



## **EMOTION—CORTISOL TRANSACTIONS OCCUR OVER MULTIPLE TIME SCALES IN DEVELOPMENT: IMPLICATIONS FOR RESEARCH ON EMOTION AND THE DEVELOPMENT OF EMOTIONAL DISORDERS**

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In understanding the associations between emotional experience and physiological processes, time is a central variable. Most physiological processes are moving targets—they change from moment to moment and over the course of days, months, and years. Stress-sensitive physiological systems, such as the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system, are in fact *designed to change over time* in relation to changing internal and external conditions. This notion of adaptive flexibility in physiological functioning has been termed “allostasis,” in contrast to models emphasizing the importance of physiological stability or “homeostasis” (McEwen, 1998; Sterling, 2003). Adaptive changes in physiology occur both in response to, and in anticipation of, experience, with the goal of helping the body prepare for, cope with, and recover from social, emotional, and physical challenges (McEwen, 1998; Sterling, 2003).

In this chapter, I focus on the HPA axis as an allostatic system and introduce a chronometric model (see Figure 2) suggesting that HPA-axis changes (as indexed by changing salivary cortisol levels) occur in response to social and emotional experience over *multiple time courses* in development. I provide examples of research on children and adolescents showing the relevance of various time courses of cortisol change (ranging from moment-to-moment changes to changes occurring over the course of days, months, and years) for understanding individual differences in state and trait emotion and the development of emotional disorders. Using illustrations from my own research on adolescents at risk for the development of major depressive disorder (MDD), I show how a consideration of multiple time scales of cortisol change, combined with careful design, measurement, and use of multilevel analyses, can

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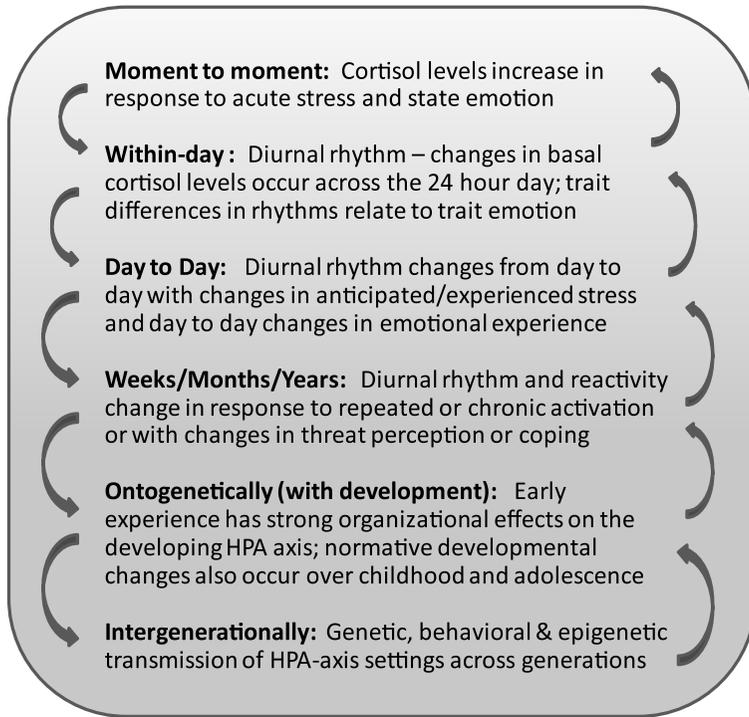


FIGURE 2.—Multiple time frames of change in the hypothalamic-pituitary-adrenal axis in relation to social and emotional experience.

reveal the subtle and dynamic interplay that occurs between emotional experience and cortisol in the course of everyday life and with development. This chapter particularly highlights the monograph themes of “time” or “time course” and “development,” illustrates other monograph themes of “context” and “specificity,” and notes how other research in this monograph fits within the chronometric model introduced herein.

#### MOMENT-TO-MOMENT CHANGES IN CORTISOL (ACUTE REACTIVITY)

The most commonly studied time scale of cortisol change is acute reactivity, in which within-person changes in cortisol in response to an acute stressor or momentary (state) emotion are measured in either laboratory (Dickerson & Kemeny, 2004; Gunnar, Talge, & Herrera, 2009) or naturalistic settings (Adam, 2006; Smyth et al., 1998; van Eck, Berkhof, Nicolson, & Sulon, 1996). As noted in Gunnar and Adam (this volume), cortisol levels

peak in saliva approximately 20–25 min poststressor, but take up to an hour to recover to prestress baseline levels. Speaking to the theme of specificity, although some studies have linked momentary negative mood states, such as worry, sadness, and anger, to acute increases in cortisol (e.g., Adam, 2006), reviews of the experimental acute reactivity literature in children, adolescents, and adults suggest that situations that pose threats to the social self are the most consistent and powerful acute activators of the HPA axis and that positive social relationships may serve as effective buffers of cortisol reactivity (Dickerson & Kemeny, 2004; Gunnar et al., 2009; Gunnar & Quevedo, 2007). Thus, social context plays a powerful role in contributing to and buffering acute cortisol reactivity, with social threat being an important ingredient for acute cortisol increase. As discussed later in this chapter, and in Gunnar and Adam (this volume), there is also some evidence that associations between state emotion and momentary cortisol change with development, with acute cortisol reactivity declining after infancy and increasing again over the transition to adolescence. Cortisol increases cannot therefore be considered a simple proxy or indicator for the presence of negative emotional states. Acute cortisol reactions are likely to occur under negative emotional conditions in which threats to the self are high, and support is low, and may change with age/developmental stage.

#### CIRCADIAN CHANGES (WITHIN-DAY CHANGES OR CORTISOL DIURNAL RHYTHMS)

Cortisol levels follow a strong circadian pattern across the day. In studies that examine cortisol levels across the full waking day, approximately 70% of the variation in cortisol is due to time of day (Adam & Gunnar, 2001). The basal or diurnal cortisol rhythm is typically characterized by high levels upon waking, a substantial (50–60%) increase in cortisol concentration in the 30–40 min after waking (the cortisol awakening response or CAR), and a subsequent decline over the remainder of the day, reaching a low point or nadir around midnight (Kirschbaum & Hellhammer, 1989; Pruessner et al., 1997; Weitzman et al., 1971).

The circadian or basal patterning in cortisol occurs as part of the basic circadian machinery for regulating alertness, appetite, and metabolic function (Dallman et al., 1994). Nonetheless, stress and emotional experience may cause cortisol levels to increase above typical basal levels at any point in the day (thus, reflecting acute reactivity, above) (Adam, 2006). Also, both individual differences in emotion (trait emotion) and changes in emotion within persons over time (daily emotional state) have been found to modify the shape of the diurnal cortisol rhythm (Doane & Adam, 2010; Hauner et al., 2008; Polk, Cohen, Doyle, Skoner, & Kirschbaum, 2004).

Two key elements of the basal rhythm that have been shown to be responsive to emotional experience are the CAR and the diurnal cortisol slope (decline in cortisol levels across the waking day) (Adam & Kumari, 2009; Saxbe, 2008). When the diurnal cortisol slope is modeled as rate of change in cortisol from wake time to bedtime (i.e., doesn't include the CAR), the size of the CAR and the steepness of the diurnal cortisol slope are not strongly correlated and relate in different ways to psychosocial and emotional variables. They thus represent relatively independent indicators of basal cortisol function (Adam & Kumari, 2009; Saxbe, 2008). Another basal cortisol indicator, the average cortisol level across the waking day, as measured by the area under the diurnal cortisol curve, does not relate as consistently with emotional experience.

How state emotional experience modifies diurnal cortisol rhythms is described later; here, I briefly describe research on trait emotional functioning and basal/diurnal cortisol. Diurnal cortisol patterns start to emerge in infants by 3 months of age (Price, 1983), and individual differences in these rhythms are evident throughout childhood and adolescence. In examining trait emotional correlates of the CAR, one study found that adolescents with high levels of introversion had a lower CAR (Hauner et al., 2008), and another found that adolescents with high levels of trait anger had a larger CAR (Adam, 2006). More research has been conducted on trait emotion and cortisol slopes. For example, among preschool-age children, flatter slopes from morning to afternoon in day care settings have been associated with greater sadness and shyness, high social fear, and poor inhibitory control (Dettling, Gunnar, & Donzella, 1999; Vermeer & van Ijzendoorn, 2006; Watamura, Donzella, Alwin, & Gunnar, 2003). However, similar associations are not obtained in the home setting (Dettling et al., 1999), suggesting that these results may reflect reactivity to the child care setting, rather than trait differences in rhythms, and highlighting the importance of social context in understanding emotion-cortisol associations. In adolescents, there is evidence of flatter slopes from wake time to bedtime among male adolescents with high levels of neuroticism (Hauner et al., 2008) and among youth with high trait loneliness (Doane & Adam, 2010); these trait associations were not explained by emotional state on the days of cortisol measurement. In interpreting associations between trait emotion and cortisol, it is helpful to examine the extent to which associations are accounted for by the measurement context and by differences in state emotion. In interpreting diurnal cortisol rhythms, it is important to note that flatter rhythms can result both from higher afternoon or evening levels and from lower morning levels (DeSantis et al., 2007; Dettling et al., 1999). Cortisol levels that follow the typical diurnal pattern—high wakeup levels, a strong decline from waking to bedtime, and a moderate CAR—tend to be associated with more desirable trait and state emotional functioning.

## DAY-TO-DAY CHANGES IN CORTISOL ACTIVITY

Studies often average cortisol rhythms across multiple days of measurement in order to improve the measurement of “trait” diurnal cortisol rhythms, as day-to-day variation is often considered “noise.” More recently, research (mostly in adults) found that cortisol rhythms change in meaningful ways from day to day in relation to changing social and emotional experience. For example, the CAR is accentuated the day after adolescents and adults experience high levels of sadness and loneliness (Adam, Hawkley, Kudielka, & Cacioppo, 2006; Doane & Adam, 2010), and diurnal cortisol levels are flatter on days with higher levels of anger/frustration (Adam, 2006). Day-to-day changes in cortisol rhythms can also be anticipatory. For example, professional ballroom dancers have a higher CAR on days they have an upcoming competition (Rohleder, Beulen, Chen, Wolf, & Kirschbaum, 2007). In preschoolers, cortisol levels at the beginning of the child care day are *lower* than corresponding levels at that time of day at home, perhaps protecting against elevations that tend to occur across the child care day (Dettling et al., 1999). Indeed, recent interpretations suggest that ability of diurnal cortisol patterns (and in particular the CAR) to flexibly adapt to changing daily demands is important hallmark of healthy HPA-axis functioning (Adam, 2006; Mikolajczak et al., 2010). Most research on day-to-day changes in cortisol rhythms has been conducted on late adolescents and adults—more developmental research on day-to-day variation in basal cortisol rhythms is needed. Examining how cortisol rhythms change in response to and in anticipation of daily experience provides insights into the potentially functional role of cortisol in mediating responses to daily challenges.

## CHANGE OVER MONTHS AND YEARS

HPA-axis changes also occur over the course of months and years. These include normative developmental changes and responses to both early and cumulative developmental experience.

*Normative developmental changes* are described in more detail in Gunnar and Adam (this volume). Briefly, cortisol reactivity is robust beginning in infancy, and diurnal cortisol rhythms are evident in infants as young as 3 months of age but continue to mature over the first few years of life (Gunnar & Quevedo, 2007; Price, Close, Fielding, 1983). A relative stress hyporesponsive period, in which reactivity is harder to achieve, occurs from approximately 2 years of age through early adolescence; as a result, it may be more difficult to identify social and emotional correlates of HPA-axis activity during this time (Gunnar & Quevedo, 2007). In early adolescence, basal cortisol and cortisol reactivity

to stressors appear to increase, particularly in girls, and increases correlate with stage of pubertal development (Adam, 2006; Gunnar, Wewerka, Frenn, Long, & Griggs, 2009; Stroud et al., 2009; Stroud, Papandonatos, Williamson, & Dahl, 2004). These latter changes are hypothesized to underly increased rates of depression, especially in girls, that also emerge over this time period (Stroud et al., 2004), but more research is needed on this point.

### *Chronic/Cumulative Stress Exposure*

Beyond the impact of momentary and daily emotional experience on concurrently measured cortisol levels, exposure to chronic stress (and presumably, accompanying chronic negative affective arousal) can cause persistent alterations in basal cortisol activity and reactivity. The timing of cortisol measurement poststressor matters—reviews of both child (Gunnar & Vazquez, 2001) and adult research (Miller, Chen, & Zhou, 2007) suggest that following a stressful life event, basal cortisol levels may initially be elevated but, over time, may drop to below normal, resulting in a profile that is as likely hypocortisolemic (chronically low basal cortisol and flatter diurnal rhythms). Thus, the HPA axis may adapt to chronic stress over the course of weeks, months, and even years, and the direction of the association found may depend on the amount of time that has passed poststressor.

Chronic social-relational, and especially family stressors, are particularly likely to be linked with chronic alterations in cortisol activity (Adam, Klimes-Dougan, & Gunnar, 2007; Repetti, Taylor, & Seeman, 2002). For example, children living in a home with low levels of marital satisfaction and low maternal warmth have higher average cortisol and flatter diurnal rhythms (Pendry & Adam, 2007). Exposure to transitions in household composition (Flinn & England, 1995) and child maltreatment (Cicchetti & Rogosch, 2001; Shea, Walsh, McMillan, & Steiner, 2004) have also been associated with alterations in cortisol activity (for a review of their research on child maltreatment and cortisol, see Cichetti and Rogosch, this volume). On a positive note, interventions designed to improve social circumstances appear to have a positive impact on HPA-axis functioning; children in foster care homes participating in caregiving interventions have diurnal cortisol profiles that are more similar to profiles of children in a normal care environment (Dozier, Peloso, Gordon, Manni, & Gunnar, 2006; Fisher, Gunnar, Dozier, Bruce, & Pears, 2006). In these studies, data on children's emotional responses to stressors are rarely available. More research is needed on whether the impacts of chronic social stress (and reductions thereof) on the HPA are mediated by immediate emotional reactions to or ongoing changes in emotional experience.

### *Early Developmental Experience*

Positive early social experiences, in particular sensitive and contingent caregiving during the first few years of life, are fundamentally important in that they contribute to lifelong patterns of both emotional and biological (including HPA axis) functioning in later interpersonal contexts, with the absence of adequate early contingent caregiving having important negative consequences for later biological regulation, including HPA-axis activity (see the chapters by Feldman and Strang, Hanson, and Pollack, this volume). Evidence from both animal models and humans suggests that stress experiences occurring in the first few years of life may have more dramatic effects on long-term emotional and HPA-axis functioning than similar stressors encountered later in childhood (Halligan, Herbert, Goodyer, & Murray, 2004; Shea et al., 2004). In addition, exposure to early life stress may modify the impact of later stress experiences on the HPA axis. Essex and colleagues (2002), for example, found that afternoon cortisol levels were elevated among 4.5-year-olds with currently depressed mothers, but only if those mothers had also been depressed during their infancy. They hypothesized that early experience had sensitized the infant HPA to be more responsive to later stressful life experiences. Heim and colleagues suggested that neurobiologically and developmentally distinct subtypes of depression exist, with altered cortisol activity (including elevated basal cortisol and increased reactivity) only likely to be present among depressed individuals who encountered early life stress (Heim, Newport, Mietzko, Miller, & Nemeroff, 2008). Thus, early social-developmental experiences may (1) alter the current functioning of the HPA axis and (2) may alter/moderate associations between later emotional experience and cortisol. Knowing about an individual's developmental past is therefore essential to understanding the present functioning of their HPA axis.

### *Genetics, Epigenetics, and Intergenerational Changes*

Some portion of trait individual differences in HPA-axis activity originates in genetic differences. Twin studies identify a heritable component to HPA-axis reactivity and various aspects of basal patterning, and numerous genetic polymorphisms relevant to the functioning of the HPA axis have been identified (Wüst et al., 2004). A purely genetic model of individual differences in HPA-axis functioning allows change only in the next generation with changes in the genome—a very slow time scale of change in HPA-axis functioning. More recent epigenetic models (Weaver et al., 2004) suggest that the effects of HPA-relevant genetic polymorphisms on later functioning are not set in stone. In rodent models, alterations in adult behavioral and HPA-axis

functioning occur as a result of early maternal care, and such changes are mediated by epigenetic modifications of glucocorticoid receptor regions of DNA (Weaver et al., 2004); it seems likely that similar epigenetic mechanisms may underlie the effects of early experience on later HPA-axis functioning in humans, described earlier. Some forms of epigenetic modification have been shown to be heritable across generations in plant and animal models (Whitelaw & Whitelaw, 2006). Should this prove to be true in humans for epigenetic modifications of HPA-axis relevant genes, epigenetics would also provide a biological mechanism (to complement known behavioral mechanisms) by which emotional experiences within a life span would be passed to the next generation.

### *Loneliness Example—Considering Three Time Courses in a Single Study*

The fact that associations between emotional experience and cortisol can occur over multiple time scales is perhaps best illustrated by research in which several time scales of emotion–cortisol associations are simultaneously examined. In a recent study of loneliness and cortisol, we predicted that trait loneliness, a form of chronic psychosocial strain, would be associated with a flattening of the diurnal cortisol rhythm, but we were also interested in whether state loneliness, including experiencing lonely moments or lonely days, would also predict more acute alterations in cortisol levels. In order to maximize the generalizability of our results, and to ensure that we were studying associations between loneliness and cortisol as they actually unfold in the context of adolescents’ daily lives, we used a modified experience sampling protocol, in which momentary diary reports, time linked with salivary cortisol samples, were gathered six times per day for 3 days in naturalistic settings (see also Dahl, Silk, and Siegle, this volume, regarding the advantages of ecologically valid measurement approach). In our study, a three-level multilevel growth curve model was employed, with momentary loneliness modeled at Level 1, day-to-day changes in loneliness modeled at Level 2, and trait loneliness (and other trait characteristics) modeled at Level 3. As expected, trait loneliness significantly predicted a flatter average diurnal cortisol rhythm across the days of testing (Doane & Adam, 2010). In addition, day-to-day changes in loneliness predicted daily changes in the CAR, with higher prior day loneliness predicting a larger CAR the next morning. We hypothesized that this increased CAR following a “lonely day” may serve to provide an energetic “boost” to assist the individual in engaging more effectively with the social world the next day (“boost hypothesis”; Adam et al., 2006). Finally, momentary increases in loneliness predicted momentary elevations in cortisol, but only for those adolescents who also had high levels of chronic interpersonal stress over the past year (Doane & Adam, 2010).

Following these adolescents forward longitudinally, we found that adolescents with a higher baseline CAR are significantly more likely to develop an episode of MDD over the following year (Adam et al., 2010). This suggests that short-term CAR “boosts” may come at a cost of long-term emotional health, a cost that may not have been apparent without following youth over a time frame of months to years. It is important to note that current MDD is *not* associated with an elevated CAR in these youth; rather, youth with current (and past) MDD have flatter diurnal cortisol slopes. This highlights the importance of *using prospective longitudinal data* to examine the role of the HPA axis in the etiology of emotional disorder. Given the allostatic nature of the HPA, *risk factors* for the development of emotional disorder may not still be identifiable among individuals already showing signs of disorder, since *changes* in the HPA axis are thought to be involved in etiology of depression, and the experience of the disorder itself may further alter the HPA (Adam, Sutton, Doane, & Mineka, 2008). Dynamic associations between emotional experience and cortisol occur over multiple time frames. Failure to identify and carefully plan data collection efforts to capture the appropriate time frame(s) of change in cortisol and emotion could result in underestimations of the associations between HPA-axis activity and emotional experience.

#### *Psychological and Neurobiological Mechanisms of HPA-Axis Change*

A full chronometric model of the HPA axis should consider (1) the extent to which acute HPA-axis activations add up to contribute to associations with occurring over longer time scales and (2) the psychological and neurobiological mechanisms mediating HPA axis change at each time scale. For this brief chapter, it must suffice to note (as depicted in Figure 2) that bidirectional cross-talk and interactions across time scales are expected and that changes across differing time scales are likely mediated by differing aspects of the underlying neurobiology of the HPA axis, ranging from genetic and epigenetic mechanisms to changes in receptor populations and responses in the pituitary and adrenal to changes in emotional and cognitive inputs to the HPA axis, such as threat appraisals and coping resources.

#### *Importance of Considering Multiple Influences on Cortisol*

It is important to note that cortisol does not respond uniquely, or specifically, to emotional experience. As summarized in Figure 3, many other aspects of current and past experience have been linked to individual differences in basal cortisol activity and reactivity. To more effectively reveal associations between emotion and cortisol, it is important measure and model various confounding and moderating influences, including factors measured on the

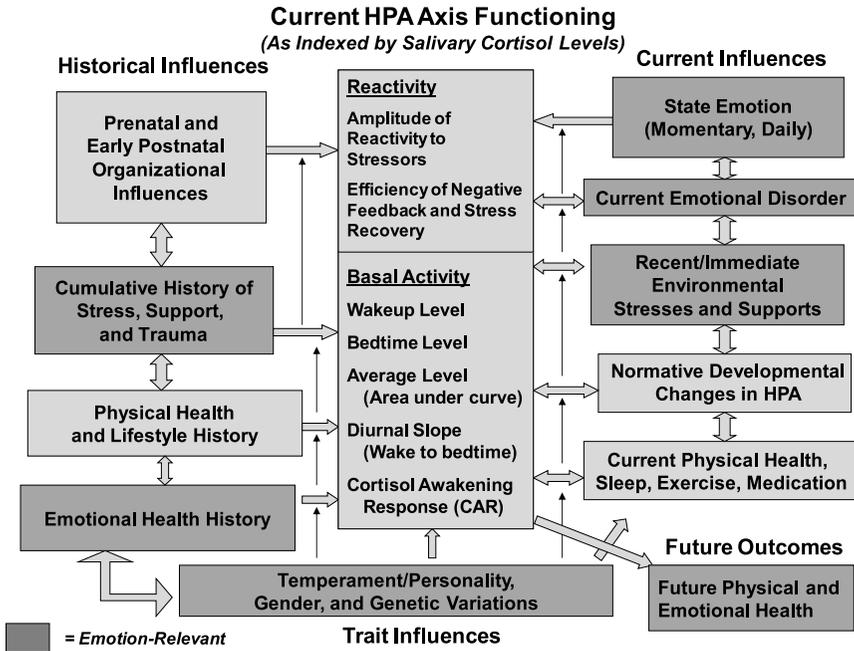


FIGURE 3.—Historical and current influences on HPA-axis functioning as indexed by salivary cortisol levels, highlighting the role of emotion and emotional disorder.

days of testing, in the recent past, and earlier in individuals' developmental histories. For example, in examining associations between state and trait loneliness and cortisol, we included day-varying covariates, such as time of waking each day, and person-level covariates, such as the presence of current MDD, caffeine, and nicotine use and recent interpersonal life stress (see Doane & Adam, 2010). Typically, we found that addition of multiple covariates for known confounding and moderating influences, rather than reducing effect sizes, tend to improve the strength and clarity of associations between emotional experience and cortisol.

### Summary and Conclusion

To understand individual differences in cortisol, and its relations with state and trait emotional experience, one must understand the dynamic quality of this hormone—that cortisol levels and patterns change over multiple time scales in response to changes in emotional experience. It is also important to understand that within-person changes and individual differences in

cortisol are not specific to emotional experience—there are many other confounding and moderating influences on HPA-axis activity. Future research should consider (and measure and model) how multiple influences on cortisol interact, over multiple time scales ranging from moments to years, to contribute to individual differences in the associations between emotional experience and cortisol. Future research should also take a multisystem, integrative approach, examining the meaning and impact of cortisol change in light of co-occurring changes in other stress-sensitive biological systems, and should attempt to identify the neurobiological mechanisms underlying the various patterns and time courses of HPA-axis change.