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Attachment and Stress in Early Development

Does Attachment Add to the Potency of Social Regulators of Infant Stress?

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ABSTRACT

For the last forty some years, studies of stress and attachment have been mainstays of primate psychoendocrine research. These studies have focused on the limbic–hypothalamic–pituitary–adrenal (LHPA) system, a system critical to adaptation and survival. They have shown that activity of this neuroendocrine system is sensitive to the availability and responsiveness of the attachment figure. Separation produces elevations in cortisol, the primary hormone of this system, in both monkey and human infants. In the presence of the attachment figure, elevations in cortisol to a range of stressors are reduced or prevented altogether. Finally, within the attachment relationship, insensitive, intrusive, or, in the extreme, abusive care stimulates increases in this stress hormone. These findings fit well with arguments that attachment provides primate infants with a secure base for exploration and that separation or loss is stressful or traumatic. In addition, because stress influences immune competence and brain development, these findings suggest one mechanism by which attachment protects the developing primate's physical and mental health. We need, however, to ask whether the significance of attachment–stress findings have been overplayed. Are any of these findings unique to attachment relationships? It will be argued that evidence, to date, fails to show that attachment plays a unique role in stress regulation in developing primates. In part, this conclusion is necessary because certain critical studies have not been done. In the absence of definitive studies, we may be wise to limit conclusions to more general statements about sensitive and responsive social relationships as powerful regulators of stress in early development.

INTRODUCTION

Among John Bowlby's seminal insights was the idea that in the primate central nervous system a motivational system evolved to insure that an infant will

attempt to maintain proximity and contact with the conspecifics who are the most likely to provide it with nurturance and protection (Bowlby 1969). He termed this system *attachment*. Protection from dangerous elements of the environment and regulation of the infant's internal state are two of the principal functions of caregiving. Thus, the ultimate function of attachment is achieved through the attachment system that operates to maintain proximity between caregivers and infants. Protection of the infant's internal state from internal and external threats to homeostasis is not solely the responsibility of the caregivers. Evolution has also conferred on mammals and their young stress-sensitive neurobiological systems that operate in the face of threat to shift and liberate metabolic resources and orchestrate behavior and physiology to increase survival. Activating these stress-sensitive systems, however, also brings costs to the organism, which in early development may include impairments in physical growth and shaping of the nervous system in ways that increase vulnerability to stress during throughout the lifespan (McEwen 1998).

In another of Bowlby's insights he argued that when the caregiving system is up to the task of providing protection and external regulation of the infant's internal milieu, the infant will be able to direct its resources to other activities (Bowlby 1969). Bowlby, thus, provided a framework that anticipated an inverse relationship between the availability and responsiveness of the attachment figure(s) and activity of stress-sensitive neurobiological systems. In this chapter, I outline the neurobiology of one of the principal components of the mammalian stress system: the limbic–hypothalamic–pituitary–adrenocortical (LHPA) system. This system has most often been the focus of research on stress and attachment in monkeys and humans. I summarize some of the key studies supporting the argument that in primates the caregiver–infant attachment system functions to regulate this stress-sensitive neurobiological system. I address studies currently available to examine whether the attachment relationship plays a unique role in stress regulation during primate development, or, alternatively, is merely a reflection of the importance of social processes in stress regulation throughout the lifespan. Finally, I discuss implications of this work for our understanding of the roles of both attachment and stress in primate development.

THE LHPA SYSTEM: A BRIEF OVERVIEW

Current views of stress neurobiology describe a loosely integrated system consisting of neuroanatomically and functionally related subsystems. In the periphery, stress biology centers on the regulation of glucocorticoids or CORT (cortisol in primates, corticosterone in rodents) and catecholamines (norepinephrine [NE] and epinephrine [EPI]; Johnson et al. 1992). CORT and catecholamines operate to increase metabolism and stimulate cardiovascular and pulmonary function. In concert with central components of the stress system, they inhibit the biology of growth and repair, including digestion, physical growth,

immune function, and reproduction. In the brain, the stress system is orchestrated through reciprocal interactions among NE and hypothalamic and extra-hypothalamic corticotropin-releasing hormone (CRH).

CRH is a neuroactive peptide produced in the hypothalamus and in extra-hypothalamic sites (Strand 1999). Its production in the hypothalamus initiates the cascade of events that culminate in increased production of CORT by the adrenal glands (see Figure 12.1). CRH and other peptides, principally, arginine vasopressin (AVP), regulate the production of adrenocorticotropic hormone (ACTH) by cells in the anterior pituitary. ACTH binds to receptors in the cortex of the adrenal glands and causes the biosynthesis and release of CORT into general circulation. CORT primarily acts by binding to receptors in the cytoplasm of cells, including nerve cells. The activated hormone-receptor complex then enters the nucleus of the cell where it regulates gene transcription on genes with glucocorticoid receptive elements (GREs). Negative feedback loops operating at the levels of the pituitary, hypothalamus, hippocampus, and possibly frontal cortex (Sullivan and Gratton 2002) terminate and contain the stress response.

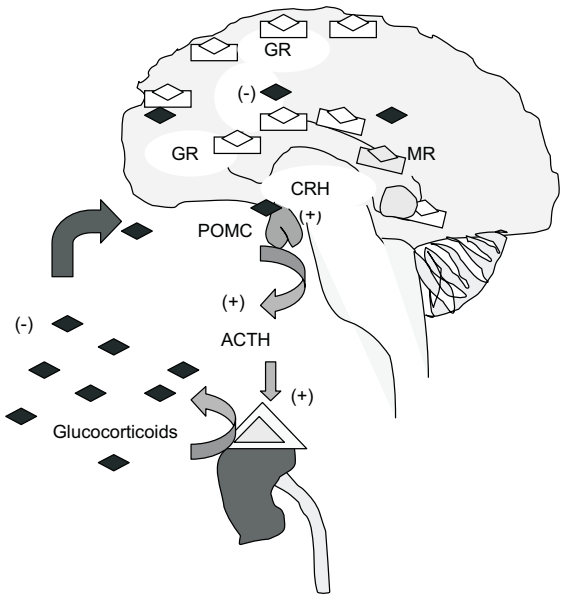

Figure 12.1 The limbic–hypothalamic–pituitary–adrenal (LHPA) axis and corticoid receptor distribution and function in brain. The corticotropin-releasing hormone (CRH) molecule originating in the hypothalamus is at the center of the activation of the system. CRH acts on the release of adrenocorticotropic hormone (ACTH) from the pituitary, which in turn acts on the adrenal to release glucocorticoids. Glucocorticoids act on tissues peripherally from the brain and are also "key" for LHPA axis "brake." Two receptors are the "locks": glucocorticoid (GR) and mineralocorticoid (MR) receptors, with GR widely distributed throughout the brain and MR localized exclusively in "the emotional brain" or limbic structures. POMC = proopiomelanocortin. Adapted from Muller et al. (2002).

Hypothalamic CRH-producing neurons receive input from other hypothalamic and brainstem nuclei, with NE being a major stimulus of increased hypothalamic CRH activity. However, there are multiple neurotransmitter and neuropeptide systems, beyond the NE system, that are involved in regulating hypothalamic CRH activity (Herman and Cullinan 1997). Activation and regulation of CRH in the hypothalamus is, thus, multifactorial, reflecting the current and previous state of the organism in conjunction with current, previous, and anticipated demands. The balancing of internal and external demands is also reflected in the regulation of what has been called extra-hypothalamic CRH. CRH is produced in many limbic structures, brainstem nuclei, and neocortical areas involved in stress reactivity and regulation. One subtype of the CRH receptor, CRH1, appears to mediate many stress and anxiety related functions; while the other subtype, CRH2, appears to mediate functions (e.g., eating, sleeping) that are often inhibited during stressful periods (Steckler and Holsboer 1999).

One common fallacy about the LHPA system is that CORT and CRH are necessarily detrimental to health and well-being. In fact, the relationship between CORT and adaptive functioning is often an inverted-U function. Both too little and too much can be detrimental (McEwen 1998). One basis for the inverted-U function may be the difference between the two major receptors for CORT, termed mineralocorticoid (MR) and glucocorticoid (GR) receptors (De Kloet 1991). In the central nervous system, MRs tend to have growth and health promotive effects, whereas GRs tend to have catabolic and potentially damaging effects. CORT has high affinity for MRs and lower affinity for GRs. Thus at low levels of the hormone, MRs in the central nervous system are primarily occupied, while at higher levels, GRs become increasingly occupied. MRs are believed to be critically involved in regulating the diurnal rhythm of CORT, whereas GRs serve in negative feedback of the system to terminate and contain stress elevations of the hormone.

In rodents, vigorous maternal care during the first weeks of life permanently increases the number of GR available to contain the stress response (Liu et al. 1997). In rodents and monkeys, negative early care experiences also increase CRH production (Coplan et al. 1996) and alter CRH receptor expression, resulting in increases in CRH1 receptors in regions involved in fearful/anxious behavior (Sanchez et al. 2001). The LHPA system also interacts with the developing serotonin (Lopez et al. 1998) and dopamine systems (Pani et al. 2000) in complex ways that may affect vulnerability to anxiety, depression, and substance abuse disorders. Cortisol and CRH also influence neural systems involved in learning and memory, including circuits in the hippocampus (McEwen 1998) and prefrontal cortex (Sullivan and Gratton 2002). With regard to the former, the same dimensions of maternal care associated with changes in LHPA activity in the rodent influence synaptogenesis and memory function (Liu et al. 2000). With regard to the latter, there is some evidence that side matters, with right prefrontal activity being more closely associated with elevated CORT

in animals and humans, consistent with evidence that right frontal EEG asymmetry is associated with depression and withdrawal behavior (Buss et al. 2003; Sullivan and Gratton 2002). The impact of early care experiences on neural systems regulating stress, emotion, and cognition provides a strong impetus for understanding how and whether experiences within the caregiver–infant attachment relationship have a unique role to play in stress regulation in primate development.

ATTACHMENT AND LHPA ACTIVITY IN DEVELOPING PRIMATES

Basic Findings

Borrowing from the human literature on stress and coping, in monkeys the mother has been conceptualized as providing a social buffer against stress. Maternal buffering describes situations in which the infant exhibits behavioral distress; nonetheless in the mother's presence, LHPA and autonomic reactions to the stressor are attenuated. A classic example is capture and handling in naïve infant monkey. Typically, this provokes marked increases in infant cortisol levels; however, when the infant is put back with the mother immediately, having never lost sight of her, the cortisol response is greatly reduced (for a review, see Levine and Wiener 1988). Physical contact with the mother does not appear to be necessary in monkey infants in order for maternal buffering to reduce cortisol increases. Infants separated and placed in cages adjacent to their mothers show markedly more distress vocalizations and behavioral agitation, but they exhibit lower cortisol increases compared to infants who cannot hear, smell, or see their mothers. In human infants it becomes difficult to elevate cortisol to a range of stressors (e.g., doctor's exams and inoculations, the approach of strangers and/or exposure to odd, anxiety-eliciting stimuli) by the end of the first year, as long as the child is in a secure attachment relationship with the parent who accompanies the child (Gunnar and Donzella 2002).

Separation from the attachment figure provokes marked elevations in cortisol in monkey infants that does not habituate over repeated trials (Levine and Wiener 1988). In human infants, brief separations such as those in the Ainsworth and Wittag Strange Situation produce increases in cortisol for infants in insecure attachment relationships (Spangler and Schieche 1998). More striking, regardless of attachment security, toddlers show marked elevations in cortisol over home baseline levels during the first several weeks after entering center-based child care (Ahnert et al. 2004). In monkey infants, separations induce long-term effects on the LHPA system. Unlike in rodents, however, where increases in LHPA axis reactivity is stimulated by single or repeated bouts of prolonged (3 to 24 hr) removal of the pup from maternal care, in monkey infants, separations of similar duration may result in blunted or suppressed activity of the LHPA system, sometimes but not always in the context of increased fearful, anxious behavior (Dettling et al. 2002; Levine et al. 1997).

If the attachment figure provides stress regulation and if separation elevates stress hormones, does rearing in the absence of an attachment figure produce marked dysregulation of the stress system? There is little evidence that such abnormal rearing environments affect the development of the HPA components of the axis, perhaps because these are well developed prior to birth in monkeys and humans (Sanchez et al. 2001). However, later developing limbic and cortical regions, which are important in the regulation of fear and stress, do show alterations. These changes include increased density of CRH1 receptors in the prefrontal cortex and down regulation of CRF2 receptors in the amygdala. Several studies of orphanage-reared children conducted several years after their adoption into families have indicated slight alterations in basal cortisol levels, particularly near the peak of the circadian cycle (for a review, see Gunnar and Donzella 2002).

In human infants, a number of studies indicate that attachment figures who are insensitive and/or intrusive provoke increases in cortisol. More intrusive, insensitive caregiving has been associated with increases in cortisol during mother–infant play bouts for infants between three and nine months of age (Spangler et al. 1994). Similarly, insensitive, intrusive mothers observed during well-child visits at two, four, and six months had infants who at those visits had higher pre-stressor levels of cortisol (Gunnar and Donzella 2002). With toddlers, mothers who were overly solicitous and who intrusively attempted to get their toddlers to approach arousing stimuli have toddlers who exhibit greater cortisol responses (Nachmias et al. 1996). In preschoolers, mothers who are less involved and responsive have children whose basal cortisol levels remain higher over the day (P. Pendry and E.K. Adam, pers. comm.). Severe failures in the caregiving system, such as those associated with abuse, produce long-term alterations in the LHPA system, perhaps especially in genetically vulnerable individuals (Heim et al. 1997). There is also evidence that manipulations which lead mother monkeys to be rejecting and unresponsive to their infants result in elevated central CRH levels measured in adulthood (Coplan et al. 1996). Noradrenergic and serotonergic systems are also affected in the same animals.

Does the Attachment Relationship Play a Unique Role in Infant Stress Regulation?

Here we explore whether the attachment relationship is unique in its stress regulatory function in primate development. I provide evidence to answer each of the following questions:

- Does the infant need to be attached to the caregiver before that individual can serve a stress regulatory function for the infant?
- Is the increase in cortisol during separation a response to separation from the attachment figure, or is it due to other changes in the environment that often co-occur with separation?

Is the Stress-buffering Effect Specific to the Attachment Relationship?

Predictability and control are two of the core psychological variables that regulate activity of the LHPA system throughout the lifespan (Levine and Ursin 1979). When we are reliant on others to exercise reliable control over threat, their sensitivity and responsiveness to our signals become principal determinants of our coping resources (Glass and Singer 1972). Caregiver sensitivity and responsivity form the basis for the development of secure attachment relationships (Ainsworth et al. 1978). However, is it necessary for the infant to be attached to a caregiver in order for their sensitivity and responsiveness to the infant's signals to regulate reactivity of the LHPA system? In some monkeys, infants receive caregiving from many female members of the troupe, whereas in others, a separated infant is less likely to direct and receive comfort from other troupe members. Studying monkeys where *aunting* or *alloparenting* is common, researchers have found that increases in cortisol upon separation return to baseline by 60–90 minutes as the infant receives care from other adult females (Levine and Wiener 1988). Because these females are familiar to the infant, one could argue that the infants might have already formed some attachment to them. More striking evidence that an attachment bond may not be necessary comes from a study of 9-month-old human infants (Gunnar and Donzella 2002). In this study, the infants were given a babysitter during a 30-minute maternal separation. The babysitter was either programmed to be sensitive and responsive or relatively cold and aloof. In the presence of the sensitive and responsive babysitter no increase in cortisol was observed, whereas elevations were observed with the colder and more distant babysitter. Certainly, the infants could not have been attached to the sensitive and responsive babysitter as they had never seen her before the moment of separation. While this study is provocative, it is important to note that we do not know whether the responsive babysitter would have been able to maintain low cortisol levels in the infant if the separation period had been extended into hours or days. Nor do we know whether infants older than nine months would have shown the same propensity to maintain baseline levels of cortisol with a high-responsive as compared to low-responsive babysitter.

Does attachment confer any added benefit to sensitive and responsive caregiving in stress regulation? Unfortunately, the aunting and babysitting studies described above do not tell us. What we need are studies that pit secure and insecure attachment against sensitive versus insensitive caregiving by individuals for whom there is no attachment bond with the child. As discussed, there is already evidence that the presence of the attachment figure in an insecure relationship results in greater cortisol responses to threatening events than it does in a secure relationship. However, it is difficult in these studies to determine whether it is the insecure relationship history or the behavior of the attachment figure during the stressor that affects the cortisol response. If it is the concurrent behavior, then we might well find that for insecurely attached infants, cortisol

reactions to potentially threatening events might be lower when they are with a sensitive and responsive stranger than when they are with their attachment figure. This would certainly argue that it is the caregiving style and not the attachment relationship that regulates the LHPA axis. Although such studies would be difficult to construct, they would be the kind of studies we need to know whether the attachment relationship confers special potency in stress regulation.

There is actually a naturally occurring situation that might be used to address this question. Dozier and colleagues (Stovall and Dozier 2000) have studied infants and toddlers in the U.S. foster care system during the first days and weeks of their transition into the care of the foster parent. Using a daily diary method, the foster mothers record the secure base behavior of the children in response to mild stressors (e.g., falling down, brief separations from the foster mother). Dozier and colleagues then classify these behaviors as secure, avoidant, or resistant and examine over days the emergence, or not, of secure attachment behaviors in the children. Some of these foster mothers are very sensitive and responsive to children in their care, others are less. One could ask, then, whether cortisol levels and reactivity in the infant during the infant's transition into the foster home track the sensitivity and responsiveness of the foster parent and whether changes in cortisol activity are noted before or after the infant begins to exhibit consistent patterns of attachment behavior towards the foster parents.

Is the LHPA Response to Separation a Response to Loss of the Attachment Figure?

Separation induces attachment behaviors (proximity/contact seeking, separation distress vocalizations), as well as other behaviors that may reflect fear and anxiety (freezing and inhibition of exploration). Separation reactions, thus, are not unitary phenomena (Kraemer et al. 1991). This may explain one of the more persistent and perplexing findings in the psychoneuroendocrine literature. Specifically, protest behaviors (crying, searching) at times are inversely related to separation-induced activity of the LHPA system. Levine and Wiener (1988) argue that protest behaviors reflect the infant's active attempt to cope with separation, whereas activation of the LHPA system reflects failed coping. An alternative explanation is that protest behaviors reflect the operation of the attachment system, and that LHPA responses reflect the operation of fear/anxiety systems in the central nervous system.

Kalin and colleagues (e.g., Kalin et al. 1988) provide support for this latter hypothesis. They have shown that calling and searching for the mother is regulated by central opioid activity. Exogenous opiates affect this type of protest behavior in infant monkeys, but they do not affect fear and defensive behaviors (e.g., freezing and threatening experimenters). Exogenous opiates also do not affect cortisol increases to maternal separation. In contrast, freezing, barking and other defensive behaviors during separation are regulated by central fear/anxiety systems orchestrated, in part, by extra-hypothalamic CRH. Central

administration of CRH mediates the intensity of defensive behaviors but does not affect protest vocalizations. Indeed, in monkey infants there seems to be a close correspondence between freezing and other defensive behaviors and measures of ACTH and cortisol in response to separation.

In human infants, separation distress (fussing, crying) varies as a function of the infant's attachment classification. Insecure avoidant attachment is associated with less protest than is insecure resistant attachment. Indeed, it has been noted that the security dimension of attachment is orthogonal to the protest dimension of reaction to separation (Belsky and Rovine 1987). Cortisol increases are noted for both low-protest, avoidant babies and high-protest, resistant babies. Among securely attached infants, protest and cortisol responses in the Strange Situation are uncorrelated, while in insecurely attached infants, significant associations are observed, consistent with evidence that resistant infants tend to be more anxious and fearful (Spangler and Schieche 1998). Similarly, there is evidence that freezing/withdrawal during separation is associated with large increases in cortisol among year-old infants (Gunnar and Donzella 2002).

Separation may stimulate fear in infants and young children, but how much fear the infant experiences likely depends on the infant's temperament and the nature of the separation environment. As already discussed above, when the infant is provided with a sensitive and responsive caregiver, this blocks increases in cortisol and likely reduces the threat the infant experiences in the separation context. However, when the infant is fearful of strangers, this may make it difficult for her to use the comfort of a strange adult to regulate stress in the separation environment. Thus, not only the quality of care provided the infant, but the child's temperament may be expected to influence increases in cortisol during periods spent away from primary attachment figures. Recent studies of cortisol activity in infants, toddlers, and preschoolers studied in out-of-home childcare arrangements confirm these predictions. Quality of care and fearful temperament are both associated with rising levels of cortisol over the childcare day (Gunnar and Donzella 2002).

Continuity with Rodent Studies

Maternal care in rodents is critical to shaping the developing nervous system and in providing protection and nurturance. Distress vocalizations and LHPA activity in response to separation, however, appear to be mediated by opiate and CRH system, as described for the monkey infant. Similarly, LHPA activity during separation does not seem to reflect loss of the mother, but rather loss of certain stimuli correlated with maternal care (Suchecki et al. 1993). Although it can be argued that pups do not form primate-like attachment bonds to their mothers, it appears from the above review that there may be considerable continuity in the social mechanisms regulating stress from rodents to monkeys to humans. The attachment motivational system may help insure that the primate infant maintains proximity to the adult who is the most likely to provide adequate social

regulation of the axis. However, there is as yet no evidence that having formed an attachment relationship, the infant loses the capacity to regulate stress physiology through interaction with other sensitive and responsive caregivers. Evidence is also lacking to indicate that separation from the attachment figure, per se, is a potent stimulator of the primate infant's LHPA system, as opposed to behavioral systems orchestrated around regaining contact (e.g., calling, searching).

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