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Stress and the Development of Self-Regulation in Context

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Abstract

This article considers the effects of psychosocial stress on child development and describes mechanisms through which early stress in the context of poverty affects the functioning of neural networks that underlie executive functions and self-regulation. It examines the effects of early experience on glucocorticoid and catecholamine levels that influence neural activity in areas of the brain associated with executive functions, primarily as studied in animal models. Finally, it considers the strengths and limitations of this research, its relevance to understanding stress reactivity from the perspective of biological sensitivity to context, and the implications for the study of risk and resilience processes and early intervention to prevent developmental delays.

Stress is a central construct in the study of psychosocial adversity. It is prominent among the several mediating mechanisms through which risk for poor physical and mental health increases in inverse relation to socioeconomic status (SES; Adler et al., 1994). Studies have linked persistently elevated levels of physiological reactivity to stress with adverse physical and mental health outcomes across the lifespan (McEwen, 2000), and a number of studies have definitively linked income poverty and low SES to children's health and development (McLeod & Shanahan, 1993; McLoyd, 1998). Until recently, however, the field has lacked in-depth examination of stress as an aspect of the link between poverty and child development (Evans, 2003).

There are many ways in which low-SES environments affect child health and development, and stress within the context of poverty is only one of them. Stress is of strong interest for children's development, however, because alterations to stress response systems resulting from the early rearing environment may have specific effects on aspects of brain development and function that promote or impede the development of reflective and goal-directed self-regulation of behavior such as that needed for success in school. Much of the research linking the early environment with alterations to the stress response and with brain development has been conducted using animal models. The purpose of this article is to briefly review some of this research and consider its implications for child development. As such, at the outset it is important to note that only by considering the context in which stress reactivity occurs can we appreciate its implications for child development. High reactivity to stress on its own does not confer risk and may even enhance development in supportive contexts (Boyce & Ellis, 2005). In high-risk environments, however, higher reactivity is likely to occur without support for the regulation of reactivity and to lead to poor developmental outcomes.

It is also important to note that the characterization of a stress response that promotes reflective self-regulation as beneficial (that is, it does not result in chronic overactivation leading to illness or to delays in the development of cognitive abilities and behaviors that are valued within socially constructed environments such as the school classroom or the

workplace) is not synonymous with its characterization as adaptive (Meaney, 2001). In unpredictable environments in which resources are scarce or social conflict is high, more reactive and less reflective patterns of cognition and behavior are likely to be adaptive and to result in short-term benefits if not longer term health and self-regulation benefits.

Animal models of early experience

Animal models have demonstrated that chronic stress in the prenatal and/or very early neonatal periods (demonstrated through manipulations that directly increase the physiological response to stress) leads to increased stress reactivity and to poor regulation of stress reactivity in the hypothalamic-pituitary-adrenal (HPA) axis component of the stress response system (Francis, Diorio, Liu, & Meaney, 1999; Huizink, Mulder, & Buitelaar, 2004; Liu et al., 1997; Ladd et al., 2000). This research has demonstrated that high levels early in life of the end product of HPA axis activity—cortisol in humans, corticosterone in rodents—influences the development of brain structures and neural circuitry in areas of the brain that are in combination important for initiating and regulating the HPA response to stress and also for cognitive abilities referred to as executive functions (EFs) that are important for learning and memory and the effortful regulation of behavior (Liu, Diorio, Day, Francis, & Meaney, 2000; Meaney & Szyf, 2005; Sanchez, Ladd, & Plotsky, 2001; Weinstock, 2001).

Several studies (Braun, Lange, Metzger, & Poeggel, 1999; Kinnunen, Keonig, & Bilbe, 2003; Lemaire, Koehl, Le Moal, & Abrous, 2000; Liu, Diorio, Day, Frances, & Meaney, 2000) have demonstrated that chronic early stress alters neural functioning and connectivity within and between limbic structures, notably the amygdala and hippocampus, associated with emotion, rapid contextually and temporally bound responses to stimulation, and the initiation and termination of the stress response; and areas of PFC, particularly ventral medial and orbital PFC important for regulating the stress response, for regulating emotion, and for coordinating thought and action in the control of behavior through EFs (Barbas & Zikopoulos, 2007; Holmes & Wellman, 2009). Numerous studies using animal models have shown the relation of corticolimbic neural circuitry to the self-regulation of behavior associated with EFs. In these models, targeted disruptions of PFC corticolimbic connectivity through lesion, transient inactivation, and pharmacological manipulation as well as stress induction procedures result in lower performance on tasks requiring EFs (Cerqueira, Mailliet, Almeida, Jay, & Sousa, 2007; Collins, Roberts, Dias, Everitt, & Robbins, 1998; Floresco, Seamans, & Phillips, 1997; Goldstein, Rasmusson, Bunney, & Roth, 1996; Mizoguchi, Ishige, Takeda, Aburada, & Tabira, 2004; Seamans, Floresco, & Phillips, 1998) and to elevated levels of reactive and inflexible behavior, as seen in fear conditioning (Champagne et al., 2008).

Relations among early experience, PFC connectivity, and EFs demonstrated in animal models are important for child development research in that EFs describe information processing abilities that allow for actively maintaining and processing task-relevant information in working memory, for flexibly sustaining and shifting attention between distinct but related aspects of a given task, and for inhibiting extraneous information and automatic responding associated with prepotent stimuli (Diamond, 2002; Zelazo, Muller, Frye, & Marcovitch, 2003). In humans, EFs have been related to multiple aspects of developing social and cognitive competence (Blair & Razza, 2007; Carlson & Moses, 2001; Hughes & Ensor, 2007), and impairments in EFs are a salient aspect of cognitive deficits in a number of developmental disorders and psychopathologies in children (Pennington & Ozonoff, 1996; Zelazo & Muller, 2002).

Early stress, brain development, and cognition

Research in animal models indicates that early experience programs the development of stress response systems to make them more or less sensitive to stress hormones, with implications for the structure and function of brain areas important for the self-regulation of cognition and behavior (Meaney, 2001). As a result, in supportive and resource-rich environments, stress response systems and PFC corticolimbic connectivity are understood to develop in a way that is conducive to effortful processing of information and reflective self-regulation associated with EFs. In low-resource, unpredictable environments, stress response systems and PFC connectivity develop in a way that promotes reactive rather than reflective self-regulation.

The pathway of this developmental effect concerns the way in which stress hormones modulate neural activity in PFC circuitry important for EFs. In both human and animal studies, glucocorticoid and catecholamine (dopamine, norepinephrine) levels demonstrate an inverted U shaped relation with EFs. Very high or very low levels of glucocorticoids and catecholamines are associated with deficits in EFs, whereas moderate increases are associated with higher level of EFs (Arnsten & Li, 2005; Lupien, Gillin, & Hauger, 1999; Mizoguchi, et al., 2004; Vijayraghavan, Wang, Birnbaum, Williams, & Arnsten, 2007). The inverted U relation between stress hormones and EFs is in part a function of the types of neural receptors present in PFC and the relative sensitivity or affinity of these receptors for glucocorticoids and catecholamines. For example, moderate increases in norepinephrine (NE), a primary neuromodulator associated with the sympathetic-adrenal system, result in increased occupation of a specific type of adrenoceptor that has a high affinity for NE and is predominantly located in PFC and associated with EF (Ramos & Arnsten, 2007). At increases beyond a moderate level, however, this type of receptor becomes saturated and adrenoceptors with a lower affinity for NE become active. These receptors are predominantly located in subcortical and posterior brain regions associated with reflexive and reactive responses to stimulation. In this way, levels of NE act to influence the neural response to stimulation, promoting neural activity in PFC associated with reflective and reasoned responses to stimulation at moderate levels of arousal, whereas at high levels, NE reduces neural activity in PFC and increases neural activity in brain areas associated with reactive, automatized responses to stimulation (Arnsten, 2000). Similarly, of the two types of glucocorticoid receptors in the brain, glucocorticoid (GR) and mineralocorticoid (MR), GRs are less sensitive to glucocorticoids than MRs and therefore remain largely unoccupied at low levels of stress arousal. However, with increasing stress and moderate glucocorticoid increase, GR occupation increases, supporting synaptic long-term potentiation. Increases in glucocorticoids with stress arousal beyond a moderate level, indicating increasingly high GR occupation, however, are associated with synaptic long-term depression rather than long-term potentiation (de Kloet, Oitzl, & Joels, 1999; Erickson, Drevets, & Schulkin, 2003).

The inverted U relation between stress levels and EFs is a manifestation at the neural level of the relation between arousal and performance that Yerkes and Dodson (1908) first described. In the Yerkes-Dodson principle, arousal at moderate levels increases performance on complex tasks but at very high or very low levels impairs performance. In this relation between stress and performance, however, the inverted U is specific to complex tasks. Although not widely recognized, Yerkes and Dodson in their original and subsequent publications demonstrated that arousal is positively and linearly related to performance on simple tasks and behaviors such as attention focusing and reactivity (Diamond, Campbell, Park, Halonen, & Zoladz, 2007). As such, in keeping with the biological sensitivity to context model, high levels of stimulation early in life, whether positive or negative, increase physiological reactivity and prime stress response systems (Ellis, Essex, & Boyce, 2005). In supportive contexts, this stimulation results in the development of physiology that is

conductive to reflective self-regulation, whereas in unsupportive, less predictable contexts, it leads to the development of physiology that is conducive to high behavioral reactivity and low reflective self-regulation.

Stress in the context of poverty

In humans, primarily in research with adults, chronically stressful environments result in sustained demands on stress response systems that are ultimately pathogenic in a variety of disease states, a phenomenon known as allostatic load (McEwen, 2000; McEwen & Wingfield, 2003). Although it is not yet established whether chronically stressful environments early in life affect the development of stress response systems in children to the extent seen in animal models, increased allostatic load is apparent in response to chronic environmental stressors in children living in poverty and similarly related to health outcomes (Evans & Kim, 2007). Given the relation of EFs to the development of cognitive and social competence in children, the effect of early stress on PFC corticolimbic connectivity and functioning seen in animal models suggests one pathway through which risk for delayed cognitive development and susceptibility to learning disorders and psychopathology is increased in children in poverty (Graham, Heim, Goodman, Miller, & Nemeroff, 1999). As we noted above, research in animal models suggests that one mechanism of this effect of poverty on child development is through structural effects of early stress on brain development in key areas important for EFs and stress regulation. Encouragingly, however, research with adult animals as well as humans suggests the reversibility to some extent of the effects of short-term stress on PFC neural circuitry and EFs (Liston, McEwen, & Casey, 2009; Radley et al., 2005). Furthermore, as we describe in detail below, animal models suggest that early intervention alters the behavioral and cognitive if not necessarily the neural consequences of early stress on development.

In addition to possible structural effects of early stress on the brain, it is also important to recognize the general relation between individual differences in stress reactivity and context. High reactive children in supportive environments are more likely to exhibit glucocorticoid and catecholamine levels that are well regulated and conducive to synaptic long-term potentiation in PFC and to the development of EFs and self-regulation abilities. In contrast, high reactive children in less supportive rearing circumstances are more likely to exhibit high glucocorticoid and catecholamine levels that are not well regulated and therefore not conducive to long-term potentiation and to EF and self-regulation. This is because higher levels of social support are associated with faster glucocorticoid (Dickerson & Kemeny, 2004) and presumably catecholamine recovery from stress. Although children in both contexts are stress reactive, those in more supportive contexts are more likely to exhibit efficient regulation of stress reactivity. For children in less supportive contexts, glucocorticoid and catecholamine receptor occupation is more likely to reach a point at which stress acts to take PFC “offline” (Arnsten & Li, 2005) and to result in reactive responses to stimulation associated with subcortical and posterior brain systems rather than reflective and reasoned responses associated with PFC.

In the developmental psychology literature, this general relation between reactivity and the quality of early experience is described in the theory of differential susceptibility to rearing influence (Belsky, Bakermans-Kranenburg, & van Ijzendoorn, 2007). In an increasing number of studies examining the differential susceptibility theory, infants and young children characterized by high levels of behavioral reactivity and negative emotionality are particularly likely to exhibit optimal regulation of behavior in high-quality environments but unfavorable outcomes in low-quality environments (Blair, 2002; Belsky, Hsieh, & Crnic, 1998; van den Boom, 1994).

A number of studies have also indicated that very high or very low levels of stress reactivity and difficulty with the up or down regulation of stress reactivity are associated with problems with EFs and self-regulation. Research on the stress response has appropriately focused on the deleterious consequences of atypically high or low stress levels, as indicated by cortisol, on development (Gunnar & Donzella, 2002; Gunnar, Tout, de Haan, Pierce, & Stansbury, 1997). In similar keeping with the inverted U relation between stress levels and EFs, studies of typically developing children, both in low-income and in middle-income homes, indicate that moderately higher levels of cortisol are associated with better performance on measures of EFs and self-regulation (Blair, Granger, & Razza, 2005; Davis, Bruce, & Gunnar, 2002). Although similar relations likely exist between catecholamine levels and EFs in children, no studies to date have demonstrated these relations because of the difficulty of noninvasively assessing catecholamine levels. However, recent work with a surrogate marker of sympathetic activation present in saliva, the protein alpha amylase, shows promise (Granger, Kivlighan, El-Sheik, Gordis, & Stroud, 2007).

Stress and development: Caregiving as a mechanism

Although animal models designed to examine the effects of early stress on development make use of a variety of types of stressors, of strong interest to child development researchers has been the examination of early rearing stress associated with naturally occurring variation in maternal behavior in the rat. Building on a research tradition that spans much of the 20th century, research in behavioral neuroscience has demonstrated that extended maternal separation and low levels of maternal specific maternal behaviors in rats are associated with problems with stress regulation and adverse cognitive and behavioral outcomes in offspring (Meaney, 2001). In contrast, brief maternal separation/handling of rat pups increases levels of maternal behaviors, notably licking and grooming upon reunion, that promote gene expression associated with the density of GR receptors in the hippocampus, the development of an efficient HPA stress response system, and what can be considered as advantageous cognitive and social developmental outcomes in typical environments with adequate resources (Caldji, Diorio, & Meaney, 2000; Liu et al., 2000; Liu et al., 1997; Weaver et al., 2004).

Although early rearing environments for children differ in many ways from those of rats, the caregiving environment for children facing low SES is more likely than typical home environments to be disorganized and lacking in appropriate stimulation and support, thereby creating conditions that are stressful for children (Evans, 2004; McLoyd, 1998; Repetti, Taylor, & Seeman, 2002). Low-quality early caregiving is highly likely to serve as a primary source of stress for children or as a mediator of environmental stressors, with stressful social and physical conditions of the home leading to stress on parents and to low-quality early care.

Several studies have demonstrated that economic adversity is associated with disruptions in parenting behaviors and that psychological distress in parents is linked to poor cognitive and behavioral outcomes in children (Brody & Flor, 1998; Jackson, Brooks-Gunn, Huang, & Glassman, 2000). However, the extent to which the experience of psychologically distressed parenting in poverty is stressful for children, and if so, whether problems with the regulation of the stress response in children in poverty is linked to poor developmental outcomes, is not well known. Studies have indicated specific contexts, more prevalent in low-income homes, that are more stressful for infants and young, such as nonoptimal attachment relationships with primary caregivers (de Haan, Gunnar, Tout, Hart, & Stansbury, 1998; Gunnar, Brodersen, Nachmias, Buss, & Rigatuso, 1996) and maternal unavailability (Bugental, Martorell, & Barraza, 2003; Haley & Stansbury, 2003). And numerous studies have shown high-quality caregiving to moderate the effects of poverty on child development outcomes

(e.g., Ramey & Campbell, 1991; Wyman et al., 1999). The extent to which such high-quality caregiving may have moderated any effects of stress on development, however, is not clear.

As we noted above, research on the stress response in adolescent children in poverty has indicated increased allostatic load associated with cumulative risk in the home, including physical (crowding, noise) and psychosocial (violence, family turmoil) risk factors. Importantly, the relation between cumulative risk and allostatic load was present only when combined with low levels of maternal responsiveness (Evans, Kim, Ting, Teshler, & Shannis, 2007). Similarly, in a large, predominantly low-income sample followed longitudinally, baseline cortisol was low and cortisol reactivity and regulation were high in response to a moderate stressor in infants at age 7 months whose mothers were high in sensitivity. Furthermore, when these infants were followed up at age 15 months, overall cortisol levels, both at baseline and in response to stress, were reduced for children of mothers high in sensitivity (Blair et al., 2008). The idea here, which finds support in the animal literature (Catalani et al., 1993; Parker, Buckmaster, Justus, Schatzberg, & Lyons, 2005), is that early care and controlled experience with stress help to produce an overall lower level of physiological reactivity to stress. Consistent with an emphasis on the role of early caregiving in animal models of stress (Meaney & Szyf, 2005), and on the relation between stress reactivity and context (Ellis, Essex, & Boyce, 2005), these studies suggest that relations between stress reactivity and later developmental outcomes are in part determined by early caregiving.

Stress and development: Implications for early intervention

Given evidence relating early rearing adversity to atypical stress responding and poor cognitive and social developmental outcomes in animal models, it is notable that these models of early stress also indicate that environmental enrichment can offset disadvantage associated with early stress exposure. For example, Francis, Diorio, Plotsky, and Meaney (2002) demonstrated reversal of the effect of early stress associated with maternal separation during the neonatal period on the HPA response to stress, as indicated by corticosterone levels, and on learning and memory among rats receiving environmental enrichment. Effects on corticosterone and behavior, however, could not be attributed to expected changes at the neural level in terms of primary processes that influence stress reactivity. Similarly, Bredy, Humpartzoomian, Cain, and Meaney (2003) demonstrated that the effects of low maternal caregiving competence on hippocampally dependent learning and memory could be reversed at the behavioral level through environmental enrichment but that the physiological function of the hippocampus was not altered in expected ways. The findings of Francis et al. (2002) and Bredy et al. (2003) indicate that the effects of enrichment as seen at the behavioral level are not necessarily mirrored in expected changes at the biological level (Fernandez-Teruel et al., 2002). Rats experiencing prenatal or postnatal stress followed by enrichment continue to some extent to look at the neural level like rats experiencing low early caregiving competence without enrichment. Consistent with the adaptive nature of the stress response, however, the findings of Francis et al. (2002) and Bredy et al. (2003) suggest a functional reversal of the effects of early stress in which environmental enrichment leads to compensatory neurobiological changes, perhaps associated with changes in frontal cortex, that alter the behavioral and cognitive consequences of high reactivity.

Neurobiological evidence from animal models suggests that early education and care interventions for children in poverty may work in part by enhancing self-regulation development in ways that overcome early risk. In the evaluation of model early intervention programs, there is an increasing recognition of the importance of personality and social competence factors associated with self-control and on aspects of cognition, such as EFs, that are distinct from general intelligence (Heckman, 2006, 2007). In what is termed human

capability formation, early inputs (parenting quality, effective preschool and early elementary education) appear to influence cognitive and personality factors that promote the capacity of the individual to benefit from later opportunities. Findings from the early intervention literature provide a wealth of evidence in favor of the efficacy of improving life outcomes in children in families at high economic and psychosocial risk (Bryant & Maxwell, 1997). The provision of competent caregiving in early compensatory care and education would be expected, in theory, to have effects on developing self-regulation in children experiencing high levels of disrupted caregiving that are in part mediated through stress reactivity and PFC functioning. Most, though not all, intervention studies have either targeted parenting behaviors directly (Barnard, 1997; Olds, 2002) or, as in the case of center-based care, provided a type of care that is characterized by high levels of caregiver sensitivity and careful structuring of experience (Gross, Spiker, & Haynes, 1997). In general, the literature on parenting and infant and child stress in the context of low SES suggests that one way in which early intervention has enhanced child developmental outcomes is through reducing the exposure of infants and children in treated groups to a type of care that is stressful in the context of adversity.

Conclusion

Although evidence from animal models is compelling because of its specificity and high level of control, the extent to which neural and physiological mechanisms relating stress, early caregiving, and developmental outcomes might be at work in human populations remains open to question. The breadth and diversity of influences on human development is far greater than that examined in nonhuman animal models (Gottlieb & Lickliter, 2004). Furthermore, there are numerous influences on neural plasticity in addition to early care, such as increased activity in enriched environments (Panksepp, Burgdorf, Turner, & Gordon, 2002; van Praag, Kempermann, & Gage, 2000), as well as individual differences in genetic background that are relevant to relations between the stress response and early environment.

Individual differences in genetic background figure largely in relations between stress and development. Increasing numbers of studies in human populations indicate that single nucleotide polymorphisms associated with glucocorticoid and catecholamine activity in PFC corticolimbic circuitry are related to variation in EF and perhaps, to some extent, susceptibility to early stress effects on cognition (Hariri, Drabant, & Weinberger, 2006; Pezawas et al., 2005; Tan et al., 2007). Examples of gene-environment interaction in the study of stress and development (Caspi et al., 2003) have also made clear that research incorporating information on genetic background can lead to a more specific understanding of the mechanisms through which the stress response and early care are likely to influence development and for whom effects will be largest. Of greatest relevance, however, is evidence of epigenetic modifications of DNA expression through early experience. Remarkably, research has shown that the maternal licking and grooming behavior in the rat that is so central to the development of the HPA stress response system produces its effect through molecular mechanisms that alter the epigenetic state of the gene that codes for GR receptor density in the hippocampus (Meaney & Szyf, 2005; Weaver, 2007; Weaver et al., 2004). And of further profound epigenetic interest is evidence indicating that levels of glucocorticoids have widespread influences on gene expression in a variety of gene classes (Datson, Morsink, Meijer, & de Kloet, 2008).

Emerging evidence of epigenetic modification of genes associated with the stress response, self-regulation, and physical and mental health is consistent with a probabilistic epigenetic model in which context and behavior play powerful roles in human development (Gottlieb, 1998, 2002). Consideration of PFC corticolimbic functioning in terms of probabilistic

epigenesis and developmental models such as the differential susceptibility model and the biological sensitivity to context model helps to illuminate the complexity of relations between nature and nurture in development. As outlined in the biological sensitivity model, both very high and very low quality of early experience can be expected to lead to high stress reactivity. This reactivity is more likely in high-quality care to promote aspects of cognition and behavior important for reflective self-regulation but in low-quality care to promote reactive responses to stimulation. In terms of probabilistic-epigenesis, it is necessary to think developmentally when considering early experience and to consider how stress reactivity in children may or may not lead to specific outcomes. Determinist developmental programming hypotheses through which early life experiences are thought to inexorably lead to later life outcomes are inconsistent with fundamental principles known to characterize development (Cairns, Elder, & Costello, 1996). As such, evidence relating rearing experience to self-regulation in animal models provides neurobiological evidence of one way in which environmental adversity associated with poverty and, conversely, early compensatory education and care, may affect developing competence in human populations. Chronic early rearing stress affects the activity of stress response systems with consequences for the regulation of cognition and behavior. As a result, early life stress, which is more frequent in the context of poverty, would attenuate developing self-regulation in children characterized by high reactivity and begin to shape developmental trajectories toward nonoptimal outcomes. Conversely, early compensatory education and care interventions to promote learning and increase the regulation of reactivity through various activities with caring and supportive others in a predictable, stimulating environment would be expected to promote competencies such as EF and self-control that are important contributors to ongoing success in life.

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