CHAPTER 5

The Influence of Early Socialization Experiences on the Development of Biological Systems

RENA REPETTI, SHELLEY E. TAYLOR, and DARBY SAXBE

Most psychologists who study socialization assess how those experiences shape social, emotional, cognitive, or health outcomes in children. Our chapter considers the effects that early experiences may have on biological systems during infancy and childhood a perspective that may inform the developmental outcomes discussed in other chapters in this handbook. We present an overview of a wide range of animal and human studies that investigate how early rearing experiences help to guide the functioning and development of the central nervous system (CNS) and endocrine and immune systems of offspring.

Nursing offers one of the clearest examples of how mothers can act as external regulators of basic biological functions in infancy in the short term and play an important role in long-term biological development. In addition to providing nourishment, maternal cells in breast milk boost the infant's immune system, supplying some of the protection from infection and disease that the offspring's immature system is not yet able to provide. Nursing also promotes skin-to-skin contact between mothers and their infant, which leads to immediate reductions in some stress response indicators (Mooncey, Giannakoulopoulos, Glover, Acolet, & Modi, 1997). In the long term, skin-to-skin contact can speed the maturation of vagal tone and sleep cycles (Feldman & Eidelman, 2003), and research suggests that tactile stimulation may enhance growth and behavioral development in human infants (Kuhn & Schanberg, 1991). Other evidence indicates that in some mammals ventral contact between mother and offspring and maternal licking and grooming behaviors lead to an immediate reduction in biological stress responses in their young (Gunnar, Gonazalez, Goodlin, & Levine, 1981; Liu et al, 1997; Mendoza, Smotherman, Miner, Kaplan, & Levine, 1978). In the case of rats, licking and grooming behaviors may also help to shape the long-term ability of offspring to prepare for and react to stress on their own (Cirulli, Berry, & Alleva, 2003). Even while the effects of early parenting experiences on biological development are being uncovered, investigators are beginning to dig deeper to discover the mechanisms by which parenting helps to craft those biological systems. For example, research discussed herein shows that early experiences can induce changes in the expression of genes that are required for neuronal development.

If physical contact with a mother and maternal behaviors such as licking and grooming play a role in shaping infant biological systems, how does the developing organism respond without the reliable presence of a sensitive parent? The chronic activation of biological stress-response systems may play a role in this process. This notion is consistent with a model of the long-term mental and physical health consequences of growing up in families characterized by conflict and aggression or by relationships that are cold, unsupportive, and neglectful. Repetti, Taylor, and Seeman's (2002) risky families model proposed that these early rearing environments can set in motion a cascade of risk reflected in disturbances in physiological and neuroendocrine system regulation, as well as deficits in the control and expression of emotion and in social competence. According to this model, the early disruptions in biological, emotional, and social development have cumulative, long-term effects in adolescence and adulthood, leading to a wide variety of physical and mental health problems.

The risky families model draws on the concept of allostatic load (McEwen, 1998; McEwen & Stellar, 1993). Allostasis is the process of activating neural, neuroendocrine, and neuroendocrine-immune mechanisms to adapt physiologically in the face of potentially stressful challenges. According to the allostatic load model, a period of recovery following physiological arousal is essential for the proper functioning of biological regulatory processes in the body; allostatic load can result when regulatory systems are overstimulated. Repetti et al. (2002) argued that the repeated activation of allostatic systems in risky family environments can disrupt the child's ability to mount a modulated physiologic/neuroendocrine response to stress and to quickly recover from that response. Chronic allostatic load, which can lead to disease over long periods, can result in maintenance of neuroendocrine activation following exposure to a stressful situation as indicated in poor recovery from stress. Long-term effects may include a flattening of the circadian rhythm of cortisol output, an indicator of hypothalamic-pituitary-adrenocortical (HPA) activity. We propose that consistent and sensitive parenting helps to control the frequency and timing of social challenges in the early rearing environment and to facilitate development of appropriate patterns of physiological regulatory processes when the young are confronted with potentially stressful situations. The links that researchers are beginning to uncover between physiological and emotional responses to stress in childhood (El-Sheikh, Cummings, & Goetsch, 1989) suggest that patterns of biological stress responding laid down in childhood may be tied to social and emotional development as well.

Although the focus of our chapter is clearly ontological, we recognize that phylogenetic questions about the evolutionary processes that may have resulted in these developmental trajectories are critical. Some of the biological responses to early negative experiences discussed in this chapter may represent adaptations. The functions of those responses (i.e., the evolutionary benefits that led to their selection) require explication. By investigating the potential short-term benefits of what appear to be adverse outcomes in

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the long run, we may come to understand some of the adaptive trade-offs that organisms make in harsh rearing environments (Simpson & Gangestad, 2001). For example, some of the evidence reviewed in our chapter may point to a quickened pace of maturation as one such trade-off. Among nonhuman primates, some of the immediate biological reactions to maternal separation include increased release of growth hormone (Laudenslager et al., 1995) and an early enhanced immune response (Coe, Lubach, Ershler, & Klopp, 1989). In the longer term, these reactions may set the stage for an acceleration of aging processes. The later outcomes of stressful early rearing conditions include earlier pubertal timing in humans (Surbey, 1990) and an increased and early vulnerability to disease in both human and nonhuman primates (Repetti et al., 2002). Because of the possibility of adaptations that maximize short-term survival benefits, even at the expense of long-term outcomes, the assignation of a "positive" or "negative" label to biological outcomes discussed in this chapter is not always possible, nor desirable. Therefore, readers who are accustomed to thinking about socialization with respect to "good" and "poor" developmental outcomes may find that the descriptions of research findings in this chapter at times seem incomplete.

Any research review must reflect the state of the field, and as should already be obvious, ours will rely heavily on studies of nonhuman mammals, particularly rats and monkeys. The rate of ontogeny of the animals commonly used in these studies and the experimental designs and invasive procedures that are possible have greatly advanced our understanding of how early rearing experiences can influence the biology of mammalian offspring. As psychologists interested in socialization, we believe it is critical to understand the concepts and findings in these fields. One of the goals of this chapter is to introduce basic research paradigms, methods, and results to socialization researchers who might not be familiar with this literature. The complexities of the biological and behavioral systems under investigation, compounded by differences among species, conspire to make this a difficult task. Nonetheless, we strive to summarize human and animal research while keeping in mind the unique socialization demands placed on human mothers and fathers.

Given the interdependence of the biological processes discussed here, the echoes of both short-term and long-term changes in one biological system should be observed throughout the organism. Indeed, the animal and human research summarized in this chapter suggests that the impact of early rearing experiences on development can be pervasive, influencing the offspring's CNS, endocrine, and immune systems. For the purposes of organizing our review of the research literature, we separate "biological systems" into different subsections of the chapter. However, these distinctions are clearly artificial when it comes to the functioning of those systems and the development of offspring.

Our chapter begins with the CNS. We present research on the effects that early experiences can have on brain structure and function, in particular neuronal activity. The second section discusses evidence from both animal and human studies that childhood family environments and other early rearing experiences influence the development of the major neuroendocrine stress-response systems, the HPA axis, and the sympathetic and parasympathetic branches of the peripheral nervous system. The third section summarizes research on the impact that early social deprivation, particularly maternal separation, has on immune functioning. The final literature review section presents research findings that link early rearing conditions to growth and sexual development in human

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ts that early expel activity. The secat childhood famevelopment of the e sympathetic and d section summamaternal separapresents research opment in human and nonhuman primates. We close with conclusions, comments about the current state of research, and suggestions for future research directions.

CENTRAL NERVOUS SYSTEM RESPONSES TO SOCIALIZATION EXPERIENCES

Research indicates that parenting behavior has enduring effects on the development and functioning of the mammalian brain. Here we summarize findings from research literatures that relate early experiences to neurotransmitter regulation, in particular the "diffuse modulatory systems," as well as brain plasticity, neuronal density and viability, the expression of genes involved in neuronal development, and electroencephalogram (EEG) patterns.

Brain activity consists of an orderly set of chemical reactions. The chemicals that regulate the transmission of neural impulses in the brain are neurotransmitters, which are released by presynaptic elements upon stimulation and activate postsynaptic receptors. There are a large number of neurotransmitter systems in the mammalian brain, each one consisting of the transmitter molecule as well as the structures and processes involved in its synthesis, storage, action, reuptake, and degradation. Many of the regulatory functions of the brain are controlled by three neurotransmitter systems: norepinephrine, dopamine, and serotonin. These monoamines comprise "diffuse modulatory systems." These systems have numerous projections that are widely dispersed in the brain and they mediate broad protracted actions involving level of arousal and mood, and individual systems appear to be essential for aspects of motor control, memory, motivation, and metabolic state. For instance, in addition to their role in the peripheral nervous system, norepinephrine-containing neurons are found in the locus ceruleus in the pons from which they fan out to almost every part of the brain. These cells seem to be involved in the regulation of attention, arousal, sleep-wake cycles, learning, memory, anxiety, pain, mood, and brain metabolism. Serotonin-containing neurons are mostly clustered in the dorsal raphe nuclei and project to different regions of the brain. They are involved in the control of sleep-wake cycles, and in the different stages of sleep and have been implicated in the control of mood and certain types of emotional behavior, including aggressive behavior and clinical depression. Although there are dopamine-containing neurons scattered throughout the brain, there are two main projections from the midbrain. One group of dopaminergic cells arises in the substantia nigra and projects axons to the striatum (i.e., the caudate nucleus and the putamen); these cells facilitate the initiation of voluntary movement. The origin of the other group of cells is in the ventral tegmental area of the midbrain with axons that innervate an area that includes the frontal cortex and the limbic system. This projection is somehow involved in reward systems and emotion (Bear, Connors, & Paradiso, 1996).

Experimental evidence shows that early rearing conditions can influence the development of each of these important modulatory systems, as well as gamma aminobutyric acid (GABA), the major inhibitory neurotransmitter in the CNS. Many psychoactive drugs affect these neurotransmitter systems, and, because of that, the systems play a very important role in current thinking and research on the biological basis of certain psychiatric disorders. However, because the exact functions of these systems in the brain are not understood, we have only a limited understanding of the possible behavioral or functional significance of the changes in those systems that result from the early environmental inputs described in

this section. Absent a mapping of the developmental consequences of observed changes in neurotransmitter systems, it is not possible to label individual research findings as contributing to beneficial or detrimental outcomes for the developing mammal.

Animal Studies

The animal research reviewed here focuses on the effects that early rearing experiences such as maternal separation, human handling, and social isolation have on the developing CNS in rodents and nonhuman primates. We know that maternal deprivation has an impact on the developing serotonin and dopamine systems of the infant rat. For example, postsynaptic serotonin receptors in the cortex and the hippocampus increased in number after infant rats were separated from their mothers for 24 hours (Vazquez, Lopez, Van Hoers, Watson, & Levine, 2000). Because the limbic-HPA axis is capable of modulating the serotonin system, modifications in the serotonin system in response to maternal separations are likely tied to the hyperresponsiveness of the limbic-HPA axis that also results from maternal deprivation (as discussed in the next section). There also appears to be a broad role for mesolimbic dopamine neurotransmitter systems in responses to social isolation, including maternal deprivation, although the specific effects may differ at different ages. For example, maternally deprived rats show enhanced release of dopamine in response to an amphetamine challenge (Hall, Wilkinson, Humby, & Robbins, 1999; Kehoe, Shoemaker, Arons, Triano, & Suresh, 1998). The dopaminergic pathways are critical to the brain's control of movement, and changes in the dopamine system are thought to play a role in the altered locomotive activity that is associated with early isolation experiences in rats.

Human handling of rat pups induces changes in maternal behavior; mothers of recently handled pups exhibit increased licking/grooming and arched-back nursing¹ (Liu et al., 1997). Research suggests that these forms of maternal stimulation mediate the human handling effects observed in rodents (though perhaps not the handling effects observed in other mammals, such as rabbits) (Denenberg, 1999). The impact of both handling and maternal deprivation on the rat brain extends to the major inhibitory neurotransmitter system. Rat pups subjected to handling showed higher GABA_A and benzodiazepine receptor bindings as adults. This contrasts with the alterations observed in adult rats subjected to repeated separations from their mothers during the first 3 weeks of life; they showed reduced GABA_A and benzodiazepine receptor bindings (Caldji, Francis, Sharma, Plotsky, & Meaney, 2000; Francis, Caldji, Champagne, Plotsky, & Meaney, 1999). These changes may partially mediate some of the behavioral responses to early rearing conditions that are observed in adult rats, such as decreased expression of fear-related behaviors in response to early handling and enhanced fearfulness among those exposed to early maternal separations.²

The handling of infant rat pups by humans also appears to improve the efficiency of synaptic connections in the rat brain and enable long-term learning through long-term potentiation. Long-term potentiation is a process that makes the links between certain synapses more powerful over time; when one synapse repeatedly triggers the firing of another, that second synapse eventually becomes more sensitive and responsive to the first. Early handling of rats seems to increase the amplitude of long-term potentiation in the hippocampus, suggesting that early handling and enhanced maternal care may bolster the offspring's eventual ability to learn (Cirulli et al., 2003).

Influences of Early Socialization Experiences

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re the efficiency of hrough long-term s between certain rs the firing of anonsive to the first. otentiation in the re may bolster the Early maternal separation seems to affect the expression of neurotrophins in rats. Neurotrophins, such as nerve growth factor, are proteins that help establish connectivity in the nervous system and promote the density, viability, and differentiation of neurons. As such, they play an important role in brain plasticity. One study found that a 1-hour maternal separation increased the expression of nerve growth factor in the hippocampus of 3-day-old rats, while a follow-up study using a longer separation time found increased nerve growth factor expression in the hypothalamus, hippocampus, and other CNS regions (Cirulli, Alleva, Antonelli, & Aloe, 2000). Maternal licking has also been shown to increase nerve growth factor. In addition to their function as neurotransmitters, monoamines have been shown to act as neurotrophic factors during cortical development. Given the effects of maternal separation and licking on monoamine systems and neurotrophins, it is not surprising that these early maternal experiences have been linked to the growth of nerve fibers in the rat brain (e.g., Braun, Lange, Metzger, & Poeggel, 2000).

Some of the research discussed in this chapter examines early environmental influences on gene expression in the rat brain (Caldji et al., 2000; Cirulli et al., 2000; Plotsky & Meaney, 1993; Vazquez et al., 2000). Gene expression can be studied by examining the amount of messenger RNA (mRNA) in a tissue sample. Messenger RNA molecules are the "templates" that encode the manufacturing instructions for proteins from strands of DNA. The amount of mRNA for a particular protein present in a tissue sample indicates the rate at which the gene for that protein was transcribed. For example, in one study researchers were interested in RC3 (neurogranin), a postsynaptic protein kinase C substrate that is expressed in the dendritic spines of some neurons. They found that rats exposed to an experimental condition comprised of moderate amounts of both maternal separation and handling showed elevated RC3 mRNA expression in the hippocampus when compared to rats that either were not separated from their mothers (no handling) or were exposed to briefer periods of separation and handling (McNamara, Huot, Lenox, & Plotsky, 2002). By showing that environmental factors, such as maternal separation and handling, may induce changes in the expression of genes that are required for the development of circuitry in the rat brain, this research is beginning to point to the mechanisms by which early experiences shape the development and functioning of the CNS.

Investigations involving nonhuman primates similarly point to an effect of early rearing conditions on developing neurotransmitter systems. This line of research grows out of observations of the behavioral and social deficits that some primate species show when reared in total or partial social isolation. For example, rhesus monkeys reared under conditions of social deprivation display numerous social deficits in affiliation (social responsiveness, sexual and maternal behavior, communication) as well as in feeding and drinking, exploratory behavior, and learning ability (Lewis, Gluck, Beauchamp, Keresztury, & Mailman, 1990). They also exhibit high rates of stereotyped and self-injurious behaviors, such as rocking, self-biting, and self-hitting. Studies of the neurobiological mechanisms that mediate these extreme and unusual behavioral deficits focus on the role of the monoamine neurotransmitter systems described earlier: norepinephrine, serotonin, and dopamine. In these studies, concentrations of neurotransmitter metabolites, obtained from samples of cerebrospinal fluid, are used as indicators of the activity of that neuronal system in the brain.

In one experiment, rhesus monkeys were raised under one of three conditions during the first month of life: mother-reared, mother-deprived, and "reared" by a terry-clothcovered surrogate mother. When samples of the monkeys' cerebrospinal fluid were tested, the surrogate-mother reared and mother-deprived monkeys had lower concentrations of norepinephrine compared to the mother-reared monkeys. However, there were no differences in the levels of dopamine and serotonin metabolites (Kraemer, Ebert, Schmidt, & McKinney, 1991). Other studies, however, have found that rhesus monkeys deprived of experience with a mother and critical aspects of peer interaction during the first 15 months of life had higher levels of metabolites of serotonin as well as lower concentrations of norepinephrine in cerebrospinal fluid (Kraemer & Clarke, 1990).

Concentrations of monoamine metabolites in cerebrospinal fluid do not provide a complete picture of the functioning of that neurotransmitter system. Therefore, it can be difficult to interpret the significance of increases or decreases of a neurotransmitter metabolite in cerebrospinal fluid. This is illustrated by the findings from a study of older adult rhesus monkeys (Lewis et al., 1990). Monkeys reared in total social isolation during the first 9 months of life were compared to monkeys that had been reared with peer and maternal contact. There were no differences in the concentrations of dopamine, serotonin, and norepinephrine metabolites in the cerebrospinal fluid taken from the two groups of monkeys. However, when a dopamine agonist (apomorphine) was administered to assess changes in dopamine receptors in the brain, the isolated monkeys had a much higher frequency of spontaneous eye blinking.³ Because the monkeys were tested in older adulthood (all older than 14 years), these findings suggest that early, prolonged social isolation results in long-term alterations in the functioning of dopamine receptors in the brain.

Another research paradigm manipulates the monkey rearing environment by altering the availability of food. The increased demands of a "variable foraging" environment, in which food is sometimes plentiful and easily obtained and sometimes not, appear to reduce maternal responsivity (Andrews & Rosenblum, 1991). Squirrel monkey mothers in high demand conditions have been observed to spend 60% more time foraging for food and stopped carrying their infants at earlier ages (Lyons & Schatzberg, 2003). In one study, bonnet macaques were reared by their mothers under two conditions. Some lived in laboratory breeding groups under stable ad libitum conditions and others experienced adverse variable foraging demands (mothers were sometimes required to dig through wood chips to obtain food) for a few months during their early life. Cerebrospinal fluid was sampled when the monkeys reached an age comparable to the peripubertal-young adult phases of human development. In this study, monkeys reared under the stressful foraging conditions had higher cerebrospinal fluid concentrations of all three monoamines that were tested: serotonin, dopamine, and norepinephrine (Coplan et al., 1998). Another study of bonnet macaques reared under the same two conditions examined the behavioral effects of probes of two neurotransmitter systems.⁴ The subjects who had been reared under variable foraging conditions were hyperresponsive to a probe of the norepinephrine system (yohimbine, an alpha-2 antagonist), but were hyporesponsive to a serotonin agonist (mCPP). Their behavioral reactions to the probes indicated that norepinephrine responses were exaggerated and serotonin responses were blunted compared to offspring reared by mothers under less stressful conditions (Rosenblum et al., 1994).

Studies by Suomi and associates suggest a role of maternal behavior in moderating genetic risk for serotonergic dysfunction. One study compared monkeys with two forms of the 5-HTT allele, a gene related to serotonin transport; the short form of the gene confers low serotonin reuptake efficiency, whereas the long form is associated with normal serotonin reuptake efficiency (Suomi, 1997). In addition, some of the monkeys were

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or in moderating with two forms of the gene conted with normal e monkeys were raised by their mothers and some were raised by peers. Being raised by peers is a risk factor for the development of a reactive, impulsive temperament and other deficits in social behavior, including more aggressive exchanges and less grooming. Monkeys with the short 5-HTT allele who were raised by peers showed lower concentrations of the primary central serotonin metabolyte (5-HIAA) than was true for monkeys with the long allele. But for monkeys raised by their mothers, primary serotonin metabolyte concentrations were identical for monkeys with either allele. This pattern clearly suggests a protective effect of maternal behavior on expression of genetic risk for low levels of serotonin. A promising direction for future research is the investigation of possible connections between early socialization experiences, serotonin functioning, and social behavior in monkeys.

Evidence also suggests that early adverse parenting experiences may cause neuronal metabolic impairments and affect neuronal density and integrity. Bonnet macaque infants reared by mothers exposed to variable foraging demand conditions for several months were studied 10 years later using proton magnetic resonance spectroscopic imaging, a method of detecting brain activity at the cellular level (Mathew et al., 2003). Compared to a matched control group, variable foraging demand monkeys displayed significantly decreased N-acetylaspartate (NAA)/Creatine (Cr) and increased glutamate-glutamineaminobutyric acid (Glx)/Cr ratios in the anterior cingulate. NAA is typically used as a marker to assess neuron density and viability, so this result would suggest decreased neuronal viability. The finding of a lower NAA/Cr ratio in the anterior cingulate in the variable foraging demand group mirrors a previous finding in human teenagers with posttraumatic stress disorder (De Bellis, Keshavan, Spencer, & Hall, 2000), and other reports on adult posttraumatic stress disorder have found reductions in NAA in hippocampal or medial temporal lobe regions (Schuff et al., 1997). The investigators also argue that because heightened glutamate neurotransmission in the prefrontal cortex may partially mediate HPA activation, the GLx findings (showing increased glutamate functioning in the variable foraging demand group) may be an indication of heightened HPA activity in those subjects.

The impact of the social environment on neurotransmitter systems is not limited to early rearing experiences. In golden hamsters, for example, social subjugation during puberty in the form of daily exposure to aggressive adults resulted in increased serotonin innervation of the anterior hypothalamus (as well as a decrease in vasopressin levels). In addition, subjugated animals were more likely to attack younger and weaker animals but were less likely to attack animals of similar age and size (Delville, Melloni, & Ferris, 1998).

Although it may be too soon to say how each of the CNS alterations reported in animals might affect subsequent behavior and functioning, we can safely conclude at this point that there is an association between social experiences during development and neurobiological changes in several diffuse modulatory systems in the brains of rats and nonhuman primates.

Studies of Human Infants and Children

Human research is much more limited than the studies summarized previously both because of the invasiveness of procedures to assess neurotransmitter functioning and because of the need to use nonexperimental designs in socialization studies. However, find-

ings are consistent with the animal literature in linking adverse early socialization experiences with differences in the developing neurotransmitter profiles of children. For example, one study compared infants of mothers who, on the basis of a 3-minute play interaction, had been classified as "intrusive" (rough tickling, poking and tugging, tense or fake facial expressions) or "withdrawn" (flat affect, rare touching and vocalizing, disengaged behaviors). Offspring of the intrusive mothers showed higher levels of monoamines (dopamine, epinephrine, and norepinephrine) in urine collected at 6 months of age, compared to infants whose mothers were withdrawn (Jones et al., 1997). The absence of a normal control group in this study makes it difficult to interpret these findings. Moreover, the long-term significance of the neurotransmitter profiles that were observed is not known. However, dysregulation of these neurotransmitters is associated with behavioral problems and psychopathology, including aggression, depression, and anxiety (Berman, Kavoussi, & Coccaro, 1997; Micallef & Blin, 2001; Thase, Jindal, & Howland, 2002).

Because the serotonergic nervous system appears to play a role in aggression, a few researchers have focused on the link between serotonin and abusive or aggressive family environments. An indirect approach to assessing central serotonergic activity in humans is the examination of responses to a serotonin challenge. An increase in serotonin activity in the brain stimulates a rise in prolactin measured in blood samples. The magnitude of the increase in peripheral prolactin is treated as an index of the increase in serotonergic activity in the CNS. An example of this approach is found in research indicating dysregulation in the serotonergic system of children who have been maltreated and abused. One study compared depressed-abused children to two groups of nonabused children; one group included depressed children and the other group consisted of nondepressed, control children (Kaufman et al., 1998). The majority of the abused children had experienced multiple forms of maltreatment, such as physical or sexual abuse. and half were living under adverse conditions, including homes in which there was ongoing spousal and emotional abuse. In response to a serotonergic challenge (intravenous administration of a serotonin precursor, L-5-HTP), the abused children secreted significantly more prolactin, indicating increased sertonergic activity. Moreover, this indicator of central serotonergic functioning (total prolactin post-L-5-HTP) was significantly correlated with ratings of aggressive behavior. The precise nature of the association between aggression and serotonin is not known. However, there is some support for a causal role of dysregulated serotonin functioning in the aggressive behavior of psychiatric patients (Berman et al., 1997).

Another study examined prolactin responses to fenfluramine hydrochloride, which increases the level of serotonin in CNS synapses (through release of serotonin from nerve terminals and by inhibiting the process of reuptake). In a sample of younger brothers of convicted delinquents, all of whose families were impoverished, less maternal regulation of child behavior was associated with a larger prolactin response to the challenge. Lower scores on the "encouragement of maturity" subscale of the HOME (Home Observation and Measurement of the Environment Inventory), which is based on observers' ratings of the degree of parental limit setting, were associated with larger increases in the boys' central serotonergic activity. A stronger prolactin response was also linked to greater aggression in this sample of prepubertal boys (Pine et al., 1997). In another report, based on the same study, an inverse relationship was found between harsh parenting and the density of 5-HT_{2A} receptors on platelets (a peripheral index of CNS serotonin profile) (Pine et al., 1996). Lower receptor density was linked to mother–child relationships characterized by

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Electroencephalographic Studies

Neurotransmitters regulate the transmission of electrical charges across neurons. The EEG uses scalp recordings to measure the resulting pattern of electrical activity in the brain. EEG studies have found differences in relative right- and left-hemisphere activation that seem to correlate with temperament, early childhood experiences, and genetic propensity. Davidson (1995, 1998) and Fox (1994) have suggested that affective styles connected with emotion regulation, such as approach and withdrawal behaviors, can be related to both state-dependent and more stable individual differences in cerebral asymmetry. The left frontal region typically appears activated during the expression of approach emotions like curiosity and joy, while the right frontal region activates during distress, fear, and other withdrawal emotions.

Several studies suggest a relationship between maternal psychopathology and infants' EEG patterns, although it is unclear whether this relationship derives from genes, maternal interaction style, or both. A study of 159 mother-infant pairs found that compared with a control group, the 13-15-month-old children of mothers diagnosed with depression were less likely to show relative left-hemisphere activation and more likely to show relative right-hemisphere activation (Dawson & Ashman, 2000). Insensitive mothering-both intrusive and withdrawn behaviors-partially mediated the association between depression and infant EEG in all mothers and fully mediated this association in the mothers who became depressed only after birth, providing support for the idea that parenting style influences infant EEG. In the study of withdrawn and intrusive mothering mentioned previously, Jones et al. (1997) found that the children of withdrawn mothers showed greater relative right frontal asymmetry than infants of intrusive mothers, whose EEG patterns showed greater relative left frontal EEG asymmetry. In a subsequent study, infants of withdrawn mothers, in comparison to infants of intrusive mothers, showed greater relative right frontal asymmetry. When a stranger modeled surprised and sad expressions, however, the infants of intrusive mothers shifted toward greater relative right frontal EEG asymmetry (Diego et al., 2002). While parenting style may influence EEG patterns, it remains unclear whether individual differences in EEG asymmetry stem from early experience or from genetic inheritance. When further elaborated, this body of research may eventually provide another line of evidence suggesting that early childhood experiences shape the brain's functioning and development.

Both animal and human research point to early rearing experiences playing a role in the development and functioning of neurons and neurotransmitter systems. However, the precise nature of the effects of socialization are difficult to interpret with currently available data. It is challenging to integrate findings from studies that are based on different species, focus on different kinds of early rearing conditions, and use a variety of strategies to assess multiple neurotransmitter systems and the activity of neurons in different parts of the brain. Moreover, because neuroscientists do not yet understand precisely how the diffuse modulatory systems function in the brain, we do not yet know what the implications are for behavior, adjustment, or development when neuron and neurotransmitter

differences are observed under various rearing conditions. The different stages of development at which subjects are studied adds another layer of complexity to the picture. Nonetheless, the research does indicate that the development and activity of neurons and neurotransmitter systems in the mammalian brain are affected by a wide variety of rearing conditions, ranging from various degrees of maternal deprivation, to rearing by mothers under high demand, to human parenting that is intrusive, abusive, harsh, and unregulated. These socialization experiences appear to change the development and functioning of the CNS in ways that may be linked to behavioral deficits later in life.

STRESS-RESPONSE SYSTEMS

An important task of the CNS is to regulate biological responses to stress. Evidence suggests that the development and functioning of the main stress-responsive systems, namely the HPA axis and the sympathetic and parasympathetic nervous system are influenced by early socialization.

Hypothalamic–Pituitary–Adrenocortical Axis

There is manifold evidence from animal and human studies to suggest an important role of early family environment in the development of the HPA axis and its engagement in response to stress. So well established are these relations that depriving a young offspring of contact with its mother through maternal separation is the most commonly employed paradigm in animal studies for understanding the impact of early stress on development (e.g., Laudenslager et al., 1995; Kuhn & Schanberg, 1998). Moreover, it is now evident that changes due to a chronically stressful early environment can have permanent effects on stress responses across an offspring's lifetime. Although most of this evidence comes from animal studies, studies of human families reveal similar patterns. We begin this section with a brief description of the functions of the HPA axis and then describe the evidence relating early family environment, especially maternal-offspring ties, to HPA axis functioning.

The HPA axis plays a central role in managing threat. Corticotropin-releasing hormone, produced in the paraventricular nuclei of the hypothalamus, stimulates the secretion of adrenocorticotropic hormone by the anterior pituitary, resulting in the release of glucocorticoids from the adrenal glands (e.g., cortisol in humans and corticosterone in rats). Glucocorticoids serve an important function at low basal levels by permitting or restoring processes that prime homeostatic defense mechanisms (Munck & Naray-Fejes-Toth, 1994). This integrated pattern of HPA axis activation modulates a wide range of somatic functions including energy release, immune activity, mental activity, growth, and reproductive function. At low basal levels, glucocorticoids promote mental and physical health as well as normal development (Gunnar, 2000).

However, larger, more frequent, and more long-lasting elevations in glucocorticoids, as occur in chronically or recurrently stressful environments, can compromise HPA axis functioning and, ultimately, health. For example, a hyperresponsive HPA axis influences the development of hypertension and cardiovascular disease, immune suppression, hyperinsulimia, and insulin resistance, enhancing risk for diabetes. Glucocorticoids are also implicated in age-related decreases in immune competence and cognitive functioning.

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n glucocorticoids, promise HPA axis PA axis influences iune suppression, lucocorticoids are nitive functioning. Hyperactivity of the HPA axis is also thought to contribute to anxiety disorders and depression, as well as to growth retardation and developmental delay. As this analysis suggests, the HPA axis interacts with other systems, including the autonomic nervous system and the immune system, such that changes in the HPA axis functioning will affect these and other systems as well. Hyporesponsiveness of the HPA axis can also have deleterious effects on health and development. It can be associated with chronic fatigue and susceptibility to autoimmune and inflammatory diseases, including rheumatoid arthritis and asthma (Gunnar, 2000).

The question arises as to the relationship between hyperresponsive and hyporesponsiveness of the HPA axis. One theory is that stressful conditions early in life lead first to hypercortisolism, as children react intensely to chronic or recurring problems, such as family conflict. Over time, however, with repeated activation, the HPA axis may lose some of its resiliency, manifested in chronically elevated basal cortisol levels, a flattened diurnal cortisol rhythm, and/or weak cortisol responses to acute stress (see Gunnar & Vazquez, 2001; McEwen, 1998, for further discussion of this issue). At present, these sequential changes in HPA axis functioning in response to chronic stress represent a hypothesis rather than a definitive conclusion, and not all empirical evidence fits this hypothesized sequence (Gunnar & Vasquez, 2001; Heim et al., 2000). Linking these changes to socioemotional functioning will also be revealing. For example, heightened HPA responses to stress may be associated with anxious responses to stress, whereas an elevated flat cortisol trajectory may be associated with psychic numbing and/or coping through withdrawal instead.

Animal Studies

Research with rodents and nonhuman primates has demonstrated conclusively that maternal behavior affects an offspring's developing HPA axis as well as HPA responses to stress. For example, studies of rhesus monkeys have found that ventral contact between offspring and mother following a threatening event promotes rapid decreases in HPA axis activity (Gunnar et al., 1981; Mendoza et al., 1978). Meaney and associates have shown that the immediate effect of maternal licking and grooming and arched-back nursing is a reduction in corticosterone responses and sympathetic activity in offspring and mother alike (Liu et al., 1997; Francis, Diorio, Liu, & Meaney, 1999). These researchers have compared the offspring of mothers who are high versus low in licking and grooming and cross-fostered offspring of high or low licking-and-grooming mothers, to demonstrate experimentally the impact of these nurturant behaviors. The rats reared by mothers who engage in more licking and grooming during the first 10 days of life show reduced plasma adrenocorticotropic hormone and corticosterone responses to acute stress, increased hippocampal glucocorticoid receptor messenger RNA expression, enhanced glucocorticoid feedback sensitivity, and decreased levels of hypothalamic corticotropin-releasing hormone messenger RNA (Cirulli et al., 2003). Through these processes, early maternal nurturant behaviors appear to shape the infant's ability to prepare for and react to stress (Champagne, Francis, Mar, & Meaney, 2003).

The long-term effects of these maternal nurturant behaviors are evident as well. Offspring who are the recipients of early maternal attention also get lifelong protection against stress. Specifically, as adults, rat pups who received nurturant maternal care early in life had reduced plasma adrenocorticotropic hormone and smaller corticosterone responses to acute stress. As they matured, the offspring also showed more open-field exploration, suggesting less anxiety in novel situations, and as adults, they were less likely to show age-related onset of HPA axis dysregulation in response to challenge and agerelated cognitive dysfunction. (Francis, Diorio, et al., 1999; Liu et al., 1999). Using a variety of correlational and experimental methods, Meaney and colleagues (Weaver et al., 2004) showed that these changes occur via alteration of the offspring epigenome at a glucocorticoid gene promoter in the hippocampus via changes in DNA methylation. Thus, early nurturant maternal care can alter the expression of genes related to HPA responses to stress in ways that persist across the lifespan.

Similarly, Rosenblum, Coplan, and colleagues (Coplan et al., 1996) manipulated the environments in which mother macaque monkeys raised their offspring through the variable foraging demand (VFD) paradigm described previously. In an environment with easily obtainable food, and also in an environment in which finding food required more effort, the mother monkeys were attentive to their offspring, whose development proceeded normally. In the VFD condition, however, the mothers became more inconsistent in their mothering. The offspring of these mothers showed elevated cortisol responses to stress, coupled with fearful and socially maladaptive behavior. We interpret these and related findings as indicating that maternal nurturance, or its absence, helps to shape the HPA axis. When maternal responses are nurturant, the offspring's HPA axis operates efficiently and returns to baseline quickly following a stressful encounter; these effects persist across an offspring's lifespan. In contrast, those animals that receive less nurturant maternal behavior develop a "hair-trigger" HPA axis response to stress. Their glucocorticoid responses to stressful events are strong and persistent and eventually carry health consequences (see Newport, Stowe, & Nemeroff, 2002, for a review).

Studies of Human Infants and Children

A broad array of evidence in humans likewise suggests that the cortisol response, reflecting HPA axis functioning, may be altered in the offspring of risky families. Indirect evidence for the role of early maternal nurturance is found in the elevated cortisol levels observed among children whose mothers suffer from psychological disorders that may affect their ability to provide consistent nurturing. For example, infants of mothers with panic disorder showed high salivary cortisol levels as well as disturbed sleep, although their behavior was not otherwise adversely reflective of their mothers' panic disorder (Warren et al., 2003). Essex, Klein, Cho, and Kalin (2002) reported that maternal depression was a significant predictor of children's cortisol levels beginning in infancy through first grade and predicted symptoms of psychological distress at this last time point. However, the extent to which altered parenting behavior associated with panic disorder and depression accounted for the differences in the children's cortisol levels and whether cortisol mediates subsequent symptoms of emotional distress are not yet clear; shared genetic inheritance may have played a role in these associations.

Harsh parenting behavior may also be linked to HPA axis functioning. A study of 264 infants, children, and adolescents found an association between abnormal cortisol profiles, diminished immunity, and frequent illnesses with a family environment characterized by few positive affectionate interactions and a high level of negative interactions, including irrational punishment and unavailable or erratic attention from parents (Flinn & England, 1997). Bugental, Martorell, and Barazza (2003) found that infants who re-

Influences of Early Socialization Experiences

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ning. A study of bnormal cortisol ronment charactive interactions, m parents (Flinn t infants who received corporal punishment showed high cortisol reactivity to stress; in addition, infants who experienced their mother's frequent emotional withdrawal demonstrated elevated basal levels of cortisol. Granger et al. (1998) reported that children's basal cortisol levels prior to a conflict-oriented mother-child task were associated with a family environment high in aggression, anger, and conflict, the child's internalizing behavior problems, the mother's childhood levels of socially withdrawn behavior (a potential indicator of a genetic contribution to this pattern), and current psychosocial problems. Spangler, Schieche, Ilg, Maier, and Ackermann (1994) found that a mother's insensitivity to her child during play predicted an increase in the child's cortisol during free play; infants of highly insensitive mothers also exhibited more negative emotional behavior during play as well. Abuse can also affect HPA axis functioning. In one study, children who had been physically abused in their families had somewhat elevated afternoon cortisol concentrations; maltreated children who were also depressed had lower morning cortisol concentrations compared to nondepressed maltreated children and were more likely to show a rise, rather than the expected decrease in cortisol, from morning to afternoon (Hart, Gunnar, & Cicchetti, 1996). In a review of the evidence, Chorpita and Barlow (1998) noted that in families characterized by low levels of warmth and high levels of restrictive, controlling parenting, HPA axis functioning may be disrupted in response to stress, leading to increased corticotrophin-releasing hormone and hypercortisolism (see also Gunnar & Donzella, 2002). These changes have been linked to a heightened risk for anxiety and depression (e.g., Chorpita & Barlow, 1998), although the causal connection between these sets of findings is not yet known.

A child's attachment to his or her parents appears to moderate cortisol responses to novel or potentially threatening conditions. For example, children with disorganized/disoriented attachment patterns are more likely to exhibit higher cortisol levels to situations that other children take in stride (Hertsgaard, Gunnar, Erickson, & Nachmias, 1995). In a series of studies, Gunnar and associates found that attachment patterns moderated cortisol responses of babies in stressful circumstances (Gunnar, Brodersen, Nachmias, Buss, & Rigatuso, 1996; Nachmias, Gunnar, Mangelsdorf, Parritz, & Buss, 1996). For example, Ahnert, Gunnar, Lamb, and Barthel (2004) examined cortisol levels in children at home before starting child care, during an adaptation phase in which their parents accompanied them, during a separation phase, and 5 months later. In the separation phase, cortisol responses rose for all children, and attachment security was unrelated to these levels, but during the adaptation phase, secure infants had significantly lower cortisol levels than insecure children did. The implications of these patterns for socioemotional development, if any, are not yet known.

The protective effects of a secure attachment relationship appear to be especially evident for socially fearful or inhibited children and children otherwise at risk. Gunnar and associates argued that temperamentally fearful children are especially vulnerable to stress, and an insecure attachment is implicated in their elevated cortisol responses to new situations, serving both as a marker of the parent–infant relationship and as a potential predictor of later anxiety disorders (Gunnar & Donzella, 2002). Children with other preexisting risk factors may also be especially vulnerable to the effects of parenting. Bugental (2004) tracked outcomes experienced by children born with medical or physical disorders and found that at-risk children who also experienced harsh parenting showed elevated cortisol and low habituation to potentially stressful events. In contrast, those at-risk children who experienced supportive parenting showed normal cortisol responses and nor-

mal habituation to stress. Unlike the research reviewed earlier, in this study the stress reactivity of children not at risk was unaffected by parenting style. This finding underscores the interactive role that parenting style may play with other risk factors, including genetic risks, in the etiology of biological and psychological stress responses.

Paralleling the animal studies, a number of findings suggest that effects of early environment on HPA axis functioning in children persist into adulthood. Several retrospective studies report that alterations in HPA axis functioning associated with a risky family environment continue to appear in young adulthood. In one study, poor family relationships, assessed by college students' ratings of their early family environment, were associated with elevated cortisol responses to a laboratory challenge (Luecken, 1998). In a second study, women who reported having been abused in childhood showed greater HPA responses to laboratory stress than did women without such histories; these responses were greater for abused women who also had symptoms of anxiety and depression (Heim et al., 2000; see also Kaufman, Plotsky, Nemeroff, & Charney, 2000). Taylor, Lerner, Sage, Lehman, and Seeman (2004) found that young adults who reported an early environment marked by conflict, by cold, unaffectionate behavior, or by neglect showed elevated baseline cortisol levels prior to a laboratory stress challenge, although responses to the challenge itself were not influenced by family background. A study of 6-12-yearold children reared in Romanian orphanages 61/2 years after they had been adopted examined diurnal cortisol patterns. Most of the children raised in the orphanages had significantly higher cortisol levels over the daytime hours than did comparison adopted samples and nonadopted children. These effects were attributed to the risky early environment in which these children were raised, which included gross neglect of basic needs and chronic exposure to infectious agents (Gunnar, Morison, Chisholm, & Schuder, 2001). Thus, the evidence clearly suggests that HPA functioning can be potentially permanently altered in response to early stressful environments.

The impact of day care on children's diurnal cortisol responses may also reflect an effect of chronic stress on HPA axis activity. Watamura Sebanc, and Gunnar (2001) reported a rise in cortisol across the day among children in full-day child care. Although the cause of this pattern is not fully understood, factors involving the interactional demands of group settings during this developmental period may be implicated. A second study (Watamura, Donzella, Alwin, & Gunnar, 2003) reported that children who were socially fearful were more likely to demonstrate this cortisol increase, whereas those children who played more with peers exhibited lower cortisol levels. Possibly, these results may be understood as gene–environment interactions whereby the highly stimulating social environment interacted to produce heightened HPA axis activity primarily in children with some initial proclivity to social fearfulness.

Although research relates qualities of the early family environment to offspring's HPA axis development and functioning, several important issues remain. A first issue concerns how the HPA axis changes over time in response to long-term stress. A working hypothesis is that initial reactions to a risky family environment are marked by elevated HPA responses to stress which yield over time to the development of elevated basal cortisol levels and a muted HPA response to stress. More research is needed on this issue, however, especially on potential implications of flattened HPA stress responses for socioemotional functioning. A second issue concerns the role of shared genetic factors in explaining some of the relations between a harsh family environment and clinical outcomes, such as anxiety, depression, and certain diseases that have genetic bases. Although dy the stress reing underscores icluding genetic

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It to offspring's n. A first issue ress. A working ked by elevated elevated basal ed on this issue, ; responses for enetic factors in nd clinical outbases. Although animal studies in which early environment is manipulated show definitively that maternal behavior can, in and of itself, affect HPA axis development and functioning, the degree to which genetic contributions figure into these relations in human offspring merits examination. A third issue concerns the fact that many different types of early adverse experience appear to affect HPA axis functioning in similar ways. As one of the primary stress systems of the body, the HPA axis is responsive to numerous insults, ranging from the harsh parenting described here to physical stressors such as malnutrition or exposure to drugs *in utero*. As such, the HPA axis may represent a general pathway to multiple mental and physical health outcomes. This hypothesis bears continued scrutiny, however, as specific effects on biological systems associated with specific types of stressors are being uncovered. This issue raises the more general point that research can now begin to examine ways in which particular stressors (such as abuse vs. neglect) may differentially shape the HPA axis and/or its interactions with other biological systems, a specificity that has largely been lacking in research findings to date.

Sympathetic and Parasympathetic Functioning

The sympathetic adrenal medullary system is also involved in the management of threat or challenge. The actions of the sympathetic system are mediated primarily by norepinephine and epinephrine. These catecholamines exert effects on adrenergic receptors in the target tissues to produce, among other changes, increases in heart rate and blood pressure, dilation of the airways, and enhanced availability of glucose and fatty acids for energy. These coordinated responses facilitate short-term mobilization of an organism's resources for the rapid, intense physical activity involved in the "fight-or-flight" response.

A few studies with human infants and children indicate that the early family environment can have an impact on the immediate and long-term functioning of the autonomic nervous system. Although most children show increases in arousal in response to familial stress (El-Sheikh et al., 1989), children in families marked by chronic conflict experience this physiological activation on a recurrent basis. One study found that boys but not girls from families characterized as unsupportive by parents had stronger heart rate responses to laboratory stressors, compared with boys from more supportive families (Woodall & Matthews, 1989). It is unclear whether elevated autonomic reactivity to stress results from chronic exposure to family conflict, or whether shared genetic heritage plays a role as well (Ballard, Cummings, & Larkin, 1993; Ewart, 1991). Moreover, because much of this research measures heart rate and blood pressure, the studies do not enable one to identify which aspects of autonomic functioning (sympathetic changes, parasympathetic changes, or a combination) are responsive to a risky family environment.

Research on young adults suggests that the early family environment has long-term effects on sympathetic nervous system functioning and on risk factors for coronary heart disease as well as related metabolic disorders. Luecken (1998) reported that college students who reported poor family relationships in childhood had higher blood pressure both at resting levels and in response to a laboratory challenge. These family characteristics were also associated with elevated anger and hostility, suggesting that these factors may contribute to stronger sympathetic responses to stress. Taylor et al. (2004) found that young adult males, but not females, showed elevated heart rate and blood pressure responses to stress, if they were from families characterized by conflict or a cold, nonnurturant parenting style.

The research evidence suggests that these heightened sympathetic nervous system responses to stress may have long-term consequences, as elevated sympathetic reactivity has been tied to risk factors for coronary heart disease. For example, heightened cardiovascular reactivity to stress among boys 8–10 years old has been tied to increased left ventricular mass, a risk factor for coronary heart disease (Allen, Matthews, & Sherman, 1997). Using evidence from 3,225 adults participating in the CARDIA study, Lehman, Taylor, Kiefe, and Seeman (2005) related reports of a risky family environment in childhood to adult metabolic function, which is a predictor of heart disease, diabetes, and other disorders. They found that individuals from families characterized by conflict, neglect, or cold, nonnurturant parenting were more likely to have dysregulations in metabolic functioning in adulthood, relations that were mediated by negative emotions and a lack of social support.

Vagal Tone

The parasympathetic branch of the peripheral nervous system, and its main nerve, the vagus, is also implicated in reactivity to stress. The vagus, the 10th cranial nerve, communicates bidirectionally between the viscera and the brain, influencing heart rate, intestinal movement, gastic acid secretion, and other important regulatory functions. The vagus is connected to the sinoatrial node, considered to be heart's pacemaker, and acts as a brake to decrease heart rate. This "vagal brake" allows individuals to regulate their responses, to engage and disengage from environmental stimuli, and to recover from arousal. In addition, the vagal system plays a role in social behaviors such as facial expression, vocalization, and head turning. Polyvagal theory (Porges, 1995) proposes that cardiac vagal tone is an index of physiological regulatory capacity in infants, given the vagus's impact on a host of relevant systems. Indeed, vagal tone and heart rate variability have been linked to emotion regulation, social competence, and temperament in infants and children (Doussard-Roosevelt, Porges, Scanlon, Alemi, & Scanlon, 1997, Doussard-Roosevelt, McClenny, & Porges, 2001). Vagal tone also appears to be coordinated with the HPA axis, such that individuals who respond to a laboratory task with an increase in cortisol show a decreased vagal tone response to the task and vice versa (Porges, 2001).

Vagal tone may be influenced by prenatal or genetic factors: The newborns of women categorized as experiencing high anxiety during the second trimester of pregnancy had lower vagal tone when tested on the first day of life, and their vagal tone appeared to be correlated with other markers such as sleep organization and alertness (Field et al., 2003). Vagal tone may also be affected by the quality of early care. A study of premature infants found that those who received more kangaroo care (i.e., protracted mother-infant skin-to-skin contact) showed greater maturation of vagal tone between 32 and 37 weeks gestational age (Feldman & Eidelman, 2003). Kangaroo-care infants also spent more time in quiet sleep or alert wakefulness and less time in active sleep and also appeared more competent than non-kangaroo-care infants on neurodevelopmental tasks such as habituation and orientation. Another study assessed first-time mothers and their 6-month-old infants and found that infants' cardiac vagal tone correlated positively to the symmetry of mother-infant communication patterns (Porter, 2003). In other words, infants with attentive and attuned mothers tended to have higher vagal tone.

More research is warranted into the specific processes influencing the maturation and mylenization of the vagal nerve. While it is possible that infants develop high vagal

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ne maturation op high vagal tone as a result of sensitive caregiving, prenatal conditions and genetics may also play a role, as studies of neonates would suggest. Also, high vagal tone might be the cause, rather than the result, of symmetrical mother-infant communication. Children adept at emotional regulation may be more capable of remaining engaged in mother-infant communications and may prompt more reciprocal attentiveness in their mothers. A study that assessed vagal tone at 2 and 4 years of age found evidence for the stability of both vagal tone and mothers' parenting practices over that timespan (Kennedy, Rubin, Hastings, & Maisel, 2004). In addition, vagal tone at age 2 predicted parenting practices at age 4; for example, low vagal tone predicted harsher parenting, while high vagal tone was associated with more supportive parenting. Exposure to marital conflict also appears to be linked to lower vagal tone in 6-month-olds (Porter, Wouden-Miller, & Porter, 2003). Again, however, the direction of influence remains unclear. Not only does marital conflict seem to impact offspring vagal tone, but vagal tone also appears to influence children's reactions to intraparental conflict. In a group of 8- to 12-year-olds, higher vagal tone appeared to buffer children exposed to marital conflict against externalizing, internalizing, and health problems as a result of that conflict (El-Sheikh, Harger, & Whitson, 2001).

As with research on the HPA axis, research on the sympathetic and parasympathetic systems has associated early childhood stress with possible impairments in the functioning of these systems. These deficits appear to manifest themselves mainly in terms of heightened reactivity—for example, exaggerated blood pressure responses to a laboratory stressor—and in terms of compromised self-regulation (e.g., low vagal tone). However, much more work remains to be done on the specific causes and consequences of sympathetic and parasympathetic dysfunctions. For example, the possible genetic bases of these systems remains poorly understood. It is also unclear precisely which types of stressors, administered at what age, might have the greatest impact on the development of the sympathetic and parasympathetic systems.

IMMUNE FUNCTIONING

Given the influence of autonomic and endocrine activity on immune responses, it is not surprising that early experiences, such as maternal separation, have been found to have an impact on immune response (Worlein & Laudenslager, 2001). In particular, glucocorticoids, which are secreted as part of the HPA response to stress, are known to have immunosuppressive effects. Much of the immunological research has been conducted on monkeys. For example, rearing without exposure to a mother, as found in isolation rearing (without maternal or peer interactions) and peer socialization paradigms, has a longlasting impact on monkey immune development (Coe et al., 1989; Coe, Lubach, Schneider, Dierschke, & Ershler, 1992; Lubach, Coe, & Ershler, 1995). As described below, experimental disruptions of the mother-infant bond produces evidence of both suppression and enhancement of immune responses in monkeys. Although an enhanced immune response was not initially expected, researchers have speculated that the absence of appropriate maternal stimulation could activate certain immune responses or alter the rate of maturation of the immune system (Coe et al., 1989). It is likely that the absence of breast feeding among the mother-deprived monkeys is also involved in this process. Breast milk can directly influence immune responses in the infant by the passage of maternal cells thereby altering the vulnerability of the young infant to infectious agents. Increased exposure to disease processes in the monkeys deprived of breast milk could affect the development of the maturing immune system (Coe et al., 1989; Lubach et al., 1995).

Two common *in vitro* measures of immune function in this literature are proliferative response and natural cytotoxicity.⁵ Disruptions of the mother–infant bond, through various separation paradigms, produce complex alterations in immune responses in the monkey as assessed by these measures, with the effects sometimes lingering for years (Laudenslager, Capitanio, & Reite, 1985; Worlein & Laudenslager, 2001). The long-term alterations can include an enhanced immune functioning, suggested by increased natural cytotoxicity of lymphocytes, but also indications of a suppressed immune response, such as reduced B- and T- cell proliferative responses to mitogens. Interestingly, the effects of chronic stress on humans include both an enhancement and a suppression of immune responses, which contribute to immune dysregulation (Robles, Glaser, & Kiecolt-Glaser, 2005).

Although the changes in immune functioning are not yet fully understood, researchers speculate that any lasting effects of early separation experiences on immune responses are probably related to long-term changes in the mother-infant relationship that follow reunion. Similar to the rat mothers described earlier, who increase nurturing behaviors following reunion with their pups, pigtail macaque mothers tend to be more attentive and more restrictive when reunited with their infants and evidence suggests that there is a lasting impact of the separation-reunion experience on maternal behavior. Previously separated mothers wean their infants at a later age and maintain greater control over their infants' physical proximity when observed at 15 months of age (Worlein & Laudenslager, 2001). It is thought that these maternal behaviors may play a role in the long-term alterations in immune responses that have been observed in monkeys who experienced early disruptions of the mother-infant bond. It is possible that lasting changes in the primate mother-infant relationship mediate long-term changes in other biological systems following separation.

The effects of maternal separation on bonnet macaques' immune system can be ameliorated by the presence of a preferred peer partner (Boccia et al., 1997). Bonnet macaques who were separated from their mothers and their social group showed an initial suppressed immune response, but those changes were not observed in the infants who had a preferred peer partner present during the 2 weeks of separation.⁶ Among the monkeys with a peer present, the magnitude of the immunological changes was related to the juvenile friend's affiliative behaviors. Infants who had more social behaviors, such as cradling, playing, and grooming, directed toward them during the separation period showed greater cytotoxicity and increased lymphocyte proliferation in response to two mitogens. This research suggests that alternative social attachments during separation can ameliorate the infant's immune response to maternal loss.

In the Boccia et al. (1997) study, the infants with friends present also showed less behavioral evidence of depression when separated from their mothers. This pattern is intriguing because of research suggesting that depression in humans is associated with compromised immune functioning (Cohen & Herbert, 1996). In fact, monkeys who show the greatest behavioral response to maternal separation (e.g, distress vocalizations, time spent in huddled, and withdrawn postures) also are the most likely to show declines in lymphocyte activation. Because the mother-infant relationship prior to the separation is known to impact behavioral responses, it may also play a role in the immune response (Worlein & Laudenslager, 2001). t the development of *5*).

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also showed less be-. This pattern is inssociated with comnkeys who show the lizations, time spent declines in lymphoeparation is known e response (Worlein Although the functional significance of the immunological changes observed in the monkey studies is not known, immune responses to abnormal rearing conditions early in life, even those that indicate enhanced immune activity, may set the stage for an increased vulnerability to disease later in life, when there is a natural decline in immunity (Lubach et al., 1995). As indicated previously, the impact of experiences like maternal separation on immune functioning can only be understood in the context of other biological responses to early stress, in particular changes in the HPA system.

GROWTH AND SEXUAL DEVELOPMENT

Research suggests that early rearing experiences can impact the secretion of growth hormone and the observed physical growth of offspring. Pubertal timing also appears to be influenced by the quality of family relationships and the presence of fathers in the home.

Growth and Growth Hormone

Growth hormone plays a role in growth, development, and immunoregulation. Appropriate maternal behavior is a stimulus for growth hormone secretion in nonhuman primates and in human infants (Kuhn & Schanberg, 1998), and growth hormone levels change in response to stress in nonhuman primates and rats (Laudenslager et al., 1995). In rat pups, maternal separation elicits a fall in serum growth hormone and a loss of tissue responsivity to exogenous growth hormone. Interestingly, stroking the pup with a paint brush restores serum growth hormone to control values, suggesting that the loss of tactile stimulation from the dam may account for the effects of separation on growth hormone (Kuhn & Schanberg, 1991). Research with human infants indicates that tactile stimulation can stimulate both somatic growth and behavioral development (Kuhn & Schanberg, 1991).

In contrast to the rat pups' response to separation, there is evidence in some monkey species that short-term responses to maternal separation may include a short-term *increase* in secretion of growth hormone. One study reported a slowly developing increase in plasma growth hormone in pigtail monkey infants in response to a 2-week maternal separation. Increases in growth hormone during the second week of separation were associated with a behavioral sign of distress, time spent in slouched huddled postures, suggesting that individual change in endocrine functioning was tied to the stressfulness of the separation for the monkey (Laudenslager et al., 1995). Although growth hormone secretion returned to baseline levels within a week following the pigtails' reunions with their mothers, frequent and prolonged repetition of reactions can be deleterious.

As in all the research discussed in this chapter, there are important distinctions between short-term responses to stressful experiences and the long-term consequences of chronically stressful early rearing experiences. For example, brief interruptions of growth hormone secretion in neonatal rats may be of little consequence. However, prolonged suppression of growth hormone reduces growth in all mammals (Kuhn & Schanberg, 1998). Early studies of human children exposed to inadequate caretaking identified consequences such as "deprivation dwarfism" and failure to thrive (Gardner, 1972; Glaser, Heagary, Bullard, & Pivchik, 1968). Contemporary research on the effects of institutionalization, particularly in Romanian orphanages, suggests that early deprivation experi-

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ences result in impairments across a wide range of domains, including cognitive and social development as well as physical growth (Zeanah et al., 2003). The findings also point to the remarkable resilience of human development to early insult, as cognitive and physical gains have been observed following adoption (O'Connor et al., 2000). However the children in these studies spent the early months or years of their lives in grossly depriving conditions that included severe malnourishment. It is therefore impossible to discern how the social deprivation that these children experienced (e.g., most of their time was spent in individual cribs and they had very limited face-to-face interactions with caregivers) contributed to their impairments. Research on stressful, though less extreme. rearing environments has also found evidence of growth retardation. For example, in one longitudinal study, growing up in a difficult and conflictual family was associated with less height attainment in assessments made at age 7 and in adulthood (Montgomery, Bartley, & Wilkinson, 1997). Another study found that infants with less sensitive mothers were not growing as well (lower weight for age) as other infants (Valenzuela, 1997). The mechanisms underlying growth retardation in children growing up in risky environments are not yet understood. Behavioral processes, such as feeding and eating, as well as altered endocrine functioning, particularly growth hormone secretion, may be implicated.

Pubertal Timing

Early socioemotional stress seems to accelerate puberty in girls. A survey of over 1,100 girls related early puberty to the number of stressful life events and to family structure, specifically father absence (Surbey, 1990). In another study, better family relationships, fewer internalizing and externalizing problems, and lower levels of depressive affect were associated with later age at menarche in girls ages 10–14 (Graber, Brooks-Gunn, & Warren, 1995). These findings held even after controlling for the effects of pubertal development on family relationships and life stress. Early puberty in girls has been linked with a number of negative outcomes, from elevated breast cancer risk to weight gain to greater promiscuity and teenage pregnancy. Early-maturing girls also report more emotional problems, like depression, and more risk-taking behavior, like alcohol consumption (Ellis & Garber, 2000).

Because the HPA axis and hypothalamic-pituitary-gonadal axis regulate pubertal development, these axes may be pathways that link family stress to pubertal maturation. As the preceding sections have indicated, HPA axis overactivation characterizes children in stressful environments, and this activation may trigger the early development of the hypothalamic-pituitary-gonadal system. Research in this area appears inconclusive and even contradictory, however (Graber et al., 1995), perhaps because genes, body fat, and athletic activity also influence pubertal timing and may be linked to HPA axis functioning as well. Therefore, it is difficult to tease out the specific impact of psychosocial stress on pubertal maturation.

Father absence seems to have a separate, specific influence on girls' pubertal timing, above and beyond general familial stress (Romans, Martin, Gendall, & Herbison, 2003, Ellis & Garber, 2000). For example, the 1995 National Survey of Family Growth found that women whose parents separated in early childhood had twice the risk of early menarche, a fourfold risk of early sexual intercourse, and more than twice the risk for early pregnancy as women who lived with both parents during childhood (Quinlan, 2003). According to an evolutionary model, early experiences shape girls' eventual reproductive strategies (Belsky, Steinberg, & Draper, 1991). From this perspective, one could argue

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The research literature on pubertal timing in boys is much less substantial than the literature on girls' pubertal development. As with girls, boys reared in father-absent homes appear to reach puberty sooner, and boys raised without fathers show higher testosterone levels and more aggressive behavior (Granger et al., 2003). Perhaps the best illustration of older males' impact on younger males' pubertal timing comes from the animal kingdom. In the early 1990s, the rangers at Pilanesberg National Park in South Africa ended a series of elephant attacks on white rhinoceroses by introducing six older males to the park's elephant population (Slotow, Van Dyk, Poole, Page, & Klocke, 2000). After the older elephants arrived, the young males' testosterone levels dropped, suggesting that the mere presence of higher-ranking males exerts regulatory effects on sex hormones.

CONCLUSION

Physiological and behavioral adaptations that optimize maturation and survival are species-specific. Therefore, any general account of the role of parenting behaviors, or the behavioral and biological strategies observed in offspring in response to early rearing conditions, must include some oversimplification. With this caution in mind, we highlight patterns that emerge in our review of data from human and animal studies. The protective effects of parental nurturing behaviors extend to numerous aspects of biological functioning in mammals. Some of the behaviors that signal sensitive and responsive parenting appear, in the short run, to influence regulatory processes in immature biological systems and, in the long run, to facilitate the development of stress response systems. In the animal literature, maternal separation is often treated as a stressor. Our analysis suggests that a maternal separation stressor is unique in that it also removes an external regulator from the infant's environment-an individual who, under normal circumstance, helps to regulate the infant's response to environmental challenges. It is therefore not surprising that disruptions of the parent-child bond (especially the mother-child bond) through prolonged separation, parental stress, or poor parenting behavior can result in health outcomes that have been associated with biological dysfunction and dysregulation. Investigations are beginning to show how those changes may be mediated through gene expression. In some cases, early activation of stress-response systems seems to lead to early maturation of biological systems and subsequent evidence of accelerated aging and disease process.

In addition to understanding the implications for physical health, a critical next step is to address how the biological responses to early rearing conditions described in this chapter may relate to behavior over the course of development. In humans, the same stressful family environments that have been linked to children's neurotransmitter profiles and to their HPA axis and autonomic functioning also appear, in the longer term, to interfere with social and emotional development in childhood, promote risky behaviors in adolescence, and lead to poor mental health outcomes in adulthood (Repetti et al., 2002). The time is right for socialization researchers to begin to link these scientific literatures. Biological, social, emotional, and behavioral development are intertwined through reciprocal connections. Therefore, causal pathways will not necessarily always lead from socialization experiences to biological processes to social-emotional developmental outcomes. For example, biological systems are also influenced by individual emotional or social factors, as seen in the impact that negative affect and depression have on immune functioning.

Unfortunately, any effort to investigate the biological underpinnings of socialization effects on social and emotional development is limited by a paucity of human research. We found little research addressing human parenting effects on the development of offspring CNS, endocrine, and immune systems. Attempts to generalize experimental findings from other species to human development are fraught with the potential for inaccuracy. For example, the animal literature emphasizes the impact of very early rearing experiences, particularly in contrast to the length of time over which human parenting is distributed. On the one hand, because children are dependent on their parents for a much longer period of time, human parents influence offspring biological development long past infancy. On the other hand, parenting effects may be much greater during neonatal development in some of the animal species discussed in this chapter. For example, some aspects of development that occur in the neonatal rat, and are therefore vulnerable to changes in mother-infant interactions, occur prenatally in humans and may be less influenced by maternal behavior after birth (Kuhn & Schanberg, 1998). Another limitation of the experimental animal literature is the practice of keeping subjects in highly controlled environments during the intervening period between the early experience under study and the assessment of the biological outcome. As Gottlieb and Lickliter (2004) have pointed out, the animals are not exposed to naturally occurring variations in social experience that may play a corrective or remedial role. They note, for example, that the effects of handling on rat pups are enhanced by subsequent rearing under social conditions. Thus, findings from the animal early rearing literature may be misinterpreted as reflecting unalterable early programming on development.

One of the most pressing questions is how positive, nurturing socialization experiences shape the development of human biological systems. Most of the research reviewed in this chapter focuses on the impact of stressful early experiences such as social deprivation (e.g., maternal separation) and harsh or abusive parenting. For example, we know that adverse rearing conditions can affect the development of important neurotransmitter systems in the mammalian brain. However, we currently have much less comparable information about how sensitive and nurturant rearing influences the development of these systems. Yet we know that nurturant behaviors observed in mammals, such as licking, grooming, and other forms of physical contact, play a role in the functioning of immature biological systems (e.g., by helping babies to recover more quickly from stress responses). In the long term, the same behaviors also promote the development of vagal tone, sleep cycles, and the HPA axis. Researchers can build on this foundation to investigate how other sensitive and responsive parenting behaviors shape the development of the CNS and other biological systems. Knowledge about these biological connections will advance current socialization models in exciting directions.

Models will also be enhanced by research on socialization provided by fathers. Our search for research beyond the mother-child dyad yielded little outside the impact of father absence. Whether studying mothers or fathers, researchers need to take special care to correctly identify the source of correlations between socialization experiences provided by a parent and offspring biological outcomes. Without the experimental designs that are used with other species, it is critical that correlational investigations of human parenting avoid incorrectly attributing environmental influences to genetic ones. velopmental outemotional or sohave on immune

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l by fathers. Our the impact of fatake special care eriences provided l designs that are numan parenting Many socialization researchers seek to understand how parenting behaviors and family environments shape critical developmental outcomes such as learning, emotion regulation, social competence, and mental health. Although most current models focus on behavioral and cognitive mediators, many of the outcomes may also be shaped by the kinds of biological changes hinted at in this chapter. For that reason, we believe that human socialization research will be advanced as we learn more about the effects that early rearing experiences and parenting have on the development and functioning of the biological systems discussed here. An important next turn in the road ahead will be an integration of what we are learning about biological responses to early rearing conditions with the social and emotional developmental processes that are the primary focus of this volume.

ACKNOWLEDGMENTS

We would like to thank Carlos Grijalva, Joan Grusek, Paul Hastings, Teresa Seeman, Joan Silk, Cindy Yee-Bradbury, and participants in the Repetti research seminar at UCLA for their helpful comments on an earlier draft of this chapter.

NOTES

- 1. Dams assume several different nursing positions, even during the same nursing bout; licking and grooming are most likely to take place during nursing while the mother is in the arched-back position.
- 2. The handling and separation paradigms are distinct. Over the course of a normal day, dams are routinely off their nests and away from the pups for more than the 15 minutes that is required for the handling manipulation. In contrast, the maternal-separation procedure involves separations that are typically longer-lasting (e.g., 180 minutes per day) and extended over several days (Francis, Caldji, et al., 1999).
- 3. Because the spontaneous eye blink is at least partially controlled by dopamine neurons in the basal ganglia, the measure of spontaneous blink rates provides a method of assessing dopamine function.
- 4. Probes are drugs that target a neurotransmitter system. Biological or behavioral responses to the drug are observed; abnormal responses are thought to reflect abnormal neurotransmitter functioning.
- 5. The proliferative response can be assessed in the lab by using mitogens (antigens) to stimulate proliferation of cell populations that have been isolated from a sample of peripheral blood. The cytotoxicity, or destructive power, of an isolated population of lymphocytes is measured by their ability to lyse (rupture) a sample of target tumor cells.
- 6. Infants who did not have a juvenile friend with them during the separation showed less B- and T-cell proliferative response to mitogens, and an initial decrease in the natural cytotoxicity of peripheral blood lymphocytes, which gradually returned to normal by the end of the first week of separation.

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