
Rees, S.L., Steiner, M., Fleming, A.S., 2006. Early deprivation, but not maternal separation, attenuates rise in corticosterone levels after exposure to a novel environment in both juvenile and adult female rats. Behav. Brain Res. 175, 383—391.
Repetti, R.L., Taylor, S.E., Seeman, T.E., 2002. Risky families: family social environments and the mental and physical health of offspring. Psychol. Bull. 128, 330—366.
Ross, L.E., Sellers, E.M., Gilbert Evans, S.E., Romach, M.K., 2004. Mood changes during pregnancy and the postpartum period: development of a biopsychosocial model. Acta Psychiatry Scand. 109, 457—466.
Ross, L.E., McLean, L.M., 2006. Anxiety disorders during pregnancy and the postpartum period: a systematic review. J. Clin. Psychiatry 67, 1285—1298.
Rutter, M., 1979. Protective factors in children's responses to stress and disadvantage. In: Kent, W.M., Rolf, J.E. (Eds.), Primary Prevention of Psychopathology, vol. 3. University Press of New England, Hanover, NH, pp. 49—74.
Sanchez, M.M., Ladd, C.O., Plotsky, P.M., 2001. Early adverse experience as a developmental risk factor for later psychopathology: evidence from rodent and primate models. Dev. Psychopathol. 13, 419—449.
Sánchez, M.M., Noble, P.M., Lyon, C.K., Plotsky, P.M., Davis, M., Nemeroff, C.B., Winslow, J.T., 2005. Alterations in diurnal cortisol rhythm and acoustic startle response in nonhuman primates with adverse rearing. Biol. Psychiatry 57, 373—381.
Shibui, K., Uchiyama, M., Okawa, M., Kudo, Y., Kim, K., Liu, X., Kamei, Y., et al., 2000. Diurnal fluctuation of sleep propensity and hormonal secretion across the menstrual cycle. Biol. Psychiatry 48, 1062—1068.
Smyth, J.M., Ockenfels, M.C., Gorin, A.A., Catley, D., Porter, L.S., Kirschbaum, C., Hellhammer, D.H., Stone, A.A., 1997. Individual differences in the diurnal cycle of cortisol. Psychoneuroendocrinology 22, 89—105.
Spangler, G., Schieche, M., 1998. Emotional and adrenocortical responses of infants to the strange situation: the differential function of emotional expression. Int. J. Behav. Dev. 22, 681—707.
Stewart, P.M., Penn, R., Holder, R., Parton, A., Ratcliffe, J.G., London, D.R., 1993. The hypothalamic—pituitary—adrenal axis across the normal menstrual cycle and in polycystic ovary syndrome. Clin. Endocrinol. 38, 387—391.
Tarullo, A.R., Gunnar, M.R., 2006. Child maltreatment and the developing HPA axis. Horm. Behav. 50, 632—639.
Trocmé, N.M., Tourigny, M., MacLaurin, B., Fallon, B., 2003. Major findings from the Canadian incidence study of reported child abuse and neglect. Child Abuse Negl. 27, 1427—1439.
Tu, M., Walker, C.D., Lupien, S.J., 2005. Feeding upon awakening in breastfeeding and bottlefeeding mothers does not affect the awakening cortisol response. Stress 8, 213—216.

Tu, M.T., Lupien, S.J., Walker, C.D., 2006. Diurnal salivary cortisol levels in postpartum mothers as a function of infant feeding choice and parity. Psychoneuroendocrinology 31, 812—824.

van Eck, M., Berkhof, H., Nicolson, N., Sulon, J., 1996. The effects of perceived stress, traits, mood states, and stressful daily events on salivary cortisol. Psychosom. Med. 58, 447—458.

van Haarst, A.D., Oitzl, M.S., Workel, J.O., de Kloet, E.R., 1996. Chronic brain glucocorticoid receptor blockade enhances the rise in circadian and stress-induced pituitary—adrenal activity. Endocrinology 137, 4935—4943.

Vermetten, E., Bremner, J.D., 2002. Circuits and systems in stress. I. Preclinical studies. Depression Anxiety 15, 126—147.

Widom, C.S., Raphael, K.G., Dumont, K.A., 2004. The case for prospective longitudinal studies in child maltreatment research: commentary on Dube, Williamson, Thompson, Felitti, and Anda (2004). Child Abuse Negl. 28, 715—722.

Wust, S., Wolf, J., Hellhammer, D.H., Federenko, I., Schommer, N., Kirschbaum, C., 2000. The cortisol awakening response-normal values and confounds. Noise Health 2, 79—88.

Young, A.H., 2004. Cortisol in mood disorders. Stress 7, 205—208.