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Sensitive Periods of Development

Implications for Risk and Resilience

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Scientists, educators, and clinicians have long been interested in the effects of early experience on social, cognitive, and adaptive behavioral development. Neuroscientists have long argued that there are periods across development of the nervous system during which experience-expected environmental stimuli have greatest impact. These periods are referred to as "sensitive periods" and are thought to be integral to physical, social, and cognitive functioning in adulthood.

In this chapter we focus on how sensitive periods may influence development and provide a survey of research on early childhood sensitive periods in cognition, brain development, and social–emotional development. This chapter is divided into two sections. First, we discuss the history, theory, and methodological considerations associated with research in sensitive periods. Second, we use research on early-life deprivation as a model to investigate sensitive periods in child development. Specifically, we concentrate on three domains known to underlie mental health: cognition, neural development, and social–emotional development.

INVESTIGATION AND INTERPRETATION OF SENSITIVE PERIODS

Work in the area of sensitive periods is part of a larger body of research on the effects of early experience on neural and behavioral development. For many years, scientists have been interested in the effects of early versus later life experiences on the emergence of multiple domains of adaptive behavior. Sensitive periods are one subset of this greater body of work. Scientists focus on the timing of experience and examine whether there is a particular window of time before which certain experiences do not change brain organization and behavior and after which experience may no longer play a significant role in shaping brain and behavior. Some of the earliest work in identifying these windows of opportunity dates back to the 1930s when ethologist Konrad Lorenz (1935) observed that greylag goslings would form a social attachment with the first moving object they encountered after hatching. This attachment was perceptively identical to how goslings would bond to their biological mother and was termed "imprinting," since imprinted goslings would subsequently avoid other moving objects. Lorenz detailed that goslings without exposure to a moving object within the first 48 hours would not form a strong attachment to the first moving object they encountered, and therefore deemed the first 48 hours to be necessary for the formation of this strong maternal-like bond, a "critical period" in gosling development.

Historically, "critical periods" were defined as rigidly demarcated windows of time during which experience provides input that is essential for normative development, and without this input development is irrevocably altered (Hensch, 2005; Knudsen, 2004). However, subsequent experimental work examining Lorenz's work on imprinting (Hess, 1964; Moltz, 1960) as well as human work examining early social deprivation (Clarke & Clarke, 1977; Rutter, 1980), has called into question whether critical periods for environmental experience are as well-defined and irreversible as originally thought, thus necessitating a reconceptualization of how experience impacts development.

"Sensitive periods," in contrast to critical periods, are a limited time window in development during which a system is particularly sensitive to experience (Bornstein, 1989; Hensch, 2005; Knudsen, 2004). Evidence of sensitive periods is found across many fields (e.g., biology, zoology, medicine, ethology). However, over the last few decades, sensitive periods have become an area of particular interest for understanding and investigating human development. Specifically, the concept of sensitive periods may provide one account as to how early experiences (or the lack thereof) have particularly strong effects on brain and behavior later in life (Bornstein, 1987, 1989; Hensch, 2003; Werker & Hensch, 2015; Werker & Tees, 2005; Zeanah, Gunnar, McCall, Kreppner, & Fox, 2011).

What Defines a Sensitive Period?

Although what defines a sensitive period varies across disciplines, there are a number of characteristics that are necessary to deem a phenomenon a "sensitive" period (for reviews, see Bornstein, 1987, 1989; Knudsen, 2004).

Bornstein (1989) indicated that each sensitive period should have a defined "system" that is being altered by a change in sensitivity to environmental experiences. Changes to this system may be easily observable and assessed (e.g., visual acuity) or a more a more complex and less easily mapped latent construct (e.g., emotion interpretation), but critically these systems should not be entirely under genetic control and therefore must rely on contributions from experience for development (Knudsen, 2004). William Greenough, a neuroscientist, first proposed two processes by which experience affects the brain: experience expectant and experience dependent. "Experience-expectant" processes are those that the emerging neural circuitry "expects" in order to form adaptive systems for behavior. A good example is vision, with particular types of visual experience playing a formative role early in life. "Experience-dependent" processes are those that form the foundation of individual differences in children's learning and development. The formation of neural circuits "depends" on the particular and unique contexts and stimuli that are provided. On the one hand, experience-expectant processes lend themselves easily to thinking about sensitive periods during which these "expected" events are to occur. Experience-dependent processes, on the other hand, may occur across the lifespan. Each system should have an *asymptote* or *direction* of change (i.e., increase or decrease); it has been suggested, however, that direction of change may not be unidirectional and may be mediated by organism-specific characteristics or prior experiences (Boyce & Ellis, 2005). For example, research examining sensitive periods in IQ development has identified periods of environmental sensitivity for two different directions of change: increased IQ (Brant et al., 2013) and decreased IQ (Fox, Almas, Degnan, Nelson, & Zeanah, 2011; van IJzendoorn, Luijk, & Juffer, 2008).

All sensitive periods should have an *onset* or *opening* period when sensitivity to a particular set of experiences begins to increase, a *duration* of increased sensitivity, and an *offset* during which sensitivity declines. While these features are rather straightforward in definition, they may vary widely across systems. For instance, onsets and offsets may be gradual or very sharp. Similarly, onsets and offsets may be defined by chronological age (time since birth) or developmental age (age at which a child functions across domains). Additionally, for an onset to occur, each system must be developed enough to function, plastic enough for changes to occur, and have the ability to be modulated via a *mechanism* or *pathway* (e.g., up-regulation–down-regulation or excitatory–inhibitory; Fagiolini & Hensch, 2000; Hensch, 2003; Knudsen, 2004).

Finally, it is important to consider that sensitive periods may have different degrees of *variability* across both individuals and species (Bornstein, 1987, 1989). Individual and species variation in duration, onset, offset, mechanism, asymptote, and pathway can make sensitive periods difficult to operationalize and measure. Investigations of variability in sensitive periods are of great interest to many, since they may infer possible areas of most optimal intervention.

Outcomes of a sensitive period affect the system in a number of different ways and include introducing a new function, altering an existing function, or maintaining an already existing function. Outcomes can have different temporal profiles, ranging from instant to emerging decades later (a "sleeper" effect), and can be short-lived or persist across the lifespan. Finally, some outcomes may be alterable by experiences outside of the sensitive period, whereas others are more permanent.

Examples of Sensitive Periods

One of the clearest and translational studies of sensitive periods comes from the experimental work of Hubel and Wiesel (1959, 1962, 1965; Wiesel & Hubel, 1963) detailing the development of the visual system. Hubel and Wiesel's work documented that when kittens are first born they show a pattern of nonspecialized neural architecture in an area of the brain integral to vision (striate cortex). However, over time, kittens with normal visual development begin to show a highly specialized neural architecture with alternating, columnar connectivity for each eye. Given that this neural specialization begins only after kittens are exposed to a complex visual environment, it was hypothesized that a sensitive period for visual development may exist. To test this hypothesis, Hubel and Wiesel occluded one eye shortly after birth and found that after a short period of time, the occluded eye becomes functionally blind and that the specialized neural representation for the eye never developed. Hubel and Weisel (1963) also demonstrated that if an eye remained occluded for an extended period, then the kitten did not recover normal vision or neuronal specialization in visual cortex. While parallel work obviously cannot be done in humans for ethical reasons, a natural experiment exists in children who are born with congenital cataracts. Consistent with the work Hubel and Weisel, children who have congenital cataracts show altered perceptual development and amorphic development of visual cortex (Lewis, Maurer, & Brent, 1995; Lewis & Maurer, 2005). Furthermore, the study of children with cataracts (binocular and monocular) and amblyopia (poor visual in a single eye due to altered brain circuitry) has identified multiple sensitive periods related to visual acuity, peripheral vision, and detection of global motion (Berardi, Pizzorusso, & Maffei, 2000; Hensch, 2005; Lewis et al., 1995; Lewis & Maurer, 2005).

While development of the visual system shows strong evidence of sensitive periods, it is important to note that a wide variety of systems in human development show similar indications of sensitive periods. Language development has been shown to have many overlapping and interacting sensitive periods during development that lead to optimal language processing (Werker & Hensch, 2015; Werker & Tees, 2005). For instance, within speech perception, separate and cascading sensitive periods appear to exist for phonetic, phonological, lexical, and reading development. Similarly, there is evidence for sensitive periods in face processing. A number of researchers have documented changes in the perception of faces and face-voice integration across the first year, with decreased discrimination across categorical boundaries with age, a phenomenon known as "perceptual narrowing" (Nelson, 2001). Beginning in the first period of life, one or more sensitive periods appear to exist for the memory of faces, race processing, gender processing, and species processing. The evidence of experience-expectant periods of development within language development and face processing provide two additional examples of sensitive periods in human development, with more examples existing across other domains. They also emphasize that within each domain there are multiple sensitive periods corresponding to the emergence of component processes involved in these complex skills.

Sensitive Periods in Human Development

While there are many well-defined sensitive periods in sensation and perception in both animal and human work, sensitive periods for more complex skills (e.g., cognition or social behaviors) are much harder to investigate for at least two reasons. First, many complex processes have a protracted period of development and rely on the development of a number of integral underlying skills. For instance, intelligence heavily relies on the development of language, executive functions, fluid cognition, and crystallized cognition. In addition to relying on many individual skills, sensitive periods in complex social skills are hard to identify, since it is difficult to delineate typical versus atypical development given the wide variation in onset and presentation of social behavior across contexts and cultures. Second, there are significant ethical considerations associated with investigations of sensitive periods in humans. While animal research allows for carefully controlled and manipulated studies that substantially alter an organism's environment (e.g., severe deprivation, knockout animals), such manipulations commonly produce long-lasting changes that would be unethical in human populations. Given these limitations, much of the research detailing sensitive periods in human development relies on so-called experiments of nature in which environmental manipulations are the result of some societal, social, medical, or genetic perturbation.

One framework that is well suited for the investigation of sensitive periods in humans is found in populations that experience early deprivation. By examining the onset, duration, and extremity of early deprivation, scientists can begin to understand what periods of childhood are critical for neural, cognitive, and social development. There are many different types of early deprivation a child can experience, such as poverty, maltreatment, and neglect, each of which is accompanied by its own constellation of environmental experiences (for review, see Sheridan & McLaughlin, 2014). One major difficulty associated with using deprivation studies to examine sensitive periods is that, for many children, deprivation is long-lasting and it is therefore difficult to parse whether environmental deprivation differentially impacts development at separate points in development. One area of deprivation research with rather abrupt changes in environmental conditions that can begin to untangle whether environmental deprivation may differentially influence development is the institutional care and international adoption literature. For the remainder of this chapter we summarize current findings that suggest sensitive periods exist for neural, cognitive, and social development, as evidenced by studies of institutional care.

Sensitive Periods in Child Development: Evidence from Studies of Institutional Care

Current estimates suggest that, worldwide, about 8 million children reside in institutional care (United Nation's Children's Fund, 2004, 2007). Children in institutional care experience adverse early experiences that influence a number of domains, including language, cognition, emotion, and attachment/social development.

While early deprivation is a useful model for identifying sensitive periods in human development, there are some important caveats that should be acknowledged. First, alterations in complex behaviors are likely to be distal outcomes of many overlapping and interacting sensitive periods in human development (Knudsen, 2004). Additionally, complex skills tend to comprise more simple subskills (which are likely to have their own individual sensitive periods and developmental cascades) that interact and rely on one another, which makes the assessment of sensitive periods very difficult (Werker & Tees, 2005). Furthermore, evolution and human development rely on multiple mechanisms that compensate for deviations in development. As such, many of the effects discussed in the following sections are likely to be conservative estimates of the effects of early sensitive periods on subsequent functioning (Zeanah et al., 2011).

In contrast to much of the work on sensitive periods in animals and sensory domains in humans, sensitive periods of complex systems in human development are methodologically more difficult to identify. As discussed previously, ethical concern over scientifically manipulating a child's environment is one of the major reasons that it is difficult to identify sensitive periods in human development. Second, many studies examining sensitive periods in human development via natural experiments do not have high degrees of control (i.e., children who are adopted from institutions may be different from those who are not) or a high degree of temporal resolution (i.e., children are more likely to be adopted in early vs. late childhood). Given these constraints, we have outlined how we identified particular components of sensitive periods in the early deprivation literature in Table 1.1.

Postinstitutionalization adoption studies allow investigation of sensitive periods in a number of ways. Children who are exposed to institutionalized care early in life and then placed in high-quality environments (adoptive homes) provide three kinds of evidence for sensitive periods in early childhood. First, extended follow-up of such children allows examination of deficits they may have at the time of adoption and also those that may emerge

TABLE 1.1. Components of Sensitive Periods in the Context of Early Deprivation

Sensitive period component	Definition	Example from early deprivation model
Asymptote	Direction of effects	Does deprivation cause development to be stunted or accelerated?
Onset	Environmental sensitivity is increased	Do children removed from deprivation before a certain age not see deficits?
Offset	Environmental sensitivity is decreased	Is there a point at which continued institutional care does not have a differential effect on development?
Variability	Differences in systems and outcomes between children	Do children with similar caregiving backgrounds show a wide array of performance?
Outcomes	Changes in the individual as a result of sensitive periods	Are children who had early deprivation at increased risk for a negative outcome?

over time. Deficits noted at the time a child is taken out of an institution and placed into care may suggest that the experiences in institutional care are associated with these deficits. This, of course, assumes that no preexisting condition contributed to these deficits. As well, variation in the age at which a child is removed from the institution may help inform whether there are sensitive periods involved in the effects of such early depriving experience. For example, if one child is removed from an institution prior to 6 months of age and another is removed a year later, differences in deficits may suggest that the timing, length of deprivation, or the age of exposure (or all three) contributed to these different outcomes. Again, this assumes that there were no preexisting differences between these two children. Second, improvement or amelioration of deficits after a child is removed from institutional care suggests that the system impacted the child during a sensitive period may be plastic, or that the timing of intervention occurred during the sensitive period (had not reached its offset), or that multiple sensitive periods may exist, or that there is no sensitive period.

Many studies have assessed the effects of institutionalized care on internationally adopted children; however, one seminal cohort worth mentioning is the English and Romanian Adoptees (ERA) Study (Rutter & ERA Study Team, 1998; Rutter, Sonuga-Barke, & Castle, 2010). The ERA Study began in the 1990s and was designed to examine the effects of early deprivation on child development. The sample was drawn from 324 children who were adopted into families in England before 42 months of age. The final sample consisted of 111 children adopted before 24 months and 54 children adopted between 24 and 42 months of age. Additionally, 52 within-country adoptees were recruited for comparison. Data from the ERA Study have demonstrated that early adversity affects organismic changes that are difficult to ameliorate and extend beyond just prolonged psychosocial deprivation. These changes are referred to as "biological programming" (Rutter, O'Connor, & ERA Study Team, 2004). Rutter and colleagues have demonstrated that children who experience early deprivation show patterns of cognitive deficits that are consistent with biological programming effects or neurological damage. Further evidence of biological programming comes from data detailing increased incidence of disinhibited attachment. Specifically, findings indicate that children who were institutionally deprived are more likely to show disinhibited attachment styles and that there is a relation between disinhibited attachment and duration of deprivation; furthermore, these patterns persist after the restoration of normative family rearing. Data from the ERA study have demonstrated the biological programming effects of early deprivation and suggested sensitive periods in child development across a number of domains (Rutter et al., 2010).

To date, there has been only one randomized controlled study of institutionalized care and early intervention, the Bucharest Early Intervention Project (BEIP). The BEIP randomly assigned young children residing in institutional care in Bucharest, Romania, to either remain in institutionalized care and continue to receive care as usual, as provided by the Romanian Government, or to receive a high-quality foster care intervention (see Zeanah et al., 2003, for more information on study design). Data from the BEIP provide evidence for the effects of early deprivation and allow inspection of the presence of sensitive periods in development by examining the age at which children were removed from the institution and placed into foster care. Continued follow-up of both groups of children (care as usual and foster care) provide evidence of how continued deprivation affects systems of interest.

For the remainder of the chapter we review the evidence of sensitive periods in neural development, cognitive development, attachment, and mental health through the lens of early deprivation.

Sensitive Periods in Neural Development

Sensitive periods in neural development are of great interest given that an understanding of aberrations in neural development may elucidate possible mechanisms associated with more complex cognitive changes, such as the differences seen in IQ and executive functioning (Nelson, Bos, Gunnar, & Sonuga-Barke, 2011). Research findings on the effects of adverse early experiences on neural development generally focus on structural, functional, or a combination of structural and functional neural changes. Structural changes are physical changes to the brain, such as increased or decreased volume, thought to reflect in part the growth of neurons or changes in diffusivity of water molecules in the brain (indicated by diffusion tensor magnetic resonance imaging) thought to reflect the integrity of white-matter tracts or myelin. Functional changes, on the other hand, reflect differential patterns of brain activity or changes in circuit connectivity reflecting a pattern of use. In the following two sections we review the evidence for sensitive periods in structural and functional brain development. While we review these two bodies of literature separately, it is important to remember that structure and function are linked, given that the use (or lack of use) of brain regions commonly leads to changes in structure. However, how function and structure interact throughout development remains empirically understudied.

Structural Differences

Structural brain development begins a few weeks after conception and continues into the second and third decades of life. Given the protracted time course of neural development, early experiences may influence development starting in the prenatal period. Neural development in the postnatal early infancy period is commonly a period of robust "synaptogenesis" (creation of brain cells), with an abundance of dendrites and axons being produced (Huttenlocher & Dabholkar, 1997). While some evidence suggests that synaptogenesis rates are experience-dependent and vary by region, with more rudimentary areas of the brain typically peaking in cell count before areas that support more complex functions (Huttenlocher & Dabholkar, 1997), other data suggest this may not be the case. For instance, studies in primates have shown that synaptogenesis occurs synchronously across all cortical areas (rather than in a pronounced order) and is independent of environmental input (Rakic, Bourgeois, & Goldman-Rakic, 1994). Following a period in the postnatal months of rapid synaptogenesis, brain regions begin experience-dependent pruning (the removal of synapses, axons, dendrites, etc.) that enables the brain to adapt and organize itself optimally based on environmental demands. Rates of synaptic pruning vary as a function of a hierarchy of circuits, with simple areas/circuits (i.e., visual and motor systems) pruning earlier and faster than more complex areas/circuits (i.e., prefrontal and limbic systems). Another aspect of neural development is "myelination," which is the process of forming a fatty sheath around the axons of neurons that aids in neuronal conduction, speed, and communication. Myelination begins in midinfancy and persists into early and midadulthood, with more complex brain structures completing myelination later than more basic structures (Benes, Turtle, Khan, & Farol, 1994; Yakovlev & LeCours, 1967).

There is much evidence that the presence of expectable, contingent caregiving early in life is essential for proper structural brain development (Sheridan, Fox, Zeanah, McLaughlin, & Nelson, 2012; Tottenham & Sheridan, 2010; Tottenham, 2012a, 2012b). Given that deprivation is associated with the absence of essential environmental experiences, the effects of deprivation on the brain tend to be robust and, in some cases, long-lasting. Here we review the major findings related to volumetric differences, amygdala development, and frontal circuitry; however, there are many other areas of the brain influenced by early deprivation (for review, see Bick & Nelson, 2016).

SENSITIVE PERIODS AND BRAIN VOLUME

Volumetric measures of brain development index, among other things, the efficiency of synaptogenesis, synaptic pruning, and myelination in the whole brain and in specific brain regions. Simply, volumetric measures usually consist of three measures: total volume, white matter volume, and grey matter volume. White matter volume is predominantly composed of myelin and glial cells, and is associated with neuronal communication and connectivity, whereas grey matter is composed of neuronal cell bodies, dendrites, and unmyelinated axons, and is associated with sensory and cognitive processing (Miller, Alston, & Corsellis, 1980; Wilke, Krägeloh-Mann, & Holland, 2007). There is converging evidence that early deprivation is associated with reductions in head size and whole-brain volume, as well as alterations in grey matter and white matter, which suggests there may be many sensitive periods for synaptogenesis, synaptic pruning, and myelin creation early in infancy and early childhood (Hanson et al., 2015; Mehta et al., 2009; Sheridan et al., 2012). Data from the BEIP indicate that early intervention may buffer against the negative effects of early deprivation on white matter but not grey matter development (Sheridan et al., 2012). These findings suggest that there may be separate sensitive periods for white and grey matter development, with the white matter sensitive period lasting longer, occurring later, or being more malleable than the sensitive period for grey matter.

EVIDENCE FOR SENSITIVE PERIODS IN THE AMYGDALA

The limbic system consists of a number of brain structures associated with emotion processing and regulation, memory, motivation, and learning (LeDoux & Phelps, 2010; Mega, Cummings, Salloway, & Malloy, 1997). The amygdala, an area essential for emotion and threat processing, appears to be influenced by institutional care; however, the asymptote (direction of change) may be influenced by a number of contextual factors (Callaghan & Tottenham, 2016). For instance, two postinstitutionalization adoption studies found evidence that early institutional care is associated with increased amygdala volume and a positive relation between amygdala volume and length of time spent in the institution (Mehta et al., 2009; Tottenham et al., 2010). Conversely, another postinstitutionalization adoption study found decreased amygdala volume in children who experienced early deprivation, with a negative relation between amygdala volume and cumulative life stressors (Hanson et al., 2015). Recent work by Tottenham (Callaghan & Tottenham, 2016; Gabard-Durnam et al., 2014; Gee et al., 2013) suggests that both amygdala functioning and connectivity between amygdala and cortical regions change across typical development and are also influenced by adverse experiences. In a series of studies, Tottenham found that children experiencing early adversity displayed more "mature" patterns of amygdala reactivity (similar to older children and adults), as well as more "mature" connectivity. One possibility is that early adverse experience speeds up the development of these connections so as to enhance possibilities for survival in a stressful environment (Callaghan & Tottenham, 2016). These findings suggest there may be sensitive periods for amygdala development early in life; however, the asymptote may vary substantially based on postinstitution environmental input and individual factors.

EVIDENCE OF SENSITIVE PERIODS IN FRONTAL CIRCUITRY

The prefrontal cortex (PFC) is implicated in a number of complex emotional and cognitive functions, such as executive functions, top-down attentional processes, and self-regulation. The PFC has one of the most protracted developmental time courses in the brain, which makes it highly susceptible to environmental influences such as stress (Arnsten, 2009; Gogtay et al., 2004; Kolb et al., 2012). To date, only two studies have reported an effect of institutional care on PFC development (Hodel et al., 2015; McLaughlin et al., 2014). Both studies found that the PFC was negatively impacted by institutional care (decreased cortical surface area or thickness). While the effects of institutionalized care on specific subregions of the PFC differed slightly across the two studies, these changes do suggest that the PFC may be particularly sensitive to environmental experiences, and that there may be a sensitive period for normative PFC development in the first few years of life.

Resting-State Functional Differences

Sensitive periods related to function while the brain is at rest have received much less attention than structural differences. To date, two studies have looked at functional connectivity in previously institutionalized children using two different neuroimaging methods: positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). Using PET to examine brain glucose metabolism, data indicate that previously institutionalized children show bilateral reductions in metabolic rates in the in the orbitofrontal gyrus, the infralimbic PFC, the medial temporal structures (amygdala and head of hippocampus), the lateral temporal cortex, and the brain stem (Chugani et al., 2001). These data suggest that many of the cognitive and mental health deficits we discuss later in this chapter may be mediated by dysfunction in these brain regions caused by early deprivation (Chugani et al., 2001). Additional evidence for functional differences is found in ventromedial PFC and amygdala connectivity. During typical development, the amygdala and PFC show a period of positive coupling early in life, followed by a period of negative coupling later in development (Callaghan & Tottenham, 2016). However, data from previously institutionalized children indicated more mature patterns of connectivity (negative connectivity) between the ventromedial PFC and amygdala early in life (Gee et al., 2013). These data suggest there may be a period for neural connectivity in circuits related to fear learning that is particularly sensitive to and accelerated by early life stress. To date, no studies have used PET or fMRI in a randomized controlled design, a necessary scientific step to test the presence of sensitive periods in brain development.

Additional evidence for sensitive periods in functional brain activity comes from studies using electroencephalography (EEG). A series of studies from the BEIP at child ages 30 months, 42 months, and 8 years have documented both the negative effect of early deprivation on neural activity, as well as the possible amelioration of these deficits with early intervention. Prior to the implementation of the BEIP intervention, when participants were 30 months of age, early neglect was related to more immature patterns of brain activity—higher levels of lower-frequency activity (theta oscillations) and lower levels of higher-frequency brain activity (alpha and beta oscillations)—when compared to community controls (Marshall & Fox, 2004). This pattern of results remained significant at 42 months and at 8 years of age for children randomized to remain in institutional care; however, a different pattern of activation emerged for children who were randomized to receive a high-quality caregiving intervention (Marshall, Reeb, Fox, Nelson, & Zeanah, 2008; Vanderwert, Marshall, Nelson, Zeanah, & Fox, 2010). At age 8, children who were removed from institutional care and placed into a therapeutic foster care setting began to show more developmentally typical patterns of neural activity (Vanderwert et al., 2010). However, these intervention effects were qualified by the age at which children were placed into foster care. By age 8, children placed into foster care before 24 months showed neural activity indistinguishable from that of never-institutionalized community controls, while children placed after 24 months of age showed activation similar to that of children randomized to remain in institutionalized care. These findings have two major implications for understanding sensitive periods in specific aspects of brain development. First, it appears that early deprivation has noticeable effects on EEG activity by 30 months of age, suggesting that the onset of sensitive periods related to neural activity begin early in life. Second, aberrations in neural activity related to early deprivation may be ameliorated with intervention at or before 2 years of age. However, given that children who received intervention after 2 years of age did not show intervention effects, it is possible that one or more sensitive periods related to neural activity may close as early as 2 years of age. Furthermore, given that children who received the foster care intervention before 24 months of age did not show improved patterns of neural activity at 30 months of age, and that these effects were only evident later in development, it is important to consider that amelioration of early deficits may rely on long-lasting environmental interventions or that outcomes related to early intervention may not appear until later in life (sleeper effect).

Sensitive Periods in Cognitive Development

IQ

IQ is commonly considered a "gold standard" among psychologists as a measure of assessing human intelligence and is heavily relied upon for the diagnosis of intellectual disabilities. Unlike many cognitive assessments, IQ is commonly standardized, age-adjusted, and thought to remain relatively stable across the lifespan, particularly in adulthood. Methods of IQ assessment vary over the lifespan, but most research is conducted using standardized assessments such as the Wechsler (1974) family of tests, Stanford–Binet (Thorndike, Hagen, & Sattler, 1986), Woodcock–Johnson (Woodcock & Johnson, 1989), and the Bayley (2006) scales for young children.

Evidence from a wide range of studies suggests that early deprivation has marked effects on the development of IQ (Fox et al., 2011; Nelson et al., 2007; Rutter et al., 2010; van IJzendoorn et al., 2008). These studies show that deprivation during early childhood is associated with lower IQ scores.

Studies examining the onset of sensitive periods related to IQ have shown that the earlier children are removed from deprivation, the less likely they are to show reduced IQs. Two studies of early deprivation provide strong evidence for the existence an IQ-related sensitive period. One postinstitutionalization adoption study (Rutter & ERA Study Team, 1998) found that children adopted under the age of 6 months did not show decreased IQ at ages 4–6 or at age 11, but children adopted between 6 and 24 months did show decreased IQ at ages 4–6 and age 11. These results suggest that the onset of an IQ-related sensitive period may begin around 6 months of age, with a duration well into early childhood.

Evidence supporting the existence of sensitive periods in IQ development also comes from the BEIP. Consistent with other studies, children in the BEIP who experienced early psychosocial deprivation showed reduced IQ scores (Smyke et al., 2007). Additionally, children removed from institutional care at younger ages showed smaller decreases in IQ at 42 and 54 months of age, suggesting that sensitive period onset is likely in late infancy or early toddlerhood (Nelson et al., 2007). However, when examining the IQ of children ages 8 and 12, a different pattern begins to emerge, showing fewer differences in IQ, based on timing of placement in foster care (Almas, Degnan, Nelson, Zeanah, & Fox, under review; Fox et al., 2011). Interestingly, these changes appear to be related to environmental experiences following initial randomization, such as reduced time in institutional care, placement into government foster care homes, and stability of home placement, suggesting either that sensitive periods related to IQ may have a long duration (into middle childhood) or that IQ outcomes are alterable by some kinds of environmental experiences following the sensitive period.

Executive Functions

"Executive functioning" is commonly defined as the skillful employment of three cognitive processes—working memory, inhibitory control, and attention shifting—in order to complete a goal. Executive skills are thought to be highly susceptible to environmental influences given that they have a protracted development across childhood and have been linked to a variety of outcomes in adulthood, such as academic achievement, incarceration, substance abuse, and overall physical and mental health (Moffitt et al., 2011). While executive functioning is essential for the assessment of IQ, studies have shown that IQ assessments do a poor job of evaluating executive functioning, and that IQ and executive functions are separable constructs (Ardila, Pineda, & Rosselli, 2000).

Similar to IQ, executive functions appear to be negatively impacted by early deprivation; however, findings vary by assessment method, age of assessment, and specific executive skill (Hostinar, Stellern, Schaefer, Carlson, & Gunnar, 2012; McDermott et al., 2013; Merz & McCall, 2011; Pollak et al., 2010). Merz and McCall (2011) found that children adopted from institutionalized care were more likely to exhibit executive function deficits. Additionally, they found that children adopted after 18 months fared worse than those adopted before 18 months, suggesting that the onset for sensitive periods related to executive functions may be within the first year of life.

Further evidence of sensitive periods in executive development comes from two studies that utilized the Cambridge Neuropsychological Test and Automated Battery (CANTAB; Cambridge Cognition, Cambridge, UK) to assess executive skills in institutionalized and previously institutionalized children at 8 years of age (Bos, Fox, Zeanah, & Nelson, 2009; Pollak et al., 2010). Pollak and colleagues found that postinstitutionalized children adopted at or after 12 months of age showed deficits in the spatial working memory and paired associated learning task, while children adopted out of institutionalized care at or before 8 months of age did not show these deficits when compared to a nonadopted comparison group. Similarly, studies from the BEIP showed children with a history of institutional care preformed worse on visual memory and executive functioning (ages 8 and 12) and learning (age 12) when compared to noninstitutionalized peers (Bick, Zeanah, Fox, & Nelson, under review; Bos et al., 2009). Additionally, early removal from institutional care was also not associated with improved memory and executive skills. Furthermore, this pattern of data may also suggest that, at least for some forms of executive function, there may be a sensitive period in infancy, with deficits difficult to remediate later in life.

Other studies examining executive functions of children who have experienced institutionalized care also show evidence of deficits when examining both behavioral and neural correlates of executive functions. One task commonly used to assess attention, inhibitory control, and error monitoring is the Go/No-go task. Data from the BEIP show that children in institutionalized care show both behavioral and neural deficits on the Go/No-go and Flanker tasks (Loman et al., 2013; McDermott, Westerlund, Zeanah, Nelson, & Fox, 2012). In a Flanker task, participants are instructed to identify the direction of a center arrow, which is surrounded by four flanking arrows that can point in the same direction or in the opposite direction of the center arrow (<<<<< or <<><<). The flanker task is thought to index conflict monitoring, selective attention, and inhibitory control. Specifically, on the Go/No-go task, children who were randomized to remain in institutionalized care showed reduced behavioral performance (accuracy and reaction time), as well as perturbed neural correlates associated with reduced attentional processing of No-go cues and poor detection of errors, while children removed from institutional care and placed in high-quality foster care only showed reduced attentional processing of No-go cues (McDermott et al., 2012). Similarly, a separate study of postinstitutionalized adopted children showed reduced behavioral performance in previously institutionalized children; however, neural correlates of attentional processing and error detection were not consistent with the findings from BEIP (Loman et al., 2013).

Another task commonly used to assess behavioral and neural correlates of executive function is the Flanker task. Similar to the Go/No-go task, the Flanker task was administered to both the BEIP sample and a postinstitutionalized sample (Loman et al., 2013; McDermott et al., 2013). In the BEIP sample, children randomized to remain in institutionalized care showed that early psychosocial deprivation was associated with impaired inhibitory control (measured behaviorally), as well as perturbed neural correlates of response monitoring (McDermott et al., 2013). Children who received the foster care intervention exhibited better response monitoring when compared to children who remained in institutional care. Furthermore, children within the foster care group who exhibited larger neural correlates associated with error monitoring exhibited less behavioral problems, indicating that executive functions may be an important component of healthy social–emotional development. Similarly, a separate sample of postinstitutionalized children adopted into the United States showed deficits in inhibitory control, with evidence that children adopted later exhibited larger deficits (Loman et al., 2013). Furthermore, postinstitutionalized adoptees showed altered neural correlates associated with error and response monitoring.

Together these findings suggest that children who experience early deprivation show behavioral problems and some neural evidence of reduction in inhibitory skills, providing further evidence for sensitive periods for executive development early in life. However, given that children who experienced prolonged institutional care showed worse deficits than those removed from institutional care on a number of measures, it is possible that the sensitive period for executive development may extend into middle childhood or that many sensitive periods for executive development may exist.

Sensitive Periods in Social and Emotional Development

The absence of consistent, contingent caregiving in institutional care has made children reared in this setting the focus of attachment research for decades. Across many studies it has been demonstrated that institutional care is related to abnormal patterns of attachment, with reduced security and increased prevalence of atypical attachment patterns (Steele, Steele, Jin, Archer, & Herreros, 2009; Vorria et al., 2003; Zeanah, Smyke, Koga, & Carlson, 2005). A meta-analysis examining whether removal from institutional care facilitates more normative patterns of attachment found that children adopted before age 12 months were more likely to be securely attached than those adopted after (van den Dries, Juffer, van IJzendoorn, & Bakermans-Kranenburg, 2009). Data from the BEIP also suggest that removal from institutional care and placement into foster care reduces insecure atypical attachment patterns and increases secure attachment (Smyke, Zeanah, Fox, Nelson, & Guthrie, 2010). These findings all suggest that a sensitive period for attachment exists early in development. During this sensitive period, the presence of a high-quality, consistent caregiver appears to be essential for the formation of secure bonds. These data also suggest that this sensitive period for attachment may open near the end of the first year of life, as evidenced by the meta-analysis of prior postinstitutionalized attachment studies.

Children in institutionalized care also show "indiscriminate friendliness," which is defined as disinhibited affectionate and friendly behavior towards all adults (including strangers) without fear (Tizard, 1977). Indiscriminate friendliness has been considered by some to be another variety of attachment disorder (O'Connor, Rutter, & ERA Study Team, 2000), whereas others believe it is an independent symptom (e.g., Zeanah, Smyke, & Dumitrescu, 2002). One of the first studies of indiscriminate behavior in institutionalized children revealed that almost 40% of children in institutionalized care exhibited indiscriminate behavior by age 4 (Tizard & Rees, 1975). Further studies of postinstitutionalized adoptees show similar patterns of increased indiscriminate behavior to that in children who were previously institutionalized (Hodges & Tizard, 1989; Rutter et al., 2007). Rutter and colleagues also demonstrated that children who were institutionalized beyond the age of 6 months were more likely to show indiscriminate friendliness, and they suggested that experience-based biological programming after 6 months of age may lead to indiscriminate behaviors. Consistent with other samples, children in the BEIP showed higher levels of indiscriminate friendliness (Zeanah et al., 2002); however, children who were identified as favorites of caregivers showed lower levels of indiscriminate behavior. Interestingly, children randomized to the foster care intervention showed similar levels of indiscriminate friendliness to that of children randomized to remain in institutional care. These findings suggest that there may be a sensitive period for indiscriminate social behavior that begins after 6 months of age. Furthermore, as evidenced by less indiscriminate behavior in children who were favorites of the institutional staff, the presence of an attached and attentive caregiver may be the expected environmental input (experience-expectant) for this sensitive period. Furthermore, given that later interventions (e.g., BEIP foster care, which began at a mean age of 22 months) did not reduce indiscriminate behavior, it is probable that the sensitive period for indiscriminate behavior may close by the second year of life.

Sensitive Periods in Mental Health

The final area of development we review for evidence of sensitive periods is mental health. One of the difficulties with identifying sensitive periods in mental health is that psychopathology is commonly considered an outcome that is measured sometimes years after the sensitive period may have occurred. Similarly, given that many psychiatric disorders do not appear until later childhood and early adolescence, it has been postulated that mental health problems may be a sleeper effect, reflective of the presence or lack of specific experiences in infancy and early childhood (Pine & Fox, 2015).

For over 50 years, it has been known that children who experience early deprivation are at increased risk for developing psychiatric disorders (Bos et al., 2011; Widom, DuMont, & Czaja, 2007). Psychopathology rates among previously institutionalized children are elevated across both internalizing and externalizing domains, with particularly high rates of attention problems, hyperactivity, poor self-regulation, attachment disorders, and anxiety (Colvert et al., 2008; Ellis, Fisher, & Zaharie, 2004; MacLean, 2003; Tizard & Rees, 1975).

Many researchers have examined the psychiatric consequences of early deprivation; however, a series of studies from the BEIP project provides a comprehensive view of both the effects of early deprivation and early intervention. The first standardized assessment of mental health in the BEIP sample, conducted at 54 months of age, found that early deprivation was associated with a higher likelihood for both externalizing and internalizing disorders (Zeanah et al., 2009). Children who received the foster care intervention were less likely to have internalizing disorders (primarily anxiety) but were equally likely to exhibit externalizing disorder. At age 12, psychiatric disorders were reassessed and, consistent with the 54-month findings, results indicated that children who experienced early deprivation were still at elevated risk for both internalizing and externalizing disorders (Humphreys, Gleason, et al., 2015). However, inconsistent with the findings at 54 months, children who received the foster care intervention were less likely to exhibit externalizing disorders but equally as likely to exhibit internalizing disorders as children randomized to remain in institutional care. Importantly, additional analyses revealed that children in the foster care intervention who had stable foster care placements showed less internalizing and externalizing symptoms than foster care children who had disrupted foster care placements. Another study from the BEIP also found that callous and unemotional traits, which are strongly related to psychopathology, were significantly higher in children who had experienced institutionalized care (Humphreys, McGoron, et al., 2015). This study also found that the BEIP foster care intervention decreased the number of callous unemotional traits in boys, with caregiver responsiveness moderating this relation. Consistent with the large body of literature detailing the negative effects of institutionalized care, findings from the BEIP project suggest that a sensitive period related to the development of internalizing and externalizing disorders may exist within the first 3 years of life. Critically, mental health outcomes associated with these early-life sensitive periods may be influenced by a number of environmental factors, such as removal from institutional care, caregiver responsiveness, and consistent caregiving placement.

CONCLUSIONS

Contemporary research on sensitive periods provides us with a framework for pinpointing the effects of early experience on adaptive and maladaptive behavior and therefore risk for mental disorders. Identification of sensitive periods, and the mechanisms and pathways that underlie them, may provide information for the design of targeted treatments and preventive interventions and inform us of the developmental ages at which such interventions may be most effective. Furthermore, while most of the examples provided in this chapter have focused on sensitive periods for maladaptive behaviors, it is important to note that there is evidence for sensitive periods for expertise and skills development as well. For instance, one recent study has demonstrated that individuals with higher intelligence show a pattern of prolonged environmental sensitivity to enhance learning, and related to IQ, suggesting that they may have an extended sensitive period for intellectual development (Brant et al., 2013). Finally, emerging research indicates that sensitive periods may be able to be reopened—particularly via pharmacological interventions (Gervain et al., 2013; Hensch & Bilimoria, 2012).

In this chapter we have used early deprivation, specifically, institutional care, as a model with which to investigate sensitive periods in neural, cognitive, and social–emotional development. Currently there are many lines of research investigating sensitive periods that use a multitude of models and systems, all of which highlight the importance of integral environmental experiences during heightened periods of sensitivity in development. Whereas we have encouraged the reader to consider how sensitive periods in child development may play a role in development, as well as risk and early intervention during the preschool years, the following chapters in this volume discuss the development of social and mental health.

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