

# Influences of Caregiving on Development: A Sensitive Period for Biological Embedding of Predictability and Safety Cues

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## Abstract

Across species, caregivers exert a powerful influence on the neural and behavioral development of offspring. Increasingly, both animal and human research has highlighted specific patterns in caregivers' behavior that may be especially important early in life, as well as neurobiological mechanisms linking early caregiving experiences with long-term affective behavior. Here we delineate evidence for an early sensitive period during infancy and toddlerhood when caregiver inputs that are predictable and associated with safety may become biologically embedded via influences on corticolimbic circuitry involved in emotion regulation. We propose that these caregiver signals prime corticolimbic circuitry to be receptive to later stage-specific caregiver influences, such as caregivers' external regulation of children's emotional reactivity. Following adversity that disrupts the predictability and safety associated with caregivers during this sensitive period, accelerated maturation of children's corticolimbic circuitry may foreshorten the protracted period of plasticity and caregiver influence that is characteristic of humans. This work has implications for both prevention and intervention efforts targeting children exposed to adversity early in life.

## Keywords

caregiving, predictability, safety, corticolimbic circuitry, emotion regulation

Caregivers have a profound impact on children's neural and behavioral development. Decades of research have shown that stable, nurturing caregiving early in life is essential for children's healthy socioemotional development, and, conversely, that severe disruption to early caregiving alters long-term development and increases risk for mental-health disorders across the life span. However, the specific mechanisms by which early caregiving experiences affect long-term neural and behavioral outcomes and, further, by which caregiving in the earliest stages of development influences the potential impact of caregivers on behavioral and neural development at later stages of development have remained unclear. That is, how does a child's experience of stable, nurturing caregiving become biologically embedded? How does the nature of the caregiving cues that a child receives early in life influence the child's capacity to optimally benefit from caregiving inputs supporting socioemotional functioning across development?

Although it has long been established that the affective quality and content of caregivers' signals to developing offspring influence neural development across species (Curley & Champagne, 2016), research has highlighted that specific patterns in caregivers' behavior—namely, the co-occurrence of predictability and safety—may be particularly important for shaping the development of corticolimbic circuitry involved in emotion regulation and for facilitating the caregiver's ability to serve a regulatory function later in development. Building on extant literature documenting infancy and toddlerhood as a sensitive period for caregiving input more generally, here we review evidence for the hypothesis that a child's receipt of early caregiving cues that are predictable (i.e., that occur in a way that is

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expected and reliable) and representative of safety (i.e., that protect a child from danger and are unlikely to cause harm) are essential for receptivity to later stage-specific caregiving influences that promote optimal development. Further, we highlight how these specific caregiving cues may become biologically embedded in the first several years of life and how accelerated maturation of corticolimbic circuitry following adverse caregiving may interfere with opportunities for caregivers' optimal influence on later stages of development.

### **Infancy and Toddlerhood as a Sensitive Period for Caregiver Inputs**

Via stage-specific inputs, caregivers support children in executing key tasks of typical development from birth through adolescence (Fig. 1). Across infancy, children learn to trust that their primary caregivers' responses are contingent on their needs and that caregivers have predictable behavior that consistently signals safety. In early infancy, caregivers serve as a critical source of comfort and protection, and they transition to serving as a source of support for children's emerging independence throughout the first year of life, as infants begin to explore the world with close caregiver support. During toddlerhood, caregivers continue to establish themselves as predictable sources of comfort and protection as children increasingly negotiate strong and, at times, competing desires for independence and exploration, on the one hand, and for security from close contact with caregivers, on the other (Lieberman et al., 2015).

Evidence suggests that caregivers may serve an external regulatory function early in life, when corticolimbic circuitry is still developing (Callaghan & Tottenham, 2016a; Gee, 2016; Gee et al., 2014). Corticolimbic circuitry involves the amygdala, which detects emotionally salient stimuli in the environment; the hippocampus, which is involved in learning and memory; and the medial prefrontal cortex, which regulates the amygdala's reactivity and controls emotion. As this circuitry matures and regulatory abilities become internalized to facilitate independent emotion regulation, children's reliance on caregivers' provision of external regulation may wane, and other major attachment figures, such as close peers, take on an increasing role in social buffering (Gee, 2016; Hostinar et al., 2014).

In the context of typical development, the period spanning infancy and toddlerhood may be a sensitive period during which predictable caregiver inputs associated with safety are particularly influential in establishing the opportunity for later modulation of corticolimbic circuitry and emotion by the caregiver.

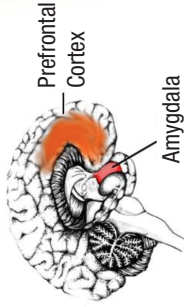
Here we define a sensitive period as a window of heightened neuroplasticity during which specific environmental inputs have an especially strong effect on later functioning (Werker & Hensch, 2015).

Although growing evidence suggests that normative variation in caregiving experiences tracks with continuous variation in corticolimbic circuitry (e.g., Gee et al., 2014), much of the evidence for an early sensitive period related to caregiving experiences comes from the literature on severe caregiving-related adversity. There is compelling evidence that exposure to caregiving adversity, such as institutionalized care or maltreatment, is more detrimental when it occurs early in life than when it occurs during later periods of development (e.g., Manly et al., 2001). For example, findings from the Bucharest Early Intervention Project, a randomized controlled trial of children in institutionalized care who were randomly assigned either to be placed in foster care or to remain in institutionalized care, have demonstrated that receiving stable and nurturing caregiving input in the first years of life is particularly influential for both short- and long-term developmental outcomes (Nelson et al., 2007). Specifically, between birth and 24 months, children's experience of institutionalized care—which likely entails exposure to a lack of both caregiver-associated predictability and caregiver-associated safety—has been shown to have particularly lasting and severe effects on a broad array of behavioral and neurodevelopmental outcomes (McLaughlin et al., 2015; see Cohodes et al., 2021, for a review related to corticolimbic circuitry). Though institutionalized care and maltreatment are multifaceted stressors that are characterized by both the absence of species-expected inputs (i.e., stable and nurturing care) and the presence of extreme stress, and that may themselves alter the timing of sensitive periods (see Gabard-Durnam & McLaughlin, 2020, for a review), these studies present empirical evidence for a potential sensitive period during which a lack of key caregiving inputs, such as predictability and safety cues, has particularly salient effects on the developing brain.

### **Predictability of Caregiving Cues**

Cross-species evidence suggests that the predictability of caregivers' responsiveness to offspring early in life is an important determinant of children's long-term cognitive and affective outcomes (Ellis et al., 2009; Glynn & Baram, 2019). One hypothesized explanation for this effect is that predictable and appropriate caregiver responses in infancy influence the developing brain because they underpin the development of secure attachment relationships, which, in turn, support social,






**Sensitive Period for Establishment of Attachment Relationships That Facilitates Stage-Specific Reliance on the Caregiver for Regulation Across Development**



**Corticolimbic Circuitry and Function**

**Reliance on Intrinsic Emotion Regulation**

**Reliance on Extrinsic Emotion Regulation**

	Infancy	Toddlerhood	Early Childhood	Childhood	Adolescence
	<b>Role of the Caregiver</b>				
	<b>Tasks of the Developmental Stage</b>				
Caregiver as a Predictable Source of Comfort and Protection	Caregiver as a Source of Support for Developing Independence	Caregiver as a Scaffold for Increased Exploration of the Physical and Social World	Caregiver as a Scaffold for Increased Exploration and as an External Source of Emotion Regulation	Caregiver as a Source of External Support and Guidance as the Adolescent Learns to Navigate the World With More Independence	
<ul style="list-style-type: none"> <li>• Infants Learn to Trust That the Caregiver Response is Contingent on Their Needs and That the Caregiver is a Reliable Safety Cue</li> <li>• Infants Feel Loved and Worthy of Care</li> <li>• Infants Establish Attachment</li> <li>• Infants Begin to Explore the World With Close Caregiver Support</li> </ul> 	<ul style="list-style-type: none"> <li>• Toddlers Negotiate Their Desire for Increased Independence and Security From Caregivers</li> <li>• Toddlers Increasingly Establish a Sense of Self Separate From Caregivers</li> <li>• Toddlers Increasingly Explore the World Around Them, With Caregivers Monitoring Their Safety and Helping Them to Navigate the World Through Developing Language and Motor Skills</li> </ul> 	<ul style="list-style-type: none"> <li>• Young Children Learn to Plan and Execute Simple Tasks With Input and Scaffolding From Caregivers</li> <li>• Young Children Continue to Explore Their World and Seek Knowledge of the Way Things Work</li> <li>• Young Children Learn to Engage in the Social World in Appropriate and Accepted Ways</li> </ul> 	<ul style="list-style-type: none"> <li>• Children Develop Mastery of Increasingly Difficult Tasks With Scaffolding From Caregivers</li> <li>• Children Internalize and Begin to Follow Rules and Community Norms</li> <li>• Children Learn New Social Skills and Develop More Complex Forms of Emotion Regulation With Input and Modeling From Caregivers</li> <li>• Children Engage in Increasingly Complex Reasoning Skills</li> <li>• Children Increasingly Cooperate With Peers and Caregivers</li> </ul> 	<ul style="list-style-type: none"> <li>• Adolescents Begin to Establish an Identity Separate From Caregivers and the Family Unit</li> <li>• Adolescents Begin to Determine Their Own Moral Values</li> <li>• Adolescents May Begin to Navigate Romantic Relationships</li> </ul> 	

**Fig. 1.** Caregiver influences on corticolimbic circuitry underlying emotion regulation across development. Evidence from both human and animal studies points to a potential sensitive period, spanning infancy and toddlerhood, during which caregiver inputs to the developing brain may have a particularly salient impact on the development of corticolimbic circuitry underlying emotion regulation. Specifically, caregiver inputs that are predictable and that are associated with safety may promote healthy neurodevelopment such that caregivers are able to support youth emotion regulation via modulation of this circuitry in later developmental stages. During infancy and toddlerhood, caregivers play a central role in regulating human amygdala function. As corticolimbic circuitry (e.g., functional connectivity between the prefrontal cortex and amygdala) matures (symbolically represented here by changing intensity of the orange horizontal band), children experience a shift from greater reliance on extrinsic emotion regulation (e.g., caregiving influences) to greater reliance on intrinsic emotion regulation (represented by the increasing intensity of the blue band as the intensity of the green band decreases). This transition also corresponds to a shift in the role of the caregiver in supporting the child's development, as the child faces novel tasks and compounding developmental challenges at each stage.

emotional, and cognitive development (Sroufe, 2005). Indeed, both contingency of caregivers' responsivity to infants (Gunnar, 1980) and synchrony in infant-caregiver behavior are key predictors of children's developmental outcomes (Feldman, 2007).

Although the mechanisms supporting the effects of predictable caregiving on neural development have been relatively unexplored in humans, a growing body of evidence from studies of rodents suggests that caregiver predictability may specifically influence the development of corticolimbic circuitry (Glynn & Baram, 2019). Paradigms in which the degree of predictability of maternal care is manipulated have provided particular insight into the specific neurobiological effects of exposure to unpredictable care in the earliest stages of development. Rodents exposed to unpredictable care exhibit atypical development of the neurobiological systems underpinning emotion-related functioning, including reduced connectivity between the medial prefrontal cortex and the amygdala (e.g., Guadagno et al., 2018). In addition, rodents exposed to unpredictable maternal care show greater amygdala activity relative to animals raised in typical conditions (Malter Cohen et al., 2013). These findings underscore possible pathways by which caregiving quality—specifically, the degree to which caregiver signals are expected and reliable—may support development of corticolimbic circuitry.

### **Association Between the Caregiver's Presence and Safety**

Caregivers' inputs to offspring are multifaceted; predictability of cues in the first several years of life is necessary but not sufficient for the priming of neural circuitry that allows caregivers to play an optimal role across development. Caregiving cues must also be associated with safety. Early in life, interactions with caregivers provide opportunities to learn about the degree to which a caregiver's presence is associated with the attenuation of fear (Moriceau & Sullivan, 2006). Over the course of repeated shared experiences between children and caregivers beginning immediately following birth and extending across postnatal development, caregivers' consistent buffering of children's fear (e.g., via physical presence and related attenuation of physiological reactivity; Callaghan & Tottenham, 2016a) reinforces the association between the caregiver's presence and safety. Caregivers' successful attenuation of children's fear, in turn, enhances the efficacy of the caregivers as a buffer and further instantiates caregivers as safety signals. It is important to note that a caregiver signaling that the child is safe is distinct from a caregiver protecting the child from all possible dangers or

preventing the child from seeking opportunities for exploration. Overprotective behaviors may signal to the child that the world is a dangerous place and interfere with the child's normative development of independent regulation of anxiety. Here we focus on the normative development of the association between the caregiver's presence and safety.

Cross-species evidence provides insight into the specific neurobiological mechanisms by which caregivers buffer children's fear and stress reactivity. In human children, the presence of a caregiver suppresses cortisol reactivity (Hostinar et al., 2014) and physically strengthens connections between the medial prefrontal cortex and the amygdala to dampen amygdala reactivity (Gee et al., 2014). These findings are consistent with evidence that a caregiver's presence suppresses corticosterone and amygdala activity in developing rodents (Moriceau & Sullivan, 2006). Perhaps in part because of the potency of buffering by a caregiver, offspring approach stimuli associated with their caregiver even when those stimuli are inherently aversive (Moriceau & Sullivan, 2006; Tottenham et al., 2019). Facilitation of approach behavior via caregiver-related cues may further promote early attachment and ensure that offspring remain close to their caregivers.

By establishing that their presence is associated with the attenuation of fear during infancy, caregivers lay the groundwork for their later modulation of corticolimbic circuitry and emotion regulation in a stage-specific manner across development. Offspring rely on caregivers to play an active role in facilitating emotion regulation and buffering amygdala reactivity during childhood, but caregivers shift to take on a supporting role as emotion regulation becomes more internalized during adolescence (Gee, 2016; Gee et al., 2014). Studies documenting the long-term effects of disrupted caregiving offer compelling evidence for the hypothesis that establishing an association between the caregiver's presence and safety facilitates optimal modulation of corticolimbic circuitry by the caregiver later in development. Even though attachment relationships can be established in the context of threatening cues (e.g., Perry & Sullivan, 2014), caregiving adversity during infancy interferes with buffering by the caregiver. Specifically, rodent pups exposed to maltreatment by their caregivers (e.g., rough handling of pups, stepping on pups) do not show expected suppression of fear-related behavior in the presence of their caregiver during infancy and, further, exhibit weakened buffering by their caregiver during the adolescent period, relative to their non-maltreatment-exposed counterparts (Opendak et al., 2019; Robinson-Drummer et al., 2019). Similarly, among nonhuman primates, maltreatment during infancy is associated with reduced effectiveness of

maternal buffering of cortisol reactivity (Sanchez et al., 2015). On average, human children who are exposed to institutionalized care early in life and are later adopted do not exhibit reduced amygdala reactivity in the presence of their adoptive caregivers (Callaghan et al., 2019).

Despite the narrative suggested by this pattern of findings—namely, that failure to form associations between caregivers and safety-related cues early in life is associated with diminished influence of the caregiver's presence in later stages of development—emerging evidence points to malleability in the impact of early disruption of caregiving relationships. In a study of particular note, Callaghan and colleagues (2019) found that, although the majority of children with caregiving-related adversity did not exhibit attenuation of amygdala reactivity in the presence of their caregivers, approximately 40% did, in fact, exhibit this age-expected modulation. Individual differences emerged: Greater security in the caregiver-child relationship was associated with greater caregiver-related attenuation of amygdala reactivity. These findings suggest that, although the absence of caregiving cues that are reliably associated with safety early in life appears to disrupt children's receptivity to later buffering by their caregivers, there is also the potential for later plasticity and reshaping. The observation of buffering among children exposed to early caregiving adversity suggests that despite "missing" the opportunity for exposure to safety-related caregiving cues in the first several years of life, these children may learn to associate their caregivers with safety during a later phase of development. Indeed, research utilizing rodent models of augmented caregiving suggests that exposure to subsequent optimal care is associated with neurodevelopment that supports adaptive responses to stress (e.g., Singh-Taylor et al., 2018). Together, these studies raise the possibility that, although specific patterns of caregiver inputs in the earliest stages of life may be crucial for priming neural circuitry to be receptive to later modulation by the caregiver, high-quality care following attachment disruption may foster plasticity in the capacity for buffering.

### **Accelerated Development Following Disruption of Caregiver Cues Associated With Predictability and Safety**

Acceleration of the corticolimbic circuit's development is a mechanism by which exposure to caregiving characterized by a lack of predictability and safety during an early sensitive period may undermine children's responsivity to buffering by the caregiver at later stages of development. The absence of predictable caregiving

that signals safety early in life is associated with accelerated maturation of the hippocampus and amygdala in both rodents (Bath et al., 2016; Manzano Nieves et al., 2020) and humans (Gee et al., 2013). One possible explanation is that unpredictable care triggers precocious activation of the stress response system, which could subsequently lead to accelerated maturation of corticolimbic circuitry (Callaghan & Tottenham, 2016b; Gee et al., 2013). Though much remains unknown about the function of such acceleration, early maturation appears to be an ontogenetic adaptation in the context of a harsh and unpredictable caregiving environment (Callaghan & Tottenham, 2016b; Ellis et al., 2009; Gee et al., 2013). However, despite evidence for some initial advantage (e.g., Gee et al., 2013), accelerated corticolimbic development may have negative long-term consequences for brain development and mental health. A protracted period of plasticity and caregiver influence in human development confers various advantages, and in the affective domain, it may provide opportunities for learning safety signals that serve a later anxiolytic function (Yang et al., 2012). Foreshortening this period of immature corticolimbic function and plasticity may ultimately limit subsequent influences of caregiver inputs to corticolimbic circuitry and reduce opportunities for learning and adaptation later in development. A potential mechanism by which exposure to caregiving adversity may confer risk for the development of mental-health disorders across the life span involves behavioral adaptations to this exposure: Behavioral adaptations that prove to be effective in the context of harsh caregiving conditions may undermine future adaptive coping in response to the novel challenges of each new developmental stage (Gee, 2016).

### **Future Directions**

Here we have highlighted cross-species evidence for a potential early sensitive period for caregiver inputs to the developing brain. Specifically, during infancy and toddlerhood, the predictability and safety associated with caregiving may facilitate an opportunity for optimal modulation of corticolimbic circuitry by the caregiver across subsequent stages of development, thereby promoting children's development of an increasingly intrinsic capacity for emotion regulation. As cross-species research continues to investigate the ways in which specific features of caregiving "get under the skin," several important questions remain.

First, though human research has established associations between exposure to predictable caregiving and generalized developmental outcomes (e.g., working memory capacity or cognitive control), future

research is needed to test the specific hypothesis that exposure to more predictable caregiving in the first several years of life is associated with both stronger modulation of corticolimbic circuitry by the caregiver later in development and a more protracted period of modulation by the caregiver's presence. Second, though research has begun to delineate the effects of early caregiving adversity on the caregiver's modulation of amygdala reactivity across development, studies to date have not examined how specific aspects of caregiving adversity (e.g., unpredictability and the extent to which a caregiver does not exhibit behaviors associated with safety), experienced in the earliest stage of human development, confer risk for this modulation to be diminished later in life (Cohodes et al., 2021). Moreover, additional research is necessary to specifically test the neural mechanisms by which these particular features become encoded (Meyer et al., 2019) and influence the processing of later caregiving cues (Opendak et al., 2020). Third, future studies that shed light on the specific mechanisms by which interventions can facilitate the establishment of capacities for later circuit modulation by caregivers despite missed opportunities for key inputs during the early sensitive period will inform interventions for children exposed to early adversity.

Given the impact of caregiving adversity in the first years of life, policy- and public-health-related efforts should focus on implementing structural changes that prevent ruptures to young children's attachment relationships, which inherently compromise their sense of safety and predictability. The extant literature suggests that young children who have experienced caregiving adversity during infancy and toddlerhood may benefit from dyadic (child-caregiver) interventions focused on providing them with opportunities to play and talk about traumatic exposures that may have compromised their sense of safety and predictability within their primary attachment relationships, and, reciprocally, providing caregivers with opportunities to reaffirm their association with safety and predictability and to scaffold the young children's emerging understanding of caregivers' capacity for repairing a diminished sense of predictability and safety (Lieberman et al., 2015). We also highlight the need to continue developing evidence-based interventions that take into account both the developmental needs of children in infancy and toddlerhood (e.g., treatments that rely on play, in addition to verbal communication) and the potential inherent in this developmental period for forming new associations between caregivers and signaling of safety and predictability due to enhanced neural plasticity and young children's reliance on support from their caregivers for nearly all aspects of functioning. Further delineating

mechanisms by which enriched caregiving environments may allow children exposed to early caregiving adversity to reestablish a sense of caregivers' predictability and association with safety will also inform the design of targeted interventions for these children.

## Conclusions

A wealth of cross-species evidence has demonstrated that early caregiving experiences can shape neural and behavioral development across the life course. Although the influences of caregiving are particularly salient early in life, caregivers play a central role in tasks of typical development throughout childhood and adolescence. Interactions between caregivers and children during infancy and toddlerhood form a foundation that allows caregivers to effectively take on stage-specific support roles across development. A rapidly evolving literature highlights predictability and safety as two key aspects of caregiving early in life that are essential for healthy development and that facilitate age-appropriate caregiver inputs to development. Specifically, encoding of caregiving cues signaling predictability and safety during an early sensitive period may shape corticolimbic development and support caregivers' role in guiding emotional learning and regulation later in development. Future research will be essential to translate emerging work on the neurobiological pathways by which caregiving cues signaling predictability and safety become embedded early in life from animal models to human development and will have implications for prevention and intervention efforts targeting children exposed to caregiving adversity early in life.

## Recommended Reading

- Callaghan, B. L., Gee, D. G., Gabard-Durnam, L., Telzer, E. H., Humphreys, K. L., Goff, B., Shapiro, M., Flannery, J., Lumian, D. S., Fareri, D. S., Caldera, C., & Tottenham, N. (2019). (See References). An empirical investigation of caregivers' buffering of children's amygdala reactivity following early caregiving adversity.
- Cohodes, E. M., Kitt, E. R., Baskin-Sommers, A., & Gee, D. G. (2021). (See References). A review of key dimensions of early adversity (including predictability and caregiver involvement) that affect the development of corticolimbic circuitry.
- Gee, D. G., Gabard-Durnam, L., Telzer, E. H., Humphreys, K. L., Goff, B., Shapiro, M., Flannery, J., Lumian, D. S., Fareri, D. S., Caldera, C., & Tottenham, N. (2014). (See References). An empirical demonstration of a neurobiological mechanism by which caregivers regulate children's anxiety.
- Glynn, L. M., & Baram, T. Z. (2019). (See References). An overview of cross-species examinations of the effects of unpredictable care on children's neurodevelopment and behavior.

Opendak, M., Robinson-Drummer, P., Blomkvist, A., Zanca, R. M., Wood, K., Jacobs, L., Chan, S., Tan, S., Woo, J., Venkataraman, G., Kirschner, E., Lundström, J. N., Wilson, D. A., Serrano, P. A., & Sullivan, R. M. (2019). (See References). An empirical examination of caregivers' buffering of rodent pups' fear following caregiving adversity.

## Transparency

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## References

- Bath, K. G., Manzano-Nieves, G., & Goodwill, H. (2016). Early life stress accelerates behavioral and neural maturation of the hippocampus in male mice. *Hormones and Behavior*, *82*, 64–71. <https://doi.org/10.1016/j.yhbeh.2016.04.010>
- Callaghan, B. L., Gee, D. G., Gabard-Durnam, L., Telzer, E. H., Humphreys, K. L., Goff, B., Shapiro, M., Flannery, J., Lumian, D. S., Fareri, D. S., Caldera, C., & Tottenham, N. (2019). Decreased amygdala reactivity to parent cues protects against anxiety following early adversity: An examination across 3 years. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *4*(7), 664–671. <https://doi.org/10.1016/j.bpsc.2019.02.001>
- Callaghan, B. L., & Tottenham, N. (2016a). The neuro-environmental loop of plasticity: A cross-species analysis of parental effects on emotion circuitry development following typical and adverse caregiving. *Neuropsychopharmacology*, *41*(1), 163–176.
- Callaghan, B. L., & Tottenham, N. (2016b). The stress acceleration hypothesis: Effects of early-life adversity on emotion circuits and behavior. *Current Opinion in Behavioral Sciences*, *7*, 76–81. <https://doi.org/10.1016/j.cobeha.2015.11.018>
- Cohodes, E. M., Kitt, E. R., Baskin-Sommers, A., & Gee, D. G. (2021). Influences of early-life stress on fronto-limbic circuitry: Harnessing a dimensional approach to elucidate the effects of heterogeneity in stress exposure. *Developmental Psychobiology*, *63*(2), 153–172.
- Curley, J. P., & Champagne, F. A. (2016). Influence of maternal care on the developing brain: Mechanisms, temporal dynamics and sensitive periods. *Frontiers in Neuroendocrinology*, *40*, 52–66. <https://doi.org/10.1016/j.yfrne.2015.11.001>
- Ellis, B. J., Figueredo, A. J., Brumbach, B. H., & Schlomer, G. L. (2009). Fundamental dimensions of environmental risk. *Human Nature*, *20*(2), 204–268.
- Feldman, R. (2007). Parent–infant synchrony and the construction of shared timing; physiological precursors, developmental outcomes, and risk conditions. *Journal of Child Psychology and Psychiatry*, *48*(3–4), 329–354. <https://doi.org/10.1111/j.1469-7610.2006.01701.x>
- Gabard-Durnam, L., & McLaughlin, K. A. (2020). Sensitive periods in human development: Charting a course for the future. *Current Opinion in Behavioral Sciences*, *36*, 120–128. <https://doi.org/10.1016/j.cobeha.2020.09.003>
- Gee, D. G. (2016). Sensitive periods of emotion regulation: Influences of parental care on frontoamygdala circuitry and plasticity: Sensitive periods of emotion regulation. *New Directions for Child and Adolescent Development*, *2016*(153), 87–110. <https://doi.org/10.1002/cad.20166>
- Gee, D. G., Gabard-Durnam, L., Telzer, E. H., Humphreys, K. L., Goff, B., Shapiro, M., Flannery, J., Lumian, D. S., Fareri, D. S., Caldera, C., & Tottenham, N. (2014). Maternal buffering of human amygdala-prefrontal circuitry during childhood but not during adolescence. *Psychological Science*, *25*(11), 2067–2078. <https://doi.org/10.1177/0956797614550878>
- Gee, D. G., Gabard-Durnam, L. J., Flannery, J., Goff, B., Humphreys, K. L., Telzer, E. H., Hare, T. A., Bookheimer, S. Y., & Tottenham, N. (2013). Early developmental emergence of human amygdala-prefrontal connectivity after maternal deprivation. *Proceedings of the National Academy of Sciences, USA*, *110*(39), 15638–15643. <https://doi.org/10.1073/pnas.1307893110>
- Glynn, L. M., & Baram, T. Z. (2019). The influence of unpredictable, fragmented parental signals on the developing brain. *Frontiers in Neuroendocrinology*, *53*, Article 100736. <https://doi.org/10.1016/j.yfrne.2019.01.002>
- Guadagno, A., Kang, M. S., Devenyi, G. A., Mathieu, A. P., Rosa-Neto, P., Chakravarty, M., & Walker, C.-D. (2018). Reduced resting-state functional connectivity of the basolateral amygdala to the medial prefrontal cortex in pre-weaning rats exposed to chronic early-life stress. *Brain Structure and Function*, *223*(8), 3711–3729.

- Gunnar, M. R. (1980). Contingent stimulation: A review of its role in early development. In S. Levine & H. Ursin (Eds.), *Coping and health* (pp. 101–119). Springer.
- Hostinar, C. E., Sullivan, R. M., & Gunnar, M. R. (2014). Psychological mechanisms underlying the social buffering of the hypothalamic–pituitary–adrenocortical axis: A review of animal models and human studies across development. *Psychological Bulletin*, *140*(1), 256–282. <https://doi.org/10.1037/a0032671>
- Lieberman, A. F., Ghosh Ippen, C., & Van Horn, P. (2015). *Don't bit my mommy! A manual for child-parent psychotherapy with young children exposed to violence and other trauma*. Zero to Three.
- Malter Cohen, M., Jing, D., Yang, R. R., Tottenham, N., Lee, F. S., & Casey, B. J. (2013). Early-life stress has persistent effects on amygdala function and development in mice and humans. *Proceedings of the National Academy of Sciences, USA*, *110*(45), 18274–18278. <https://doi.org/10.1073/pnas.1310163110>
- Manly, J. T., Kim, J. E., Rogosch, F. A., & Cicchetti, D. (2001). Dimensions of child maltreatment and children's adjustment: Contributions of developmental timing and subtype. *Development and Psychopathology*, *13*(4), 759–782.
- Manzano Nieves, G., Bravo, M., Baskoylu, S., & Bath, K. G. (2020). Early life adversity decreases pre-adolescent fear expression by accelerating amygdala PV cell development. *eLife*, *9*, Article e55263. <https://doi.org/10.7554/eLife.55263>
- McLaughlin, K. A., Sheridan, M. A., Tibu, F., Fox, N. A., Zeanah, C. H., & Nelson, C. A. (2015). Causal effects of the early caregiving environment on development of stress response systems in children. *Proceedings of the National Academy of Sciences, USA*, *112*(18), 5637–5642. <https://doi.org/10.1073/pnas.1423363112>
- Meyer, H. C., Odriozola, P., Cohodes, E. M., Mandell, J. D., Li, A., Yang, R., Hall, B. S., Haberman, J. T., Zacharek, S. J., Liston, C., Lee, F. S., & Gee, D. G. (2019). Ventral hippocampus interacts with prelimbic cortex during inhibition of threat response via learned safety in both mice and humans. *Proceedings of the National Academy of Sciences, USA*, *116*(52), 26970–26979. <https://doi.org/10.1073/pnas.1910481116>
- Moriceau, S., & Sullivan, R. M. (2006). Maternal presence serves as a switch between learning fear and attraction in infancy. *Nature Neuroscience*, *9*(8), 1004–1006.
- Nelson, C. A., Zeanah, C. H., Fox, N. A., Marshall, P. J., Smyke, A. T., & Guthrie, D. (2007). Cognitive recovery in socially deprived young children: The Bucharest Early Intervention Project. *Science*, *318*(5858), 1937–1940. <https://doi.org/10.1126/science.1143921>
- Opendak, M., Robinson-Drummer, P., Blomkvist, A., Zanca, R. M., Wood, K., Jacobs, L., Chan, S., Tan, S., Woo, J., Venkataraman, G., Kirschner, E., Lundström, J. N., Wilson, D. A., Serrano, P. A., & Sullivan, R. M. (2019). Neurobiology of maternal regulation of infant fear: The role of mesolimbic dopamine and its disruption by maltreatment. *Neuropsychopharmacology*, *44*, 1247–1257. <https://doi.org/10.1038/s41386-019-0340-9>
- Opendak, M., Theisen, E., Blomkvist, A., Hollis, K., Lind, T., Sarro, E., Lundström, J. N., Tottenham, N., Dozier, M., Wilson, D. A., & Sullivan, R. M. (2020). Adverse caregiving in infancy blunts neural processing of the mother. *Nature Communications*, *11*(1), 1119. <https://doi.org/10.1038/s41467-020-14801-3>
- Perry, R., & Sullivan, R. M. (2014). Neurobiology of attachment to an abusive caregiver: Short-term benefits and long-term costs. *Developmental Psychobiology*, *56*(8), 1626–1634. <https://doi.org/10.1002/dev.21219>
- Robinson-Drummer, P. A., Opendak, M., Blomkvist, A., Chan, S., Tan, S., Delmer, C., Wood, K., Sloan, A., Jacobs, L., Fine, E., Chopra, D., Sandler, C., Kamenetzky, G., & Sullivan, R. M. (2019). Infant trauma alters social buffering of threat learning: Emerging role of prefrontal cortex in preadolescence. *Frontiers in Behavioral Neuroscience*, *13*, Article 132. <https://doi.org/10.3389/fnbeh.2019.00132>
- Sanchez, M. M., McCormack, K. M., & Howell, B. R. (2015). Social buffering of stress responses in nonhuman primates: Maternal regulation of the development of emotional regulatory brain circuits. *Social Neuroscience*, *10*(5), 512–526. <https://doi.org/10.1080/17470919.2015.1087426>
- Singh-Taylor, A., Molet, J., Jiang, S., Korosi, A., Bolton, J. L., Noam, Y., Simeone, K., Cope, J., Chen, Y., Mortazavi, A., & Baram, T. Z. (2018). NRSF-dependent epigenetic mechanisms contribute to programming of stress-sensitive neurons by neonatal experience, promoting resilience. *Molecular Psychiatry*, *23*(3), 648–657. <https://doi.org/10.1038/mp.2016.240>
- Sroufe, L. A. (2005). Attachment and development: A prospective, longitudinal study from birth to adulthood. *Attachment & Human Development*, *7*(4), 349–367. <https://doi.org/10.1080/14616730500365928>
- Tottenham, N., Shapiro, M., Flannery, J., Caldera, C., & Sullivan, R. M. (2019). Parental presence switches avoidance to attraction learning in children. *Nature Human Behaviour*, *3*(10), 1070–1077. <https://doi.org/10.1038/s41562-019-0656-9>
- Werker, J. F., & Hensch, T. K. (2015). Critical periods in speech perception: New directions. *Annual Review of Psychology*, *66*, 173–196.
- Yang, E.-J., Lin, E. W., & Hensch, T. K. (2012). Critical period for acoustic preference in mice. *Proceedings of the National Academy of Sciences, USA*, *109*(Suppl. 2), 17213–17220. <https://doi.org/10.1073/pnas.1200705109>