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The role of early experience in shaping behavioral and brain development and its implications for social policy

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Abstract
This article provides a targeted review of the scientific literature on the effects of experience on early brain and behavioral development and later outcome as it pertains to risk for some forms of child psychopathology. It is argued that ample evidence exists indicating that the prenatal and early postnatal years likely represent a sensitive period with respect to the effects of stress on the developing nervous system and behavioral outcome, and with respect to the long-term beneficial effects of early interventions on brain and behavioral development for some genetically based disorders, such as phenylketonuria and autism. Moreover, evidence suggests that parental mental health during the first years of life has a significant influence on early brain activity and behavior, and long-term behavioral outcome. It is concluded that, although prevention and early intervention efforts should not exclusively focus on the earliest years of development, such efforts should begin during this period. By directing such efforts toward promoting optimal prenatal and infant–toddler development, the long-term negative consequences of factors that have their greatest influences during early development and which set the stage for future development can be minimized or avoided entirely. Several recommendations for public policy and future research pertaining to the effects of early experience on child outcome are offered.

In the past few decades, efforts at promoting optimal development in children have increasingly focused on the earliest years of life, including the prenatal period, infancy, and toddlerhood. Broad-based policy changes reflecting a focus on early development have included PL 99-457 enacted in 1986, which provided services to handicapped children from birth to 3 years; the Family and Medical Leave Act enacted in 1993, which recognized the importance of parents spending time with their young infants after birth before returning to work; and Early Head Start created in 1994, which provided education and childcare to at-risk children from birth to 3 years. The rationale behind these efforts has been based largely on an increased understanding of normal infant behavior and development and of the negative influences of factors such as poor nutrition, drug exposure, abuse and neglect, and parent psychopathology and stress on early development and later outcome (Nelson, in press).

The idea that early experience is important for promoting optimal long-term outcomes for children has been supported by studies of behavioral outcomes and early intervention in various at-risk and developmentally disabled populations. Examples of such research in-

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clude studies of (a) the effects of prenatal nutrition and exposure to toxic substances on brain and behavioral development (Morgan & Gibson, 1991; Sonderegger, 1992; Spohr, Williams, & Steinhausen, 1993); (b) the effects of maternal depression during pregnancy and infancy on later cognitive and emotional functioning in children (Goodman & Gotlib, 1999); and (c) the effects of early interventions for improving cognitive, social, and academic functioning in children from economically and socially disadvantaged backgrounds (Campbell & Ramey, 1994) and in children with genetic disorders that affect brain development, such as autism and phenylketonuria (PKU; Dawson & Osterling, 1997; Wappner, Cho, Kronmal, Schuett, & Seashore, 1999).

At the same time that research and policy have increasingly stressed the importance of early experience in the development of children, new techniques for studying infant behavior and brain activity have been developed, allowing developmental scientists to begin to learn more about relations between biology and behavior in infants and children (reviewed in Dawson & Fischer, 1994). In the 1990s, as these intriguing studies were published and discussed in the popular media, public interest in early brain development and behavior began to swell. The effects of early experience on the developing brain, in particular, became of interest after a White House conference on the topic was held in the spring of 1997. The White House conference coincided with a national media campaign focused on early development, which included broadcasts on "Good Morning America" and feature articles in *Newsweek*. Concurrently, public policy documents on the relation between brain science and early development were published by major foundations interested in promoting the health and welfare of children, including *Starting Points,* published by the Carnegie Corporation, and *Rethinking the Brain: New Insights Into Early Development,* published in conjunction with the White House conference. These documents were covered in the popular media and read by policymakers and politicians interested in public health and child development. Keynote speakers at the 1997 National Governor's Association discussed the importance of the new brain science for understanding children's development and for public policy. As a result, leaders in several states enacted policy changes based on what they viewed as the new research on brain development. Numerous policy initiatives and exploratory panels emerged to address the issue of early experience and brain development in several states (Groginsky, Christian, & McConnell, 1998). In 1997, the Federal Early Childhood Development Act was introduced, stressing the importance of early experience on brain development and outcome for children.

The recent public and political enthusiasm over the effects of early environment on brain development subsequently led to a backlash among some scientists who were concerned that the public and policymakers have oversimplified a complex issue. In fact, the public hype over the implications of brain science and the resulting recent critiques and controversy may have had the unfortunate effect of a waning of interest in early childhood, with a loss of policies with the potential to benefit children (Thompson & Nelson, in press). Nevertheless, scientists such as Bruer (1999), Greenough (1997), and others have raised important questions regarding what is actually known about the effects of early experience on brain development. In his recent book, Bruer (1999) argues that the media have been misguided in promoting the myth that the first 3 years of a baby's life can determine a child's long-range outcome. He further describes what he refers to as "three neuroscientific strands" that taken together form the "myth of the first three years." In this article, we will discuss each of these strands and what can be scientifically concluded about their importance for understanding the effects of early experience on later outcome. We will cover in some detail what is known about the development and underlying mechanisms involved in synaptic formation and efficiency. We will, in addition, describe the growing body of evidence demonstrating that exposure to early maladaptive experiences, such as prenatal and postnatal stress and parental psychopathology, does indeed have long-term implications for brain and behavioral development. The implications of the research pertaining to the effects of early experience on brain and behavior for public policy will be considered in the concluding section of this paper.

Synaptogenesis and the Remarkable Period of Early Brain Growth

The first neuroscientific strand that Bruer describes pertains to the fact that the brain develops rapidly during the prenatal and early postnatal months. Remarkably, early in a child's life the brain produces trillions more synapses than are found in adulthood. During the first 3 years of life, synapses form at a phenomenal rate. In humans, it appears that rapid synapse formation begins during the first few postnatal months and reaches highest densities at about 3 months for sensory cortex and about 2–3.5 years for frontal cortex (Huttenlocher, 1994; Huttenlocher & Dabholkar, 1997; Rakic, Bourgeois, & Goldman–Rakic, 1994). Furthermore, this period of peak synaptic density coincides in time with the emergence of important cognitive skills, including early manifestations of working memory (Diamond & Goldman–Rakic, 1989). For example, a study by Bell and Fox (1994) showed that infants who are able to achieve early frontal tasks involving working memory displayed increased electrical brain activity over the frontal scalp region. Put simply, neuroscience and developmental science have shown that early life is a time of truly remarkable growth in terms of both brain and behavior. However, as Bruer points out, there is still relatively little known about how early experiences, such as parenting, actually affect brain development, such as the rate or patterns of synaptic formation and pruning, or even about the relation between changes in regional synaptic densities and specific cognitive skills (e.g., peak synaptic densities in the frontal region and the emergence of early frontal lobe skills). Although it is intriguing that certain biological events such as rapid synaptic proliferation and the emergence of certain cognitive skills co-occur in development, such a cooccurrence does not prove that there is any causal relation between these two processes.

There are, however, several things that are known about the relation between early synaptic formation and pruning and behavioral development. First, it is known that some disorders that involve mental retardation, such as Fragile X, are associated with abnormal synaptic pruning, specifically with excess synapses (Comery, Harris, Willems, Oostra, Irwin, Weiler, & Greenough, 1997). While these disorders are caused by genetic abnormalities rather than faulty early experiences, it is noteworthy that there does appear to be a relation between synaptic density and intelligence, with higher numbers of synapses associated with lower intelligence.

Second, it appears that increased early environmental stimulation does not *necessarily* lead to increases in synaptic formation during the period of rapid synaptic proliferation and pruning, at least for the visual system in nonhuman primates (Bourgeois, Jastreboff, & Rakic, 1989). It is clear, however, that experience in some instances can alter the synaptic formation and organization in the cortex (see Kolb, Forgie, Gibb, Gorny, & Rowntree, 1998, for a review of this rich set of data). Animals raised in complex, enriched environments have more synapses in certain parts of their brains compared to animals raised in nonenriched environments (Greenough, Black, & Wallace, 1987). Furthermore, changes in synaptic organization as a result of experience are correlated with changes in behavioral performance in both animals and humans (Kolb et al., 1998). For example, Jacobs and Scheibel (1993) and Jacobs, Schall, and Scheibel (1993) reported a relation between extent of dendritic arborization (which would act to increase the number of synapses) and the amount of education received. Interestingly, research has shown that the effect of enriched experience on synaptic number and organization is highly dependent upon the age. Enriched experience during early postnatal life appears to lead to a decrease in spine density on the neuron but to have no effect on dendritic length (Kolb et al., 1998).

Science is still addressing the question of precisely how experiences affect the *pattern of selective elimination and responsiveness* of neural networks formed during early development, as opposed to the sheer quantity of synapses, which appears, in large part, to be under genetic control. It is known that experience can and does play a role in selecting and establishing preferentially active synapses. Selective amplification of specific neural groups occurs via a competitive process as a result of the frequency and intensity of stimulation (Edelman, 1987; Hebb, 1949). Once a specific pattern of neuronal groups is selected in a mapped area, exposure to the same or similar stimuli is likely to preferentially activate previously selected neuronal groups. In this way, it is hypothesized, developing neural patterns become stabilized and less susceptible to change over time (Edelman, 1989). Such maps are believed to involve cortical sensory and motor maps as well as the brain regions with which these cortical areas interact, such as limbic regions. Research is shedding light on the mechanisms involved in selecting and establishing preferentially active neural patterns. Repeated and synchronous activation of neighboring neurons strengthens the connections between them, and allows them to fire more efficiently.

Decades ago, Hebb (1949) suggested that either morphological or metabolic changes might underlie changes in synaptic efficiency. Much attention has been focused on long-term potentiation (LTP), which may be a metabolic mechanism for memory formation (Chen & Tonegawa, 1997; Malenka & Nicoll, 1999). In LTP, high-frequency activation of glutamate receptors results in a long-lasting strengthening of the synaptic connection such that for intervals of up to hours the synapse responds more readily and efficiently to activation. In LTP, non-*N*-methyl-D-aspartate (NMDA) glutamate receptors are activated, depolarizing the postsynaptic membrane and allowing for activation of NMDA glutamate receptors. Most likely, both postsynaptic and presynaptic mechanisms are involved in this process. Removal of the magnesium block that typically prevents activation of the NMDA receptor allows calcium to enter the postsynaptic cell, beginning a cascade of second-messenger events that ultimately leads to long-lasting changes in synaptic strength. In addition to the metabolic changes that are involved in LTP, structural changes have been identified and such changes may also contribute to memory. A recent report described the formation of new dendritic spines following LTP (Toni, Buchs, Nikonenko, Bron, & Muller, 1999). This morphological synaptic change may also lead to changes in synapse responsiveness.

Consistent with the idea that LTP underlies the formation of memories, a number of studies have shown that blocking LTP through receptor antagonists or genetic manipulations leads to impaired memory performance in experimental animals (Lu, Jia, Janus, Henderson, Gerlai, Wojtowicz, & Roder, 1997; Mayford, Bach, Huang, Wang, Hawkins, & Kandel, 1996). In addition, enhancing LTP by manipulating second-messenger cascades involved in LTP is correlated with improved memory performance (Barad, Bourtchouladze, Winder, Golan, & Kandel, 1998). In addition to memory formation, some research suggests that components of LTP that are involved in gene regulation are important for consolidation of memory traces (Bourtchouladze, Frenguelli, Blendy, Cioffi, Schutz, & Silva, 1994). Thus, although there are some reports that eliminating or decreasing LTP does not affect memory (Meiri, Sun, Segal, & Alkon, 1998), most research suggests that they are related.

Although it is becoming increasingly clear that LTP is likely involved in memory formation, there are a number of aspects of the physiological basis of memory that still must be understood. LTP is most frequently studied in the hippocampus, a structure thought to be involved in the formation of memory traces (Chen & Tonegawa, 1997; Malenka & Nicoll, 1999). It has yet to be determined, however, how memory traces are stored in long-term memory and what role, if any, synaptic plasticity plays in the storage process. There is some suggestion that, in addition to memory, LTP may be involved in activity-dependent formation of neural circuitry, certainly in sensory systems (Chen & Tonegawa, 1997; Katz & Shatz, 1996). One hypothesis yet to be tested is that experience-dependent mechanisms such as LTP might also be involved in building associative networks that form the basis for memories as well.

In summary, ample scientific evidence indicates that experiences can influence the formation, strength, and efficiency of synapses. Research is revealing the mechanisms involved in experience-dependent changes in synaptic efficiency. However, it is unknown to what extent the early years of life, because of the tremendous changes in the sheer number of synapses that take place during this time, represent a particularly sensitive period for selecting and establishing preferentially active patterns of neural networks that are less susceptible to change later in life.

Sensitive Periods and Long-Term Effect of Early Experience

This brings us to the second and third neuroscientific strands that, according to Bruer, form the "myth of the first three years." These pertain to the related notions that (a) the early years of development represent a sensitive period for brain and behavioral development and (b) early experiences can have long-term influences on brain and behavioral development. To begin, it is known that there are sensitive periods in brain development (Knudsen, 1999); that is, there are periods in development during which specific types of experience are needed for the brain to develop normally. The term "experience-expectant" development has been used to refer to developmental processes that involve a readiness of the brain to receive specific types of information from the environment (Greenough et al., 1987). This readiness occurs during sensitive periods in which specific types of information are reliably present for most members of the species. This information can be visual, social, affective, and cognitive. It has been argued that the overproliferation of synapses during early postnatal life reflects the brain's readiness to receive expected information during this period, with the subset of synapses being selectively retained depending on experience (Black, Jones, Nelson, & Greenough, 1998).

Studies have clearly demonstrated sensitive periods for the development of language and visual systems (Levay, Wiesel, & Hubel, 1980; Newport, 1990). Also, studies of children at risk for cognitive and social impairment due to genetic disorders that affect brain development, such as PKU and autism, have shown that optimal long-term outcome in terms of IQ and adaptive behavior critically depends on intervention during the early years of life. For PKU, intervention must begin when the infant is less than 21 days old (Wappner et al., 1999). It has been demonstrated that children with autism who receive intensive interventions by 2–3 years of age fare substantially better than those who receive intervention after this age (see Dawson & Osterling, 1997, for review of early intervention studies in autism). Moreover, recent research has shown that relatively common variations in early experience related to stress and maladaptive parenting can have long-term effects on development. In the next sections, we will review in detail what is known about the influences of early stress and maternal depression on development. It will be concluded that early stress and maternal depression represent relatively common deviations in early experience that appear to negatively influence both brain and behavioral development.

Effects of early stress

Numerous studies, most involving animals but some in humans, have documented the negative effects of early exposure to stress and social deprivation on both brain and behavioral development, and on long-term outcome. Prenatal stress, for example, has been shown to have numerous and varied effects on the subsequent development of offspring. The function of the hypothalamic–pituitary–adrenal (HPA) axis, the major hormonal stress response system, is affected in the offspring of rats exposed to high levels of stress hormones either by injection or by exposure to stress-inducing events (e.g., handling, restraint, light, heat, cold). Offspring of pregnant rats injected with adrenocorticotropin hormone (ACTH) showed increased basal levels of corticosterone and decreased levels in response to stress (Fameli, Kitraki, & Stylianopoulou, 1994). In these offspring, the HPA system was hyperaroused during baseline conditions and was overwhelmed and unable to respond during stressful conditions. This result suggests that the systems that typically regulate the activity of the HPA system do not function normally in cases of prenatal stress. The HPA axis is regulated by a complex system involving Type I glucocorticoid receptors in the hippocampus and Type II receptors throughout the brain (Weinstock, 1997). Disregulation of this feedback system can lead to increased response to stressors, as well as an inability to adapt to ongoing stress (Weinstock, 1997).

In nonhuman primates, prenatal stress is associated with increased basal levels of ACTH in plasma, as well as increased ACTH levels in response to stress situations of varying degree in the offspring (Clarke, Wittwer, Abbott, & Schneider, 1994). Behavioral effects have also been reported in infant monkeys born to mothers that were stressed during pregnancy. Monkeys that were exposed to repeated unpredictable noise in a darkened room gave birth to infants that exhibited increased behaviors associated with disturbance (clinging to another monkey, clinging to an artificial surrogate monkey, or self-directed motor activity) and decreased motor and exploratory behaviors (locomotion, play, exploration of the environment, and climbing) compared to infant monkeys born to nonstressed mothers (Schneider, 1992a). Changes in cognitive ability have also been noted in prenatally stressed rats and monkeys. In rats, performance on a delayed alteration task was impaired in the offspring of females exposed to the presence of a cat during the gestational period (Lordi, Protais, Mellier, & Caston, 1997). In prenatally stressed rhesus monkeys, the development of object permanence was delayed compared to controls (Schneider, 1992b).

The mechanism responsible for these behavioral changes may lie in brain development changes that occur as a result of prenatal stress. In rats exposed to prenatal stress, mild stressors resulted in an increase in acetylcholine in the hippocampus (Day, Koehl, Deroche, Le Moal, & Maccari, 1998). In addition, decreases in levels of dopamine and increases in levels of serotonin were discovered in the brains of adult rats exposed to stress hormones prenatally (Fameli et al., 1994).

Interestingly, in many studies the effects of prenatal stress on regulation of the HPA axis and on brain development seem to be stronger for females than for males (e.g., Fride & Weinstock, 1989; Kinsley, Mann, & Bridges, 1989). The maternal behavior of rats that were themselves stressed prenatally clearly differs from that of nonprenatally stressed dams (Weinstock, Fride, & Hertzberg, 1988). This raises the interesting possibility of multigenerational effects of prenatal stress, an issue that has yet to be well examined in the literature. In summary, there is evidence to suggest that prenatal stress results in long-term changes in both brain and behavior in animals.

In comparison to the animal literature, less is known about the effects of prenatal stress in humans. The majority of research in the area is retrospective, such as studies in which parents respond to questionnaires about their pregnancy history (Lobel, 1994). Children whose mothers' were exposed to a variety of stressors during pregnancy were found to have less optimal outcomes, including emotion regulation problems and motor delays (Meier, 1985; Stott, 1973). The prospective studies that have been done have primarily focused on very basic indicators of health and brain development such as birth weight, head size, and risk for prematurity. Although these are likely important factors in the future cognitive and social development of the child, there is little direct evidence from studies investigating outcomes in children exposed to stress in prenatal or early life. Indirect links between head size and HPA responsiveness (Ramsay & Lewis, 1995) suggest that prenatal stress may be related to later HPA responsiveness (Glover, 1997), but the relation between stress and head size is not made directly in the Ramsay and Lewis study. Thus, a relation between stress response and prenatal stress in the human is hypothetical at best: infants prenatally exposed to stress have small heads, and infants with small heads have abnormal stress responses. Direct measures of the activity of the HPA axis are required to determine precisely the effects on the system of prenatal stress in the developing human before it can concluded that results are truly parallel to those found in nonhuman primates and rats.

Studies of animals and humans also have

demonstrated that early social deprivation and exposure to high levels of stress during the early postnatal period are related to poor social outcomes and alterations in psychobiological functioning. Exposure to stress during the postnatal period is associated with increased levels of glucocorticoids, and glucocorticoids have been shown to have harmful effects on the developing brain. Evidence now indicates that maternal behavior is important for regulation of the stress response. In rats, maternal separation stimulates HPA axis activity and leads to elevated corticosterone levels, as well as changes in, corticotropin releasing factor (CRF) concentrations and receptor number (Kuhn, Pauk, & Schanberg, 1990; Kuhn & Schanberg, 1998; Pihoker, Owens, Kuhn, Schanberg, & Nemeroff, 1993). Maternal behaviors, such as feeding and stroking, can weaken this adrenocortical response to maternal separation. Suchecki, Rosenfeld, and Levine (1993) have shown that, in maternally deprived rat pups, feeding inhibits corticosterone secretion, while stroking suppresses ACTH secretion. Moreover, the attenuating effects of tactile stimulation appear to be specific to maternal stimulation (Stanton & Levine, 1990).

Similar research with nonhuman primates has shown that plasma cortisol increases following maternal separation as a function of its duration (Levine & Wiener, 1988). In nonhuman primates, the presence of a familiar social group can serve to reduce the endocrine effects of maternal separation. Monkeys who were separated from their mothers and then isolated displayed a more profound increase in plasma cortisol levels and a slower return to baseline. It has been hypothesized that the lower stress response in the presence of a familiar social group reflects the continued availability of a stable, predictable social environment (Levine & Wiener, 1988).

Importantly, animal studies involving both rodents and nonhuman primates indicate that the effects of maternal separation can persist into adulthood (Anisman, Zaharia, Meaney, & Merali, 1998; Ladd, Owens, & Nemeroff, 1996; Plotsky & Meaney, 1993). Ladd et al. (1996) found that adult rats who had been maternally deprived showed increased baseline and stress-induced plasma ACTH concentrations as well as changes in CRF neural systems. Similarly, Plotsky and Meaney (1993) found that maternal separation during the first 2 weeks of life resulted in elevated stress responses in adult rats.

Studies of nonhuman primates have demonstrated similar long-term consequences of early life stress (Capitanio, Rasmussen, Snyder, Laudenslager, & Reite, 1986; Coplan, Andrews, Rosenblum, Owens, Friedman, Gorman, & Nemeroff, 1996). Coplan et al. (1996) exposed bonnet macaques to either predictable or unpredictable rearing conditions by varying the amount and predictability of foraging that mothers needed to do to acquire food. Years later, compared to primates exposed to predictable high foraging or predictable low foraging conditions, primates exposed to variable foraging conditions exhibited elevated cerebrospinal fluid concentrations of CRF. Capitanio et al. (1986) reported that monkeys who had experienced maternal separations as infants displayed more disturbed behavior as adults.

What is known about the influence of early postnatal stress on human development? Researchers have investigated how the mother–infant relationship affects cortisol levels by exploring the relationship between attachment security and cortisol reactivity. Nachmias, Gunnar, Mangelsdorf, Parritz, and Buss (1996) reported that a secure attachment relationship buffers the cortisol responses of behaviorally inhibited 18-month-olds to a novel situation. Only the inhibited toddlers who were also insecurely attached to their mothers exhibited significant elevations in salivary cortisol. Gunnar, Brodersen, Nachmias, Buss, and Rigatuso (1996) found that attachment security moderates the cortisol response of 15-month-olds to inoculation distress. Fearful toddlers who were also insecurely attached exhibited elevated cortisol levels. These data suggest that, especially for temperamentally inhibited or fearful children, sensitive, responsive caretaking may be an important factor in the modulation of the HPA axis.

One of the most profound, long-term naturalistic studies of early deprivation has occurred with Romanian orphanage children. These children experienced significant deprivation until their adoption into homes in Europe, Canada, and the United States. About 6 years after adoption, Gunnar and Chisholm (1999) examined the effects of early institutional rearing on cortisol levels and attachment quality. They found that children who had experienced 8 or more months of institutional rearing had significantly higher salivary cortisol compared to sex, age, and socioeconomic status matched controls and compared to children who had experienced 4 or fewer months of institutional life. Also, there was a significant positive correlation between evening cortisol levels and time in institution, suggesting that the longer exposure to deprivation is related to greater effects on the HPA axis. Moreover, securely attached institutionalized children were more likely to show normal cortisol levels.

Effects of maternal depression

Bruer argues that examples involving such unusual and severe deprivation as occurs in the studies of children in orphanages cited above do not really bear upon the concerns that typical parents might have about the appropriate kinds of emotional stimulation and responsiveness they should provide their children. But, in fact, even less extreme variations in early parenting related to the parent's own emotional well-being appear to have significant long-term influence on children's emotional development, and possibly on their brain development as well. Evidence for this comes from studies of the effects of maternal depression, which is a fairly common risk factor for children, even for those children who grow up in otherwise advantaged environments. Children of mothers experiencing affective disorders, including depression and bipolar disorder, during the early postnatal years are at risk for developing problems in self-regulation, peer relationships, and sleep regulation, and for having behavioral problems, academic difficulties, and affective disorders (Alpern & Lyons–Ruth, 1993; Coghill, Caplan, Alexandra, Robson, & Kumar, 1986; Denham, Zahn–Waxler, Cummings, & Iannotti, 1991; Downey & Coyne, 1990; Erickson, Sroufe, & Egeland, 1985; Ghodsian, Zajicek, & Wolkind, 1984; Goodman, Brogan, Lynch, & Fielding, 1993; Grunebaum, Cohler, Kaufman, & Gallant, 1978; Hammen, Burge, Burney, & Adrian, 1990; Orvaschel, Welsh–Allis, & Weijai, 1988; Redding, Harmon, & Morgan, 1990). By early childhood, children of depressed mothers have a 29% chance of developing an emotional or behavioral disorder, compared to an 8% chance for children of medically ill parents (Hammen et al., 1990). Later, we will review evidence that maternal depression is associated not only with risk for maladaptive behavior but also with risk for alterations in brain activity.

The behavioral disturbances associated with maternal depression are evident even in young infants. Infants of depressed mothers tend to be withdrawn and less active and to display lower levels of positive affect (Field, 1986, 1992; Field, Healy, Goldstein, Perry, Bendall, Schanberg, Zimmerman, & Kuhn, 1988; Field, Healy, Goldstein, & Guthertz, 1990). They also have difficulty sustaining their attention and exhibit poor mastery motivation (Radke–Yarrow, Cummings, Kuczynski, & Chapman, 1985; Zahn–Waxler, Cummings, McKnew, & Radke–Yarrow, 1984). Cognitive and language delays have been observed by 1 year of age (Radke–Yarrow et al., 1985; Zahn–Waxler et al., 1984).

Thus, it appears that maternal depression may have adverse consequences on a young infant's early development and increase the risk for affective or behavioral disorder in childhood (Hammen et al., 1990). The biological and social mechanisms mediating these effects are not yet understood. One proposed mechanism involves the influence of the mother's depression on her ability to interact with her infant in a way that facilitates emotional and cognitive development. Numerous studies have shown that a mother experiencing depression is less likely to interact in an adaptive way with her young infant. Depressed mothers often find it difficult to provide contingent responses and optimal levels of stimulation, and tend to show less positive and more negative affect when interacting with their infants (Cohn, Matias, Tronick, Connell, & Lyons–Ruth, 1986; Cohn & Tronick, 1989; Field et al., 1988, 1990; Field, Sandberg, Garcia, Vega–Lahr, Goldstein, &

Guy, 1985). During mother–infant interactions, there is less frequent sharing of positive emotional states and more frequent matching of negative emotional states (Field et al., 1990).

When the child reaches toddlerhood, it has been found that toddlers of depressed mothers are less likely to maintain interactions and display less coordinated interactions. Toddlers of depressed mothers have also been found to display fewer positive affiliative behaviors toward their mothers and higher levels of hostile and aggressive behavior (Dawson, Frey, Self, Panagiotides, Hessl, Yamada, & Rinaldi, 1999). Depressed mothers also are less likely to repair interrupted interactions (Jameson, Gelfand, Kulcsar, & Teti, 1997). When interacting with their preschool-aged children, depressed mothers have been found to use a less positive tone, display more negative affect, express more anxiety, and provide fewer direct commands (Cox, Puckering, Pound, & Mills, 1987; Kochanska, Kuczynski, & Maguire, 1989; Radke–Yarrow, Nottelmann, Belmont, & Welsh, 1993).

To explain the effect of maternal depression on children's behavior, some investigators have suggested that children may be imitating the mother's depressed behavior. Others have hypothesized that children of depressed mothers may fail to develop adequate means for regulating arousal and negative affect because of the mother's difficulty in providing appropriate levels of stimulation, responsiveness, and arousal modulation. Later, in toddlerhood, these mothers may have difficulty helping the young child to develop adequate self-regulatory strategies, leading to maladaptive affective, attentional, social, and cognitive behavior. Early in the toddler years, a major achievement is the ability to inhibit inappropriate responses and the use of self-generated mental images to guide appropriate behavior. For example, Piaget's A not B task, believed to be an early prefrontal task that requires both inhibition of a prepotent response and working memory to guide behavior, is achieved some time in the 2nd year of life (Diamond & Goldman–Rakic, 1989). It has been hypothesized that inhibitory skills mediated by the frontal lobe play a central role in emotion and attention regulation and that poor regulatory skills contribute to several different types of psychopathology (Dawson, 1994). Furthermore, there is increasing evidence that parents play a central role in facilitating the development of self-regulatory skills in young infants and children (Cicchetti, Ganiban, & Barnett, 1991; Malatesta & Haviland, 1982; Tronick & Gianino, 1986; Tronick, 1989). In the case of maternal depression, it is likely that the inability to provide adequate positive emotion and regulatory input affects not only the infant's behavioral regulation abilities but also the brain systems that underlie these abilities (Dawson, 1994).

Although the studies described above have focused on the role of the depressed mother's behavior, other mechanisms mediating the effects of maternal depression on children must be considered. Research has shown, for example, that neonates born to depressed mothers tend to be less active, less socially responsive, and fussier than those born to nondepressed mothers (Field et al., 1985; Whiffen & Gottlib, 1989; Zuckerman, Als, Bauchner, Parker, & Cabral, 1990). Prenatal exposure to maternal depression may be associated with a less than optimal intrauterine environment. The contribution of genetic factors that increase risk for depression is another important factor, although it is unlikely that genetic factors alone can account for the high risk for emotional and behavioral disturbances found in children of depressed mothers (Moldin, Reich, & Rice, 1991; Todd, Neuman, Geller, Fox, & Hickok, 1993).

There is some evidence that the first few years of life may represent a time of increased vulnerability for enduring effects of maternal depression (Alpern & Lyons–Ruth, 1993). Wolkind, Zajicek–Coleman, and Ghodsian (1980) reported that maternal depression occurring when the infants were 14 months old was predictive of later behavioral problems during the preschool years, even when the depression was absent by the time the children were in preschool. Coghill and colleagues (1986) found that maternal depression during the infant's 1st year of life was predictive of lower cognitive ability at 4 years of age, regardless of mother's depression status when the child was 4 years old. Similarly, Alpern and Lyons–Ruth (1993) found that infants of mothers who were depressed when their infants were 18–24 months but not depressed when their children were 5 years were nevertheless at increased risk for anxiety symptoms at age 5 years.

As stated earlier, children of depressed mothers are not only a higher risk for cognitive, social, and affective disturbances; they also exhibit changes in brain activity early in life. Dawson and colleagues have demonstrated that 13- to 15-month-old infants of depressed mothers show reduced electrical brain activity over the left frontal scalp region, as compared to infants of nondepressed mothers (Dawson, Grofer–Klinger, Panagiotides, Hill, & Spieker, 1992; Dawson, Frey, Panagiotides, Osterling, & Hessl, 1997). This finding has been demonstrated in two independent samples, one involving teenaged mothers with multiple risk factors and another involving middle-income, primarily married, adult mothers who were carefully screened for a variety of other risk factors that could potentially influence infant behavior and brain activity (e.g., other major psychiatric disorders, substance abuse, contact with Child Protective Services, and prenatal and birth difficulties). In the latter longitudinal study involving 159 mothers and their infants, Dawson and colleagues (1997) found that infants' atypical frontal electroencephalogram (EEG) patterns were linearly related to the severity of maternal depression. Interestingly, infant frontal EEG patterns were not found to be related to mothers' levels of anxiety or hostility, even though depressed mothers reported significantly higher levels of these symptoms (Dawson et al., 1997). It was also found that the pattern of atypical frontal electrical brain activity in infants of depressed mothers generalized to a range of situations in which we recorded brain activity, including a "nonsocial" baseline condition and a standardized playful condition carried out with a familiar experimenter (Dawson, Frey, Panagiotides, Yamada, Hessl, & Osterling, 1999). Importantly, infants of depressed and nondepressed mothers were not found to differ in terms of their affective behavior during these brief, relatively structured conditions. Thus, it does not appear that the differences in brain activity were simply the result of differences in the infants' patterns of emotional expression during EEG recording.

Dawson and her coworkers also examined the relation between individual differences in frontal brain activity and infant behavior, which were observed in naturalistic situations involving mother–infant play outside the psychophysiology laboratory. Based on previous theoretical and experimental work linking the left frontal region with approach behaviors and the right frontal region with withdrawal behaviors (Davidson, Ekman, Saron, Senulis, & Freisen, 1990; Fox, 1991), it was predicted that reduced left frontal activity would be related to lower frequencies of positive approach behaviors in the infants. In addition, based on a previous finding from our laboratory that infants of depressed mothers also show increased *generalized* frontal activation during the expression of negative emotions (Dawson, Panagiotides, Grofer–Klinger, & Spieker, 1997), it was predicted that increased levels of generalized frontal activation would be related to increased levels of intense negative affect.

In this study (Dawson, Frey, Self, et al., 1999), it was found that infants of depressed mothers were less affectionate and less likely to touch their mothers during free play. They also had more difficulty quietly occupying themselves while their mothers filled out a questionnaire, and thus appeared to have more difficulty with self-regulation. Reduced left frontal activity was correlated with lower levels of positive approach behaviors (affection toward mother during free play) and higher frequencies of negative bids for attention (grabbing mother's clipboard or pen while she attempted to fill out questionnaire). In addition, increased generalized frontal brain activity was associated with higher levels of negative affect, hostility, tantrums, and aggression. Thus, the behaviors that were found to be associated with frontal brain activity appear to reflect the dimensions of positive approach and affiliative behaviors and regulation of negative emotions. These findings suggest that maternal depression is associated with alterations in infant brain activity and that atypical frontal brain activity is associated with lower levels of approach behaviors and increased intensity of negative affect or difficulty in regulating negative affect.

Dawson (1999) also found that mothers experiencing depression displayed higher levels of insensitive behaviors when interacting with their infants. Insensitive behaviors broadly included behaviors that reflected a difficulty in sensitively following the cues of the infant, including behaviors such as poking, tickling, responding to infant's bid for attention by withdrawing from or rejecting solicited physical contact, and unsolicited holding. Furthermore, path analyses indicated that mother's insensitivity with her infant mediated the relation between maternal depression and infant frontal EEG activity (Dawson, 1999). These results provide support for the hypothesis that the behavior of a depressed mother toward her infant—in particular, the degree of maternal insensitivity—can influence patterns of infant frontal brain activity. Specifically, high levels of maternal insensitivity appear to be associated with lower levels of infant left frontal electrical brain activity. These results, taken together with previous studies on the effects of maternal depression on infant behavior and brain activity, suggest that relatively common variations in early parenting that are related to a parent's emotional well-being are associated with alterations in infant brain activity and behavior. Other studies have shown that maternal depression early in life is a risk factor for later psychopathology in childhood (Goodman & Gotlib, 1999). The question of whether altered brain activity early in life constitutes a risk factor for later psychopathology is as yet unanswered and is currently being addressed in a longitudinal study being conducted by Dawson and colleagues.

Implications for Social Policy and Future Research

What can we say about the effects of early experience on brain development and later outcome and their implications for social policy? Shonkoff (in press) outlined three levels of analysis that should be applied to critically evaluate assumptions at the intersection of science, policy, and clinical practice. First, the current state of scientific findings on the issue must be understood. Second, reasonable hypotheses can be generated as logical extensions of these scientific findings. Finally, unwarranted assertions need to be assessed. Such an analysis can then lead to well-justified policy recommendations. Let us consider such an analysis and its implications for social policy recommendations.

Regarding the current state of the science, critics agree that from the perspective of established scientific knowledge our understanding of the neurobiology of the effects of early experience on developmental outcome is still in its infancy (Bruer, 1999; Nelson, 1999a, 1999b; Shonkoff, in press). Nevertheless, a number of reasonable assertions and hypotheses can be generated from what is known based on both brain and behavioral science. First, it is clear that the prenatal and early postnatal years are a time during which remarkable growth in multiple domains of functioning (e.g., social, linguistic, cognitive, motor) occurs in terms of both brain and behavioral development. Second, ample evidence exists indicating that these years likely represent a sensitive period with respect to the effects of nutrition, exposure to toxins, and possibly stress. Third, this period also seems to represent a sensitive period with respect to the long-term beneficial effects of early intervention on brain and behavioral development for some genetically based disorders, such as PKU and autism. Fourth, evidence suggests that parental mental health during the first years of life is a significant factor with respect to early brain activity and behavior and long-term behavioral outcome. This paper has focused on early stress and maternal depression, but similar evidence exists with respect to the influence of other forms of maladaptive parenting, such as maltreatment (DeBellis, Keshavan, Clark, Casey, Giedd, Boring, Frustaci, & Ryan, 1999; Pollak, Cicchetti, Klorman, & Brumaghim, 1997).

Understanding the factors that determine social and emotional outcome in humans is a complex task that requires integrating information about the genetic, physical, and social environment. Outcome is variable because of the nondeterministic, probabilistic nature of development. As Cicchetti and Cannon (1999) state, "Epigenesis is viewed as probabilistic rather than predetermined or preformational, with the bidirectional and transactional nature of genetic, neural, behavioral, and environmental influence over the life course capturing the essence of probabilistic epigensis" (p. 377). Although early experiences are important for later outcome, this does not imply that the effects of any one type of early experience are necessarily causal or permanent. Systems theory principles such as the notion that multiple pathways can converge on a common outcome (equifinality) and vice versa (multifinality) are well accepted by developmental psychopathologists and must be incorporated into any theory about the effects of early experience on later outcome (Cicchetti & Rogosch, 1996). In developmental psychopathology, the term "pathway" is used to refer to the cumulative influence of an individual's specific genetic makeup and experiences that together operate in a complex and probabilistic fashion to influence outcome (Gottlieb, 1991, 1992). An experience involving a depressed mother most likely is moderated by a host of other factors, including genetic factors, other significant relationships, the child's intelligence and schooling, peers, and so on. Each individual has a unique combination of factors influencing outcome. Thus, in most cases it is not reasonable to consider one type of experience as having a permanent and specific effect on later outcome. On the other hand, the term "pathway" implies that, at any point in an individual's development, that individual has, indeed, developed along a specific pathway involving a complex set of risk and protective factors, and to alter this trajectory one must intervene through planned therapeutic activities that focus on changing behavioral and neural patterns of conditioning, through insight and self-will, or through serendipitous advantageous experiences (a positive role model or mentor). However it occurs, real energy is required; it rarely, if ever, happens spontaneously or easily. Fortunately, inherent plasticity appears to be a characteristic of at least some brain structures (Johnson, 1999). As Cicchetti and Cannon (1999) point out, our hopes of finding new avenues for intervention rest on discovery of the mechanisms that constrain plasticity and change.

Early development is a period that is comprised of many fundamental "experience expectant" processes. Unfortunately, there are many conditions, such as autism, in which genetic or acquired brain abnormalities preclude having a normal experience of an otherwise normal environment. As described by Black et al. (1998), neuropathology can result in

> . . . a developmental "groove" that will carry development forward. Therapeutic manipulations may perturb this trajectory initially, but development will fall back into the existing track if the canalization is sufficiently entrenched. However, if the perturbation is large enough, then the trajectory can be shifted out of one equilibrium into another, and from there brain development will proceed down a different pathway. As development proceeds, canalization generally deepens—developmental trajectories progressively become more difficult to redirect by experience. This perspective supports the common therapeutic strategies that early intervention is better than late and that more intervention may work better than less. (pp. 46–47)

The substantial effect of early intervention has been dramatically demonstrated in the case of autism. If very intensive behavioral intervention is commenced by 2 years of age, a substantial number of children with autism show a remarkable improvement in this condition (see Dawson & Osterling, 1997).

Furthermore, there are many common conditions, such as exposure to stress and maternal depression, in which the variation in early, expected environment falls outside the norm, and these conditions do appear to have an influence on long-term outcome. Because we have the knowledge of many early factors that promote optimal development, it is imperative that we translate that knowledge into social policy so that society can benefit from the scientific knowledge that has been gained. In the case of our understanding of the importance of early experience on brain and behavioral development, evidence from the neurosciences and the behavioral sciences offers a firm base for identifying optimal conditions for children's development. Public understanding of the importance of such conditions is a critical first step that must be followed by the design and implementation of policy and intervention efforts. There is much more we do as a society to provide an optimal environment in the first years of life and beyond. Policy should focus on primary prevention of adverse outcomes by reducing known risk factors related to early environment and experience so that such factors can be thwarted before they have any influence on outcome, as well as on secondary prevention by identifying environmental factors that are modifiable moderators or mediators of outcome so that we can mitigate the negative influence of such risk factors on children's development and outcome. Specifically, we believe that the following policy recommendations are well justified based on the current state of knowledge regarding the effects of early experience on brain and behavioral development.

1. In general, although prevention and early intervention efforts should not exclusively focus on the earliest years of development, it is clear from the research discussed above that such efforts should begin as early as possible. By directing such efforts toward promoting optimal prenatal and infant–toddler development, the long-term negative consequences of factors that have their greatest influences during early development and which set the stage for future development can be minimized or avoided entirely.

2. Prevention efforts that promote healthy prenatal development should focus on increasing public awareness, outreach efforts, and intervention programs related to improving prenatal nutrition, reducing fetal exposure to toxins (alcohol, drugs), and minimizing maternal stress and psychopathology during pregnancy. In light of findings that prenatal depression and stress can influence fetal and neonatal behavior, prenatal screening should include a brief assessment of maternal mental health so that appropriate medical or psychological interventions can begin at this time. Moreover, intervention programs for pregnant women suffering from alcohol or drug addiction are needed.

3. Similarly, a brief assessment of mother's mental health should be included as part of the regular well-baby checkups, along with educational materials related to infant nutrition and behavioral development. Continued efforts to improve identification of psychopathology in infants during well-baby checkups should also be supported.

4. Increased efforts to train health care workers in how to detect and respond when parents are experiencing mental health problems are needed.

5. Communities struggling with poverty and the host of associated problems that are associated with poverty (stress, violence, poor nutrition, parental psychopathology, impoverished educational opportunities) should be a direct and substantial focus of programs related to optimal prenatal and early postnatal environments because children growing up in such communities are most likely to be exposed to multiple risk factors that are associated with poor long-term outcome.

6. Because the prenatal and early postnatal years represent a sensitive period with respect to the long-term beneficial effects of early intervention on brain and behavioral development for some genetically based disorders, such as autism, increased efforts at early identification of such disorders is needed. Greater public awareness and education of health care providers with respect how to detect developmental disorders during infancy and toddlerhood and how to facilitate access to appropriate interventions are needed.

7. Efforts aimed at early identification, prevention, and remediation of developmental disorders should be enhanced. To provide one example, autism has become recognized as a relatively prevalent (1 in 500–1000 persons) developmental disorder that can and should be detected during infancy in most cases (Osterling & Dawson, 1994,

1999). Unfortunately, autism is not typically diagnosed in children until around the age of 3–4 years (Siegel, Pliner, Eschler, & Elliot, 1988). Pediatricians and other health care professionals need to be aware of how to assess early symptoms of autism in infants and toddlers so that appropriate screening and referral can occur. Moreover, given the dramatic impact of early intervention in autism, funding for early behavioral intervention programs for infants and toddlers at risk for autism is clearly justified and cost effective.

8. In general, financial, emotional, and practical support needs to be provided to families who are struggling to access appropriate intervention for their children who have been identified as having a developmental disorder, chronic illness, or mental health problem. Denial of such support to families by insurance companies and government agencies is shortsighted on the part of these health care systems in light of what is known about the critical impact of early intervention on long-term outcome.

Future research should focus on increasing our understanding of the multiple influences on children's development and outcome, and thus will depend upon multidisciplinary, longitudinal approaches that integrate biological and environmental factors. Among the important issues that need to be addressed in future research are the following:

1. Given that different biological systems develop on different timetables, it needs to be determined whether and how specific environmental events, such as exposure to stress and maternal depression, selectively affect the development of specific neurobiological systems depending on the timing and duration of the exposure to such events and whether and how timing influences risk for psychopathology. In particular, studies that address these issues in humans are needed.
2. The role of the environment in promoting optimal brain function in children needs to be better understood. For example, the contribution of parenting factors to the development of self-regulatory brain mechanisms that have been hypothesized to relate to affective and attentional disorders is still poorly understood.
3. It needs to be determined whether psychobiological measures such as neuropsychological performance, cortisol levels, autonomic responses, and brain electrical activity will be useful in identifying children at risk for psychopathology.
4. Continued research on the neurobiological bases of different types of child psychopathology will be important for understanding the etiology, nature, and treatment of such disorders. Such research will lay the foundation for identifying phenotypic markers for childhood disorders, which will be essential for early identification, designing interventions, and discovering genetic mechanisms.
5. There is also a need to develop neurobiological frameworks for interventions for children at risk for psychopathology because of genetic or environmental factors. For example, the use of neurocognitive and psychophysiological assessments that target specific brain regions, such as prefrontal functioning, may allow us to design individualized treatment approaches based on neurobiological frameworks.
6. Similarly, measures of response to interventions should include neuropsychological and psychophysiological indices of brain function to determine whether and how specific brain systems may be influenced by interventions.
7. The degree of plasticity in neural systems as it relates to risk for child psychopathology needs to be understood. For example, issues related to timing, duration, and type of early interventions that may influence outcome in children at risk for psychopathology need to be explored.

In conclusion, technological advances in brain research continue to make this an exciting time with respect to our ability to understand the neural bases of normal and abnormal development. As science continues to move this effort forward at a remarkably fast pace, it has become apparent that our most difficult challenge will not be the understanding of brain and behavioral development but rather the translation of that knowledge into meaningful policy and action. This responsibility, shared by the general public, scientists, practitioners, and policymakers, should be a central focus of our efforts.

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