Parenting and Brain Development

Caitlin C. Turpyn & Eva H. Telzer

University of North Carolina at Chapel Hill

Abstract

The quality of the caregiving environment is one of the most impactful elements on youth's development, with evidence suggesting these experiences are embedded at the neural level. This chapter reviews empirical research characterizing relations between parenting and child and adolescent brain development with respect to a full continuum of maladaptive to adaptive parenting behavior. We consider evidence directly linking parental factors on neural indices of development, as well as growing evidence characterizing individual differences in neurobiological susceptibility to the caregiving environment. We conclude with a discussion of future directions for this research.

Keywords: parenting, family, brain development, neuroimaging

Experience shapes brain development, and the quality of the caregiving environment is one of the most impactful elements of experience for the developing child. A longstanding body of research underscores the central role of parents in child development, with maladaptive parenting practices—characterized by parental insensitivity and harshness—consistently linked with poorer social, emotional, and cognitive outcomes (e.g., Amato & Fowler, 2002; Valiente, Lemery-Chalfant, & Reiser, 2007). While associations between parenting and child development are inextricably linked by shared genetic factors, evidence shows that the quality of the caregiving environment exerts effects over and above shared genetics (Plomin, DeFries, McClearn, & McGuffin, 2008), underscoring parenting as a key leverage point for enhancing healthy development.

Given its effects on development, there has been a rising interest in how the caregiving environment is embedded at the neural level, especially in view of the notion that changes in brain function and structure may explain, in part, individual differences in trajectories of adjustment. The most prominent body of knowledge characterizing the effects of parenting on brain development comes from studies focusing on the most extreme forms of maladaptive parenting—child abuse, neglect, or maltreatment. While research of this kind, often focusing on clinical populations or highly victimized youth, is undoubtedly important, models of developmental psychopathology emphasize the importance of studying individual differences characteristic of both abnormal and normative development, as this knowledge is mutually informative and may allow for greater understanding of mechanistic processes involved in a full continuum of development (Cicchetti & Cohen, 1995). Researchers within the last decade have reinforced this perspective, calling for research not just among clinical populations of maltreated children but also among children who have experienced normative ranges of parenting behavior

(Belsky & de Haan, 2011).

To this end, this chapter begins with a brief primer on methods used to study neural development, and then summarizers research on the effects of child maltreatment on human brain development. We focus more comprehensively on recent studies of the effects of normative variations in parenting. With respect to the latter, we first discuss research modelling parenting's direct influence on youth brain development, and follow this with a review of a small but promising area of research modelling youths' differential susceptibility to the caregiving environment. We conclude with a discussion of future directions.

Methods for Measuring the Developing Brain

Technological advancements over the past two decades have allowed us to understand how the brain changes across childhood, adolescence, and into adulthood. The most common neuroimaging methods to study the developing brain in the context of parenting include structural MRI (sMRI), which measures the anatomy of the brain, as well task-based and resting-state functional MRI (fMRI), which measure the function of the brain. See Table 1 for a description of these modalities.

Structural MRI. sMRI seeks to measure changes in the anatomy of the brain in both grey and white matter. The most common metric is cortical volume, which is measured in terms of thickness (i.e., the distance between the white matter/grey matter cortical boundary and the grey matter/CSF cortical boundary) and surface area (i.e., the area of the white matter/grey matter cortical boundary and the grey matter/CSF cortical boundary; Vijayakumar, Mills, Alexander-Bloch, Tamnes, & Whittle, 2018). One of the most consistent findings from longitudinal sMRI research is that grey matter volume in the frontal and parietal lobes increases during childhood followed by a decline (i.e., thinning) in adolescence, before stabilizing in

young adulthood (Mills, Lalonde, Clasen, Giedd, & Blakemore, 2014). In contrast to cortical grey matter volume, cerebral white matter volume increases from birth and across the second decade of life before stabilizing in young adulthood (Mills, Goddings, Herting, Meuwese, Blakemore, et al., 2016). The regions exhibiting the most robust decreases in grey matter volume during adolescence are in regions implicated in higher-order cognition (e.g., the dorsal prefrontal cortex), and are the same regions showing the most robust increases in white matter volume (Mills et al., 2014). Grey matter changes are thought to reflect synaptic reorganization, including synaptic proliferation followed by synaptic pruning, whereas increases in white matter is thought to reflect continued axonal myelination that promotes efficient information flow in the brain (Blakemore, 2012). Other structural imaging modalities include diffusion MRI, which seeks to measure microstructural properties of the connecting white matter fiber bundles in the brain; however, this method has less commonly been used in the study of parenting and brain development.

Task-Based Functional MRI. fMRI seeks to understand how the brain functions during different psychological processes. fMRI measures the blood oxygenation level dependent (or BOLD) signal, which is an indirect measure of neural activity. When neural activity increases, there is an increase in blood oxygenation associated with blood flow to different regions of the brain. Because blood oxygenation varies according to the level of neural activity, these differences can be used to detect brain activity. While most research to date has focused on functional brain activation in isolated brain regions, there has been a growing emphasis on understanding functional connectivity, or how neural regions are co-activated. A hierarchical cascade of changes in functional connectivity patterns is proposed to occur, whereby development of subcortico-subcortical connectivity (e.g., amygdala-ventral striatum

connectivity) occurs before that of cortico-subcortical connectivity (e.g., amygdala-prefrontal cortex), which serves as a necessary precursor to more complex neural interactions (Casey, Heller, Gee, & Cohen, 2019). This shift in connectivity patterns is thought to underlie emotional development across adolescence. Other methods utilized less commonly in the literature of parenting and brain development include event-related potentials (ERP), which measures the timing of electrical activity in the brain in response to discrete events (Burani et al., 2019) and functional near-infrared spectroscopy (fNIRS), which is an optical imaging technique that measures changes in hemoglobin concentrations within the brain (Cai, Dong, & Niu, 2018).

Resting State MRI. Other research has employed resting state fMRI to examine organization within and between functional networks during task-independent activity or at rest. A consistent finding emerging across this research is enhanced connectivity *within* large-scale functional brain networks, such as the executive control network, coupled with reduced connectivity *between* networks during the adolescence period (Dosenbach et al., 2010). This shift to greater within network connectivity is thought to reflect better specialization and increasing efficiency in neural processing (Blakemore, 2012).

Evidence from studies of childhood maltreatment

Seminal work on the neural consequences of maltreatment includes studies of physical, sexual, and emotional abuse, and neglect, including research with youth raised in extreme circumstances of social-emotional deprivation characteristic of institutional rearing. Given the high levels of co-occurrence among maltreatment experiences and other forms of trauma and adversity (e.g., exposure to violence, poverty, abuse by extra-familial members), many studies in this domain have more broadly examined the effects of early life stress or adversity on the developing brain. While a comprehensive review of this subject can be found elsewhere (e.g. see,

Teicher, Samson, Anderson, & Ohashi, 2016, for further review), we briefly summarize evidence on childhood maltreatment and alterations in brain structure and function.

The majority of research in this area has focused on the effects of childhood maltreatment involved in stress or threat systems. In particular, disruptions in the hypothalamic pituitary adrenal (HPA) axis and its effects on brain development have been a predominant focus. In this pathway, excessive release of glucocorticoids due to repeated or prolonged stress is thought to result in altered morphology (i.e., via neuronal loss, disruptions in neurogenesis) and function in neural regions densely populated with glucocorticoid receptors. These regions include key structures of the limbic system involved in emotional processing, learning, and memory, such as the amygdala and hippocampus. Neuroendocrine and neural effects of this kind have been well-documented in translational research with rodent and non-human primates exposed to caregiving deprivation and early stress (Liu et al., 1997; Plotsky & Meany, 1993).

Consistent with stress models, a growing body of work in humans demonstrates structural and functional anomalies in areas of the limbic system among maltreated individuals. With respect to morphological abnormalities, numerous magnetic resonance imaging (MRI) studies indicate reduced hippocampal volumes among *adults* with a history of childhood maltreatment (e.g., Bremner et al., 1997; Teicher, Anderson, & Polcari, 2012). The hippocampus is a posterior limbic structure involved in learning and memory, and with its reciprocal connections to other limbic regions, is thought to also play a role in emotional behavior. Interestingly, evidence has not consistently indicated atypical hippocampal volumes in samples of maltreated children and adolescents, suggesting that hippocampal effects may not emerge until later in development. Some evidence also suggests early adversity may impact hippocampal function in youth. Reduced hippocampal recruitment in youth exposed to early-life stress has been reported along

with disruptions in aspects of memory and learning (Lambert et al. 2017; Lambert & McLaughlin, 2019).

Findings of structural differences in other stress-susceptible subcortical brain regions, such as the amygdala, in maltreated youth are more mixed. A few studies have reported larger amygdala volumes in maltreated children and early adolescents (e.g., Mehta et al., 2009; Tottenham et al., 2010), possibly suggesting accelerated structural maturation of the amygdalae. Yet, other studies have not observed significant differences in amygdala volume (e.g., Gorka, Hanson, Radtke, & Hariri, 2015; McLaughlin et al., 2014a) or found opposite effects (e.g., Hansen et al., 2015). What has emerged consistently, however, is a pattern of heightened amygdala functional response to threatening stimuli in maltreated youth. This evidence is borne out of neuroimaging studies most commonly employing emotional face paradigms, in which participants view angry, sad, fearful, and neutral faces during functional MRI (fMRI). In one recent meta-analysis investigating differences in brain function between maltreated individuals and healthy controls, higher levels of bilateral amygdala activation in response to negative versus neutral faces were identified in maltreated groups (Hein & Monk, 2017). The amygdala is involved in processing emotionally salient information and is thought to facilitate rapid orientation to and recognition of threatening stimuli (Phelps & LeDoux, 2005). Hypervigilance to threatening stimuli, as mediated in part by amygdala hyperactivity, may functionally prepare an individual to respond quickly to future danger in the environment. While heightened vigilance may be adaptive in the short run, this affective endophenotype may place youth at risk for long-term negative physical and mental health outcomes (McCrory, Gerin, & Viding, 2017).

Moreover, it has been suggested that early adversity may accelerate the development of threat-related neural circuitry, including the amygdala, hippocampus, and medial prefrontal

cortex (Callaghan & Tottenham, 2016). Accelerated neural maturation is postulated to be a functional adaptation to the environment, allowing the organism to reach reproductive maturation more quickly for the sake of species survival and putatively equipping an organism with more mature cognitive capacities to meet the challenges of the environment. Evidence has supported such a hypothesis with respect to accelerated aging, including studies documenting decreased cortical thickness among children exposed to adversity (Busso et al., 2017; Gold et al., 2016) and earlier pubertal timing, and cellular aging (Colich, Rosen, Williams, & McLaughlin, 2020). Despite potential benefits in the short run with respect to enhanced regulatory abilities that may come with accelerated development, Callaghan and Tottenham (2016) posited that "stress acceleration" of neural circuitry may hinder later plasticity, or the ability to adapt to environmental demands and contexts.

A smaller but growing body of evidence also implicates neural pathways involved in reward and motivation, including mesolimbic dopamine pathways in the ventral striatum and medial prefrontal cortex. Several neuroimaging studies in humans find blunted striatal brain activity during the anticipation of monetary rewards in maltreated individuals (Dillon et al., 2009; Goff et al., 2013, Hanson et al., 2015; Mehta et al., 2010). This is consistent with preclinical studies showing evidence of chronic stress effects on dopamine signaling and reward-mediated behavior, including diminished dopamine transmission in the ventral striatum and decreased approach behaviors (e.g., Brenhouse, Lukkes, & Andersen, 2013; Matthews &Robbins, 2003). Altered dopamine signaling may occur via stress-related alterations in HPA axis function (Nusslock & Miller, 2016). From an evolutionary perspective, some have argued that these effects are advantageous in a threatening or dangerous environment, pushing an individual toward avoidance behavior rather than approach as a means of safety (Teicher &

Samson, 2016). Again, however, long term consequences of this neural endophenotype may include increased risk for poor mental health outcomes, as blunted neural reward processing has been linked with anhedonia and depressive symptoms (Corral-Frias et al., 2015).

Given the heterogeneity of maltreatment experiences, it has recently been proposed that specific dimensions of maltreatment (e.g., threat versus deprivation) may have differential impacts on brain development (McLaughlin, Sheridan, & Lambert, 2014a). Threat or abuse exposures may impact neurobiological stress systems, primarily in the ways discussed above. In contrast however, environmental deprivation, as in the case of severe caregiving neglect or institutional rearing, may uniquely impact cortical development. Specifically, in contexts of severe neglect or deprivation, over-pruning of synaptic connections (especially during sensitive periods of neural development) may occur in order to accommodate low stimulation and low complexity environments (McLaughlin et al., 2014a). This over-pruning is thought to result in lower cortical volume in areas of the association cortex involved in social and cognitive processing. Indeed, children raised in institutional care show overall lower levels of grey matter volume (Mehta et al., 2009) and reduced cortical thickness in regions of prefrontal, inferior parietal, and superior temporal cortex (McLaughlin et al., 2014b).

Models of Direct Influence of Normative Parenting on Brain Development

A growing body of work, largely within the last decade, has sought to characterize the effects of what has commonly been referred to as “normative variations” in parenting, or parental behaviors below the threshold of abuse or neglect. Normative variations in parenting, such as individual differences in parental warmth, consistency, and harshness, are consistently related to behavioral development and adjustment in youth and are associated with alterations in offspring neurobiology in preclinical research (Champagne & Cheney, 2005). In human models, recent

attention has been paid to the ways in which normative variations in parenting are associated with youth's structural development and functional neural activation particularly with respect to the neural substrates of emotion-related reactivity and regulation (see Tan, Oppenheimer, Ladouceur, Butterfield, & Silk, 2020) including networks involved in salience processing (negative and positively valenced systems) and cognitive/regulatory control. Together, this work suggests that a full continuum of the quality of the caregiving environment, from adversity to sensitivity, may be neurally embedded.

Brain Structure. Variations in normative parenting have been linked with differences in subcortical and cortical morphometric indices in youth, with some findings mirroring those from maltreatment studies. Whereas research has documented higher amygdala volumes in maltreated youth, higher levels of positive parenting are associated with lower amygdala volume in adolescents (Whittle et al., 2009, Whittle et al., 2014) and infants (age 1, Bernier et al., 2019). Evidence also points to associations between aspects of adaptive caregiving and *larger* hippocampal volumes (e.g., Luby et al., 2012; Rifkin-Graboi et al., 2015) and greater gray matter density (Schneider et al., 2012), complementing research suggesting maltreatment exposure is associated with *smaller* hippocampal volumes in adults. In one longitudinal study, Luby et al (2012) found that young children (ages 3 to 5 years) exposed to greater maternal supportive behavior showed larger hippocampal volumes at ages 7 to 13 years. Interestingly, however, Rao et al. (2010) noted contrasting results, finding that higher maternal support and availability at age 4 predicted *smaller* hippocampal volumes in adolescent youth (ages 13 to 16). Given that certain subdivisions of hippocampal development follow an inverted u-shape, peaking in early adolescence, authors reasoned that early supportive parenting may set the stage for accelerated hippocampal maturation during adolescence.

Research documenting associations between cortical morphology and parenting have focused mostly on adolescent samples to date. One of the only studies to assess brain structure in children as a function of normative parenting variations found that early positive parental behavior (at age 4) predicted larger total grey matter volumes at age 8 (Kok et al., 2015). Interestingly, age 8 parenting behavior was not associated with structural development, suggesting an earlier sensitive window for parental effects. Findings from this study show that sensitive parenting is associated with *larger* gray matter volumes and complement those from the maltreatment literature, which indicate early adversity is associated with *lower* grey matter volumes in children.

Studies with adolescents, however, evidence a different pattern of effects—specifically that higher levels of sensitive parenting may be associated with accelerated maturation of cortical systems (Schneider et al., 2012; Whittle et al., 2014). For example, findings from the *Orygen Adolescent Development Study* showed that higher frequencies of maternal positive behaviors (e.g., affection, validation) during a parent-adolescent interaction predicted increased cortical thinning from early (approximately 12 years) to later in adolescence (approximately 16 years) (Whittle et al., 2014). Conversely, evidence suggests maladaptive parenting, such as maternal aggression and inconsistent parenting, is associated with metrics suggestive of immature cortical development, including higher cortical volumes (i.e., ACC, OFC, Whittle et al., 2009), longitudinal increases in lateral parietal, supramarginal gyrus, and SFG thickness (Whittle et al., 2016), and greater overall cortical thickness and asymmetry (Frye, Malmberg, Swank, Smith, & Landry, 2010) in adolescent samples. Together, this suggests that while adaptive parenting may impose accelerating effects on normative brain development in adolescence, normative variations in maladaptive parenting may impose delaying maturational effects.

This pattern of findings is interesting given evidence that children reared in extreme cases of deprivation (i.e., institutionalized rearing) also show reduced cortical thickness, suggestive of accelerated synaptic pruning in these youth, as well as evidence and theory described above suggesting that early adversity is associated with accelerated neurobiological development (Callaghan & Tottenham, 2016). This evidence on maltreated youth, however, primarily comes from studies of children; whereas, evidence of delayed cortical development as a function of normative variations in maladaptive caregiving comes from studies of adolescents. This collectively may suggest differential patterns based on stage of development, such that adversity in the caregiving environment is related to accelerated cortical development during childhood but delayed cortical development during adolescence. Along those lines, it has been proposed that adolescence is a period of neurobiological re-adaptation, as neurobiological stress systems resurvey the current environment and reorganize if conditions are significantly different than earlier periods (Gunnar, DePasquale, Reid, & Donzella, 2019). Thus, it is plausible that during this sensitive period, neural patterns of adaptation emerge that differ in direction than earlier periods. Alternatively, this evidence may suggest that maltreatment relative to normative variations in maladaptive caregiving exerts qualitatively different effects on brain development, with moderate levels of adversity linked to delayed maturation and with extreme adversity "tripping" evolutionary mechanisms to accelerate development. More research is clearly needed across childhood and adolescent periods and across a full continuum of caregiving to understand these findings.

Brain Function. Accumulating evidence linking normative variations in parenting with youths' brain function has primarily emerged from functional neuroimaging studies probing neural recruitment of salience processing systems—negative valence (e.g., threat response),

positive valence (e.g., reward anticipation)—and cognitive control (e.g., inhibition). While structural brain studies may be well equipped to characterize relatively stable neural markers of caregiving effects, functional brain imaging studies allow for *in vivo* and implicit neural processes to be captured.

Consistent with maltreatment studies, neural circuits subserving threat or negative valence systems may be sensitive to normative variations in caregiving. This has been demonstrated with respect to individual differences in lower parental warmth (Romund et al., 2016) and maternal negative affect and dysregulation (Pozzi et al., 2019; Turpyn, Poon, Ross, Thompson, & Chaplin, 2018), with these factors related to youths' higher amygdala and salience network response to negatively valenced stimuli. Moreover, altered patterns of amygdala and salience network resting state functional connectivity (e.g., amygdala, medial prefrontal cortex) associated with maladaptive parenting have been observed, with coupling between these subcortical-cortical regions suggestive of accelerated development (Kopala-Sibley et al., 2018; Thijssen et al., 2017). This evidence is consistent with proposed models of emotion-related brain development in the context of parenting (Tan et al., 2020), most consistently with aspects of maladaptive parenting conferring risk for higher levels of negative affect.

Interestingly, while such patterns of heightened amygdala engagement have been linked to internalizing psychopathology and trauma-related disorders in youth and adults (Kuwaja & Burkehouse, 2017), blunted amygdala reactivity has also been linked to externalizing psychopathology (Blair, Veroude, & Buitelaar, 2018). With respect to the latter, findings from one longitudinal study suggest that harsher parenting may confer risk via an externalizing pathway. Specifically, Gard et al. (2017) found that harsher parenting measured at age 2 was related to *lower* amygdala reactivity at age 20, which in turn was associated with higher levels of

antisocial behaviors in adulthood in a male sample. Thus, while most evidence supports harsher parenting is associated with increased salience processing, multiple neural pathways to maladjustment may occur.

Recent research also highlights potential biological sex differences in parental influences on youth brain function in negative valence systems. For example, one recent study observed sex-differentiated neural associations with negative parenting behaviors (Chaplin et al., 2018). For adolescent boys, higher negative parenting predicted blunted neural responses in affective salience regions (i.e., anterior insula, left anterior cingulate cortex); whereas, for girls, negative parenting predicted higher neural responsivity. Other evidence has documented interactions with sex and pubertal timing, finding differential brain responses to threatening stimuli in late developing boys versus girls in lateral prefrontal cortex for children exposed to higher levels of corporal punishment (Barbosa et al., 2018). These studies highlight important features of biological context and underscore the need to investigate differential patterns by sex or gender.

Additionally, an accumulating body of evidence links variations in the caregiving environment with the positive valence system or reward processing, including regions such as the ventral and dorsal striatum and medial prefrontal cortex (mPFC). Lower levels of parent-adolescent relationship quality (Qu, Fuligni, Galvan, & Telzer, 2015), lower parental warmth (Casement et al., 2014, Morgan, Shaw, & Forbes, 2014), insecure early attachment history (McCormick, McElwain, & Telzer, 2019) and higher maternal depressive symptoms (Qu, Fuligni, Galván, Lieberman, & Telzer, 2016) have been linked with youths' increased reward-related striatal or mPFC response (but see Schneider et al., 2012). For example, although Qu et al. (2015) did not observe significant relations between parent-adolescent relationship quality and adolescent reward-related brain function measured concurrently, findings indicated that

longitudinal decreases in parent-adolescent relationship quality were associated with longitudinal increases in activity in the ventral striatum and dlPFC in response to monetary rewards. Moreover, increases in ventral striatum response mediated the association between decreased positive parent-adolescent relationship quality and adolescents' greater risk-taking behavior. This suggests that lower levels of warmth or connectedness in the parent-child relationship may sensitize reward circuitry to secondary rewards (i.e., money), and this heightened responsivity may confer risk for negative behavioral outcomes. In contrast to this pattern of results, Tan et al. (2014) documented that higher levels of maternal negative affect, observed during a parent-adolescent interaction, was associated with lower brain response in reward and salience network regions (i.e., nucleus accumbens, amygdala, anterior insula, and sgACC) during a socially rewarding context in which youth received positive feedback from peers (i.e., peer acceptance). This could suggest that poorer parent-child relationship quality may differentially relate to reward circuitry response as a function of context—orienting youth away from socially relevant rewards and instead toward nonsocial rewards. Further research is needed to explore this potential pattern.

On a whole, however, evidence points to a pattern of increased reward-related striatal sensitivity in youth experiencing elevated levels of maladaptive parenting. This is in contrast to evidence from maltreatment studies, suggesting that maltreatment exposure is related to blunted striatal sensitivity. It may be that maladaptive parenting exerts sensitizing effects on the mesolimbic dopamine system, up until more extreme or chronic circumstances (i.e., maltreatment) are experienced. The latter then results in reward-related blunting effects. This is in line with evidence from rodent models indicating that acute stress enhances reward salience via modulation in the dopamine system (Abercrombie, Keefe, DiFrischia, & Zigmond, 1989)

through increases in glucocorticoids (Rouge-Pont, Deroche, Le Moal, & Piazza, 1998). However, chronic exposure to stressors results in attenuated dopamine release in the striatum (Cabib & Puglisi-Allegra, 1996) and decreased basal dopamine levels (Mangiavacchi et al., 2001).

Finally, some prior work has also shown that aspects of the caregiving environment may be correlated with neural function facilitating cognitive control and decision-making. Higher levels of anterior insula response (Marusak et al., 2018), greater anterior insula connectivity (Guassi Moreira & Telzer, 2018), and higher ventrolateral PFC (McCormick et al., 2015) response during cognitive control and decision-making contexts have been observed in youth with more negative family factors, including parental psychological control, high family conflict, and low family cohesion. For example, higher levels of family conflict were associated with greater ventral striatum-anterior insula coupling during safe decision-making in the presence of one's mother in a risky driving task, when adolescents presumably inhibited risky responses in the face of potentially rewarding stimuli. This neural pattern was in turn associated with greater risk-taking behaviors in adolescents longitudinally (Guassi Moreira & Telzer, 2018). The anterior insula is thought to be involved in integrating affective and cognitive processes, and may be a critical relay point for recruiting other networks (Menon & Uddin, 2010). Thus, aberrant anterior insula response and connectivity may disrupt effective cognitive regulation. Together, parenting may not only influence emotion generating, reward, and motivational neural systems, but may also be tied to how affective and cognitive control systems interface.

Developmental timing of parental influence. Notably, some research has suggested that parental influences on brain development may vary based on the developmental timing of exposure. The brain undergoes sensitive periods of development, or high levels of plasticity

which may render developing neural circuitry vulnerable to environmental inputs (Tottenham & Sheridan, 2010). Identifying these temporal effects is difficult to capture in human research, as maladaptive caregiving exposures rarely occur in isolated windows and cannot be experimentally manipulated. However, initial evidence of sensitive periods of neural development as it relates to parenting in humans largely stems from research on childhood maltreatment and adversity. For example, one study indicated reduced hippocampal volume was most strongly related to maltreatment exposure occurring during early childhood (ages 3 to 5 years) and early adolescence (ages 11 to 13 years) relative to other periods in a sample of adult females (Andersen et al., 2008). Other work has suggested that the preadolescent period may also represent a time of heightened sensitivity, with one study finding peak amygdala effects of maltreatment exposure occurring at ages 10 to 11 years (Pechtel, Lyons-Ruth, Anderson, & Teicher, 2014). Given that different neural regions follow different growth rates across development, it may be that specific circuitry possess unique windows of sensitivity to the caregiving environment. Due to the preliminary nature of this empirical work in humans however, further research is certainly needed in this arena.

Neural synchrony. The above studies conceptualize the developing brain in the context of direct or longterm influences of parenting, although links between parenting behavior and neural development are inevitably reciprocal, occurring on micro and macro level time scales. An important example of this comes from evidence characterizing parent-child synchrony (for review, see Feldman, 2012). Synchrony refers to the coordinated response of behavioral and biological processes across close social partners, with this coupled exchange of social signals beginning early in human development and creating a foundation for attachment relationships (Feldman, 2012). Brain-based measures of parent-child synchrony offer one example of these

coordinated social responses, with evidence suggesting that parent-child neural synchrony may represent greater social connectedness and have implications for youth adjustment. For example, one study utilizing resting state functional connectivity found that parents and adolescents with more similar resting state intrinsic networks showed greater day to day emotional synchrony and higher adolescent emotional competence (Lee, Miernicki, Telzer, 2017). Several studies using fNIRS have also found greater neural synchrony during cooperative parent-child interactions compared to individual activity in prefrontal and temporal-parietal areas (e.g., Miller et al., 2019;; Reindl, Gerloff, Scharke, & Konrad, 2018), and that higher levels of parent-child neural synchrony are associated with adaptive outcomes (e.g., higher emotion regulation, problem solving). These studies show intriguing avenues for understanding brain-based synchrony between parent and child that may compliment longitudinal research designs of parental influence on brain development.

Models of Neurobiological Susceptibility to Normative Parenting

Above, we reviewed evidence from models suggesting that parenting directly influences aspects of youths' brain development, although further research is required to clarify contradictory findings and understand longitudinal relations. However, theory has posited that aspects of neural function and structure may not only be affected by environmental inputs but may dictate the extent to which adversity or support influences developmental outcomes. Indeed, the notion that children differ in their susceptibility to the social environment, such as negative psychosocial effects of maladaptive parenting, has long been recognized in the study of child development. One theory, referred herein as differential susceptibility theory (Belsky & Pluess, 2009; see also biological sensitivity to context, Boyce & Ellis, 2005), posits that individuals differ in their neurobiological susceptibility to the environment in an evolutionarily adaptive

manner, such that some children are more susceptible or adapt more highly in response to environmental inputs than others. Central to this theory is that neurobiological susceptibility functions in a "for better or for worse" fashion (Belsky & Pluess, 2009). That is, youth who are most susceptible to their social environments are the same youth most likely to thrive in supportive social environments or to suffer in harsh social environments.

The majority of research to date on differential susceptibility has investigated behavioral markers of susceptibility, such as temperament or genetic markers of susceptibility (see Belsky & Pluess, 2009). More recently, however, brain function and structure have been discussed as optimal endophenotypic markers of susceptibility, as these measures may offer a summary of genomic expression and may allow one to make inferences regarding specific processes based on neural circuitry involved (e.g., cognitive, affective mechanisms) (Schriber & Guyer, 2016). Thus, while research discussed above illustrates the potential direct effects of parenting, differential susceptibility offers a window into how such differences in neurobiology may interact with one's environment to determine health and behavior.

Neurobiological susceptibility is thought to be a product of both genetic as well as early environmental influences that shape brain development. Thus, ostensibly, parenting may 1) directly impact neurobiological susceptibility (as reviewed in the section above) and 2) interact with individual differences in susceptibility at any point in development to predict adjustment and behavior (see Figure 1 for proposed model). Social environmental influences on neurobiological susceptibility is hypothesized to occur most strongly during early sensitive periods of development; whereas, interactions between the social environment and neurobiology reflective of differential susceptibility may manifest more prominently later in development (e.g., adolescence). Given that adolescence is both a time of significant neurodevelopment and that

psychopathology (e.g., depression) tends to emerge during this time, adolescence may represent an especially important development period for individual differences in susceptibility to manifest (Schriber & Guyer, 2016). Not surprisingly then, existing studies investigating neurobiological susceptibility patterns in youth to date have focused primarily on this period.

Brain Structure. A small handful of studies to date have examined youth brain structure as an endophenotypic marker of susceptibility to parenting. In particular, a few studies have examined key limbic structures as differential susceptibility markers in adolescent samples. Findings indicated that under maladaptive family circumstances (e.g., maternal aggression, low family connectedness), larger hippocampal volumes were predictive of depressive symptoms in adolescents. Specifically, in maladaptive family contexts, larger hippocampal volumes were predictive of higher levels of depressive symptoms; whereas, in more adaptive family contexts, larger volumes were associated with lower levels of depressive symptoms (Whittle et al., 2011; Schriber et al., 2017). Thus, the same neural profile that conferred risk in one parenting context conferred benefits in another. Further, for adolescents with smaller than average hippocampal volumes, no significant relations emerged between family context and adolescent adjustment, suggesting that these adolescents may be less sensitive to parenting in general.

For amygdala, gender differences in susceptibility profiles were observed (Yap et al., 2008). For girls, smaller amygdala volumes represented a susceptibility factor to maternal aggression, predicting greater adjustment for girls exposed to *high* levels of maternal aggression and poorer adjustment for girls exposed to *low* levels of maternal aggression (Yap et al., 2008). An opposite pattern emerged for boys, with larger amygdala volumes representing susceptibility. Youth were not uniformly affected by maladaptive parenting, however, as maternal aggression was not related to adjustment for adolescents with low (for girls) or average (for boys) amygdala

volumes. These initial studies (notably using nonclinical community samples) suggest that neurobiological susceptibility patterns, particularly in key limbic structures known to be susceptible to early adversity and stress more generally, may be evident during the adolescent period of development.

In a recent study of adolescents, differential susceptibility patterns were also identified with respect to cortical thickness (Deane et al., 2019). Under contexts of high maternal aggression, lower levels of cortical thinning were associated with lower well-being. In contrast, under conditions of low maternal aggression, lower cortical thinning was associated with greater well-being. As above, a neural profile (i.e., increased cortical thinning) distinguishing youth less susceptible to maternal behavior emerged. Unlike previous studies, neural susceptibility findings did not extend to measures of depression. Still, this initial evidence suggests that not only does parenting directly influence cortical development, neural structure may independently interact with parenting resulting in differential patterns of adjustment and behavior.

Brain Function. Only two studies to our knowledge have tested models of neurobiological susceptibility to the caregiving environment with respect to youths' brain function via MRI. In one study of adolescent girls, higher neural sensitivity to social exclusion in affective salience regions (e.g., anterior insula, dACC, and sgACC) was associated with fewer depressive symptoms in the context of supportive parent-adolescent relationships, but associated with greater depressive symptoms in the context of conflictual parent-adolescent relationships (Rudolph et al., 2018). Girls with lower activation in affective salience regions, however, were less sensitive to poorer parent-adolescent relationship quality, showing low to average levels of depressive symptoms regardless of relationship quality. In another study, youth evidencing higher caudate activation to parental praise reported greater depressive symptoms under contexts

of low maternal acceptance and high peer victimization (Sequeira et al., 2019). In contrast, for youth with lower levels of caudate activation to parental praise, peer and maternal factors were not significantly associated with adolescent depression, again perhaps illuminating a marker of reduced susceptibility to social influence more generally. These studies suggest that heightened sensitivity in affective salience regions, in response to either positive or negatively valenced affective stimuli, may represent a neurobiological marker of susceptibility in adolescent youth, once again predicting internalizing symptoms during this period.

Altogether, initial evidence underscores that parenting may not influence youth behavior uniformly, in part as a function of neurobiological factors. However, it is important to note that this evidence to date is correlational in nature and further research is needed to support the directionality of such associations.

Summary and Integration

Parenting, from its most extreme forms of maladaptation to more normative variations in healthy parental behavior, exerts diverse effects on developing neural structure and function. Extant research suggests that like maltreatment exposure, normative variations in maladaptive parenting impact developing neural circuitry most consistently within stress and negative valence systems. Although no study to our knowledge has examined both maltreatment and normative variations of parenting within one study, this cumulative evidence makes possible the notion that maladaptive parenting may function on a continuum, ostensibly impacting stress and affective systems in the brain in a linear fashion. That is, as negative features of the caregiving environment increase in quality, frequency, and/or intensity, so too do neural impacts.

While these bodies of research show similarities, diverging patterns distinguishing maltreatment from normative variations in maladaptive parenting emerge in some key areas.

First, whereas maltreatment exposure has been linked to blunted neural reward sensitivity in mesolimbic systems, normative variations in maladaptive parenting is associated with heightened reward sensitivity as measured at the neural level (e.g., Casement et al., 2014; Qu et al., 2015). Second, aspects of maltreatment have been related to reduced thickness in association cortex and accelerated cortical maturation (e.g., McLaughlin et al., 2014b); however, studies of normative variations in parenting suggest that maladaptive parenting is associated with increased cortical maturation in adolescent samples (e.g., Whittle et al., 2009, 2014, 2016). On a whole, these diverging findings may suggest that extreme adversities in the caregiving environment, such as maltreatment exposure, relative to normative variations in parenting may produce qualitatively disparate effects on neural function. It is possible that effects on these systems do not function in a linear fashion, with extreme maladaptive parenting associated with blunted (e.g., reward system function) or accelerated (e.g., association cortex structure) development.

Finally, an intriguing and nascent literature in human brain development points out that not only does the quality of parenting impact the developing brain, but aspects of brain structure and function at any given point in development may interact with social inputs such as parenting to predict adjustment. In particular, differential susceptibility theory posits that certain neural endophenotypes may place youth at particular risk for psychopathology when exposed to maladaptive parenting, but may confer benefits when exposed to supportive or sensitive parenting. This framework highlights the complexity of how parenting and the social environment are neurobiologically embedded, as neural systems may be an output, mediator, or moderator when predicting future health and behavior.

Future Directions

Human studies reviewed herein have primarily utilized observational or correlational

research methods to investigate the effects of parenting on youths' brain development. This research has undoubtedly enriched our understanding; however, correlational designs in human research may limit causal inferences in understanding the effects of parenting. It is important to note that preclinical studies documenting caregiving effects in animal models have afforded the ability to experimentally manipulate the caregiving environment and thus complement observational research in humans (Sanchez, Ladd, & Plotsky, 2001). Still, opportunities exist to take steps forward in research design for human models, especially given that animal models do not universally translate to human development. As an example, in a randomized control trial, Milgrom and colleagues (2010) randomly assigned parents of infants to a parent sensitivity training or control intervention, and uniquely measured infant brain volumes and white matter microstructure using DTI following the intervention. Results indicated that infants of parents who received sensitivity training showed greater white matter connectivity and maturation compared to controls. Such controlled designs may be one avenue for future research to empirically test parenting's effect on human brain development.

Further, most research to date has focused on maternal behavior exclusively as it relates to youth brain development. However, youth are likely exposed to other caregivers and diverse family structures. Contextual factors within the family system—including the number and gender identity of caregivers, multigenerational structure, movement of family in and out of the home, and biological relation—are rarely considered. Future research exploring this diversity is needed, and may be relevant to parental influence on neural structure and function as well as youth's susceptibility to such exposures.

Relatedly, most research to date has been done within largely Western, White, higher socioeconomic samples (Qu, Jorgensen, & Telzer, in press) without taking into consideration

how parenting and its effects on the brain may differ across ethnic, cultural, religious, and economic contexts. Indeed, the goals, values, and parenting strategies of families significantly differ based on ethnic background. For instance, Chinese and other Asian families traditionally emphasize the importance of family harmony and respect, families from Mexican and other Latin American backgrounds have a strong sense of family connection, interdependence, and support often referred to as familism, and African American families tend to value interdependence and perseverance in the face of adversity (Fuligni, 1998; Hill, 2006; McLoyd, Dodge, & Lansford, 2005). These family values often translate into more authoritarian parenting strategies, including the use of discipline (Hill, 2006). Thus, adolescents from these cultural groups may benefit more from family harmony and suffer less from parenting that utilizes harsh discipline. European American families tend to endorse individualism and individual achievement, family values that often translate into more authoritative parenting strategies that emphasize reasoning and discussion (Hill, 2006). Importantly, within each culture, the parenting practices that are valued are associated with more positive and adaptive outcomes.

While most research on parenting and brain development has been conducted in White samples, emerging theory and research suggests that the brain may be shaped by cultural experiences within the family context (Qu, Jorgensen, & Telzer, in press). For example, Mexican American adolescents who tend to place higher value on familism, show greater activation in the ventral striatum when making decisions to contribute to their family that involve self-sacrifice, compared to European American adolescents who show more ventral striatum activation when gaining for themselves and not their family (Telzer et al., 2010). Importantly, heightened ventral striatum activation when contributing to their family predicts longitudinal decreases in risk-taking behavior and depression among Mexican American adolescents (Telzer et al., 2013,

2014), suggesting that culturally shaped neural processes have implications for youths' adjustment and well-being over time. These findings underscore the importance of broadening samples to include families from diverse backgrounds to augment current theory and support culturally sensitive policies and family-based interventions that are sensitive to variations in cultural values across families. This is particularly important for culturally grounded intervention efforts that may have iatrogenic effects if non-culturally sensitive efforts are implemented (Hecht et al., 2003).

Conclusions

Altogether, this chapter reviewed literature characterizing relations between parenting and human brain development, describing research underscoring direct effects of the full continuum of parenting as well as interactive effects through early childhood to adolescence. Evidence to date makes clear that not only is extreme adversity in the caregiving environment, as in the case of abuse and neglect, related to the function and structure of the developing brain, but also that normative and perhaps more subtle variations in parenting quality are tied to youth's neural development as well. This notion provides optimism that prevention efforts targeting parenting practices and family functioning may have the potential to significantly impact youth development and that even brief preventative interventions may have important cascading effects. Moreover, families experiencing a wider range of hardship, from severe adversity to more normative stressors, can benefit from parenting support, education, and intervention.

References

Abercrombie, E. D., Keefe, K. A., DiFrischia, D. S., & Zigmond, M. J. (1989). Differential effect of stress on in vivo dopamine release in striatum, nucleus accumbens, and medial frontal cortex. *Journal of Neurochemistry*, *52*, 1655-1658. 10.1111/j.1471-4159.1989.tb09224.x

Amato, P. R., & Fowler, F. (2002). Parenting practices, child adjustment, and family diversity. *Journal of Marriage and Family*, *64*, 703-716. 10.1111/j.1741-3737.2002.00703.x

Andersen, S. L., Tomada, A., Vincow, E. S., Valente, E., Polcari, A., & Teicher, M. H. (2008). Preliminary evidence for sensitive periods in the effect of childhood sexual abuse on regional brain development. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *20*, 292-301.

Barbosa, C., Simmons, J. G., Vijayakumar, N., Dudgeon, P., Patton, G. C., Mundy, L. K., ... & Whittle, S. (2018). Interaction between parenting styles and adrenarcheal timing associated with affective brain function in late childhood. *Journal of the American Academy of Child & Adolescent Psychiatry*, *57*, 678-686. 10.1016/j.jaac.2018.05.016

Belsky, J., & de Haan, M. (2011). Annual research review: Parenting and children's brain development: The end of the beginning. *Journal of Child Psychology and Psychiatry*, *52*, 409-428. 10.1111/j.1467-8721.2007.00525.x

Belsky, J., & Pluess, M. (2009). Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychological Bulletin*, *135*, 885-908. 10.1037/a0017376

Bernier, A., Dégeilh, F., Leblanc, É., Daneault, V., Bailey, H. N., & Beauchamp, M. H. (2019). Mother–infant interaction and child brain morphology: A multidimensional approach to maternal sensitivity. *Infancy*, *24*, 120–138. 10.1111/infa.12270

Blair, R. J. R., Veroude, K., & Buitelaar, J. K. (2018). Neuro-cognitive system dysfunction and symptom sets: A review of fMRI studies in youth with conduct problems. *Neuroscience & Biobehavioral Reviews*, *91*, 69-90. 10.1016/j.neubiorev.2016.10.022

Blakemore, S. J. (2012). Imaging brain development: the adolescent brain. *Neuroimage*, *61*, 397-406. 10.1016/j.neuroimage.2011.11.080

Boyce, W. T., & Ellis, B. J. (2005). Biological sensitivity to context: I. An evolutionary–developmental theory of the origins and functions of stress reactivity. *Development and Psychopathology*, *17*, 271-301. 10.10170S0954579405050145

Busso, D. S., McLaughlin, K. A., Brueck, S., Peverill, M., Gold, A. L., & Sheridan, M. A. (2017). Child abuse, neural structure, and adolescent psychopathology: A longitudinal study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *56*, 321-328. 10.1016/j.jaac.2017.01.013

Bremner, J. D., Randall, P., Vermetten, E., Staib, L., Bronen, R. A., Mazure, C., ... & Charney, D. S. (1997). Magnetic resonance imaging-based measurement of hippocampal volume in posttraumatic stress disorder related to childhood physical and sexual abuse—a preliminary report. *Biological Psychiatry*, *41*, 23-32. 10.1016/S0006-3223(96)00162-X

Brenhouse, H., Lukkes, J., & Andersen, S. (2013). Early life adversity alters the developmental profiles of addiction-related prefrontal cortex circuitry. *Brain Sciences*, *3*, 143-158. 10.3390/brainsci3010143

Burani, K., Mulligan, E. M., Klawohn, J., Luking, K. R., Nelson, B. D., & Hajcak, G. (2019). Longitudinal increases in reward-related neural activity in early adolescence: Evidence from event-related potentials (ERPs). *Developmental Cognitive Neuroscience*, *36*, e100620. 10.1016/j.dcn.2019.100620

Cabib, S., & Puglisi-Allegra, S. (1996). Stress, depression and the mesolimbic dopamine system. *Psychopharmacology*, *128*, 331-342.

Cai, L., Dong, Q., & Niu, H. (2018). The development of functional network organization in early childhood and early adolescence: A resting-state fNIRS study. *Developmental Cognitive Neuroscience*, *30*, 223-235. 10.1016/j.dcn.2018.03.003

Callaghan, B. L., & Tottenham, N. (2016). The stress acceleration hypothesis: Effects of early-life adversity on emotion circuits and behavior. *Current Opinion in Behavioral Sciences*, *7*, 76-81. 10.1016/j.cobeha.2015.11.018

Casement, M. D., Guyer, A. E., Hipwell, A. E., McAloon, R. L., Hoffmann, A. M., Keenan, K. E., & Forbes, E. E. (2014). Girls' challenging social experiences in early adolescence predict neural response to rewards and depressive symptoms. *Developmental Cognitive Neuroscience*, *8*, 18-27. 10.1016/j.dcn.2013.12.003

Casey, B. J., Heller, A. S., Gee, D. G., & Cohen, A. O. (2019). Development of the emotional brain. *Neuroscience Letters*, *693*, 29-34. 10.1016/j.neulet.2017.11.055

Chaplin, T. M., Poon, J. A., Thompson, J. C., Hansen, A., Dziura, S. L., Turpyn, C. C., ... & Ansell, E. B. (2019). Sex-differentiated associations among negative parenting, emotion-related brain function, and adolescent substance use and psychopathology symptoms. *Social Development*, *28*, 637-656. 10.1111/sode.12364

Cicchetti, D., & Cohen, D. J. (1995). Perspectives on developmental psychopathology. In D. Cicchetti & D. J. Cohen (Eds.), *Developmental psychopathology, Vol. 1. Theory and methods* (pp. 3–20). New York: John Wiley & Sons.

Corral-Frías, N. S., Nikolova, Y. S., Michalski, L. J., Baranger, D. A., Hariri, A. R., & Bogdan, R. (2015). Stress-related anhedonia is associated with ventral striatum reactivity to

reward and transdiagnostic psychiatric symptomatology. *Psychological Medicine*, *45*, 2605-2617. 10.1017/S0033291715000525

Colich, N. L., Rosen, M. L., Williams, E. S., & McLaughlin, K. A. (2020). Biological aging in childhood and adolescence following experiences of threat and deprivation: A systematic review and meta-analysis. *Psychological Bulletin, 146*, 721–764. 10.1037/bul0000270

Deane, C., Vijayakumar, N., Allen, N. B., Schwartz, O., Simmons, J. G., Bousman, C. A., ... & Whittle, S. (2019). Parenting x brain development interactions as predictors of adolescent depressive symptoms and well-being: Differential susceptibility or diathesis-stress?. *Development and Psychopathology*, 1-12. 10.1017/S0954579418001475

Dillon, D. G., Holmes, A. J., Birk, J. L., Brooks, N., Lyons-Ruth, K., & Pizzagalli, D. A. (2009). Childhood adversity is associated with left basal ganglia dysfunction during reward anticipation in adulthood. *Biological Psychiatry*, *66*, 206-213. 10.1016/j.biopsych.2009.02.019

Dosenbach, N. U., Nardos, B., Cohen, A. L., Fair, D. A., Power, J. D., Church, J. A., ... & Barnes, K. A. (2010). Prediction of individual brain maturity using fMRI. *Science*, *329*, 1358-1361. 10.1126/science.1194144

Feldman, R. (2012). Parent–infant synchrony: A biobehavioral model of mutual influences in the formation of affiliative bonds. *Monographs of the Society for Research in Child Development*, *77*, 42-51. 10.1080/15295192.2012.683342

Frye, R. E., Malmberg, B., Swank, P., Smith, K., & Landry, S. (2010). Preterm birth and maternal responsiveness during childhood are associated with brain morphology in adolescence. *Journal of the International Neuropsychological Society*, *16*, 784-794. 10.1017/S1355617710000585

Fuligni, A. J. (1998). The adjustment of children from immigrant families. *Current Directions in Psychological Science*, *7*, 99-103. 10.1111/1467-8721.ep10774731

Gard, A. M., Waller, R., Shaw, D. S., Forbes, E. E., Hariri, A. R., & Hyde, L. W. (2017). The long reach of early adversity: Parenting, stress, and neural pathways to antisocial behavior in adulthood. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *2*, 582-590. 10.1016/j.bpsc.2017.06.005

Goff, B., Gee, D. G., Telzer, E. H., Humphreys, K. L., Gabard-Durnam, L., Flannery, J., & Tottenham, N. (2013). Reduced nucleus accumbens reactivity and adolescent depression following early-life stress. *Neuroscience*, *249*, 129-138. 10.1016/j.neuroscience.2012.12.010

Gold, A. L., Sheridan, M. A., Peverill, M., Busso, D. S., Lambert, H. K., Alves, S., ... & McLaughlin, K. A. (2016). Childhood abuse and reduced cortical thickness in brain regions involved in emotional processing. *Journal of Child Psychology and Psychiatry*, *57*, 1154-1164. 10.1111/jcpp.12630

Gorka, A. X., Hanson, J. L., Radtke, S. R., & Hariri, A. R. (2014). Reduced hippocampal and medial prefrontal gray matter mediate the association between reported childhood maltreatment and trait anxiety in adulthood and predict sensitivity to future life stress. *Biology of Mood & Anxiety Disorders*, *4*, e12. 0.1186/2045-5380-4-12

Guassi Moreira, J. F., & Telzer, E. H. (2018). Mother still knows best: Maternal influence uniquely modulates adolescent reward sensitivity during risk taking. *Developmental Science*, *21*, e12484. 10.1111/desc.12484

Gunnar, M. R., DePasquale, C. E., Reid, B. M., & Donzella, B. (2019). Pubertal stress recalibration reverses the effects of early life stress in postinstitutionalized

children. *Proceedings of the National Academy of Sciences*, *116*, 23984-23988. 10.1073/pnas.1909699116

Hanson, J. L., Nacewicz, B. M., Sutterer, M. J., Cayo, A. A., Schaefer, S. M., Rudolph, K. D., ... & Davidson, R. J. (2015). Behavioral problems after early life stress: Contributions of the hippocampus and amygdala. *Biological Psychiatry*, *77*, 314-323. 10.1016/j.biopsych.2014.04.020

Hecht, M. L., Marsiglia, F. F., Elek, E., Wagstaff, D. A., Kulis, S., Dustman, P., et al. (2003). Culturally grounded substance use prevention: An evaluation of the keepin' it R.E.A.L. curriculum. *Prevention Science*, 4, 233–248. 10.1023/A:1026016131401

Hein, T. C., & Monk, C. S. (2017). Research Review: Neural response to threat in children, adolescents, and adults after child maltreatment–a quantitative meta-analysis. *Journal of Child Psychology and Psychiatry*, *58*, 222-230. 10.1111/jcpp.12651

Hill, N. E. (2006). Disentangling ethnicity, socioeconomic status and parenting: Interactions, influences and meaning. *Vulnerable Children and Youth Studies*, *1*, 114-124. 10.1080/17450120600659069

Kok, R., Thijssen, S., Bakermans-Kranenburg, M. J., Jaddoe, V. W., Verhulst, F. C., White, T., ... & Tiemeier, H. (2015). Normal variation in early parental sensitivity predicts child structural brain development. *Journal of the American Academy of Child & Adolescent Psychiatry*, *54*, 824-831. 10.1016/j.jaac.2015.07.009

Kopala-Sibley, D. C., Cyr, M., Finsaas, M. C., Orawe, J., Huang, A., Tottenham, N., & Klein, D. N. (2018). Early childhood parenting predicts late childhood brain functional connectivity during emotion perception and reward processing. *Child Development*, *91*, 110–128. 10.1111/cdev.13126

Lambert, H. K., & McLaughlin, K. A. (2019). Impaired hippocampus-dependent associative learning as a mechanism underlying PTSD: A meta-analysis. *Neuroscience & Biobehavioral Reviews, 107*, 729-749. 0.1016/j.neubiorev.2019.09.024

Lambert, H. K., Sheridan, M. A., Sambrook, K. A., Rosen, M. L., Askren, M. K., & McLaughlin, K. A. (2017). Hippocampal contribution to context encoding across development is disrupted following early-life adversity. *Journal of Neuroscience*, *37*, 1925-1934. 10.1523/JNEUROSCI.2618-16.2017

Lee, T. H., Miernicki, M. E., & Telzer, E. H. (2017). Families that fire together smile together: resting state connectome similarity and daily emotional synchrony in parent-child dyads. *Neuroimage*, *152*, 31-37. 10.1016/j.neuroimage.2017.02.078

Liu, D., Diorio, J., Tannenbaum, B., Caldji, C., Francis, D., Freedman, A., ... & Meaney, M. J. (1997). Maternal care, hippocampal glucocorticoid receptors, and hypothalamic-pituitary-adrenal responses to stress. *Science*, *277*, 1659-1662. 10.1126/science.277.5332.1659

Luby, J. L., Barch, D. M., Belden, A., Gaffrey, M. S., Tillman, R., Babb, C., ... & Botteron, K. N. (2012). Maternal support in early childhood predicts larger hippocampal volumes at school age. *Proceedings of the National Academy of Sciences*, *109*, 2854-2859. 10.1073/pnas.1118003109

Mangiavacchi, S., Masi, F., Scheggi, S., Leggio, B., De Montis, M. G., & Gambarana, C. (2001). Long-term behavioral and neurochemical effects of chronic stress exposure in rats. *Journal of Neurochemistry*, *79*, 1113-1121. 10.1046/j.1471-4159.2001.00665.x

Marusak, H. A., Thomason, M. E., Sala-Hamrick, K., Crespo, L., & Rabinak, C. A. (2018). What's parenting got to do with it: Emotional autonomy and brain and behavioral responses to emotional conflict in children and adolescents. *Developmental Science*, *21*,

e12605. 10.1111/desc.12605

Matthews, K., & Robbins, T. W. (2003). Early experience as a determinant of adult behavioural responses to reward: The effects of repeated maternal separation in the rat. *Neuroscience & Biobehavioral Reviews*, *27*, 45-55. 10.1016/S0149-7634(03)00008-3

McCormick, E. M., McElwain, N. A., & Telzer, E. H. (2019). Alterations in adolescent dopaminergic systems as a function of early mother-toddler attachment: A prospective longitudinal examination. *International Journal of Developmental Neuroscience, 78*, 122-129. 10.1016/j.ijdevneu.2019.06.010

McCormick, E. M., Qu, Y., & Telzer, E. H. (2015). Adolescent neurodevelopment of cognitive control and risk-taking in negative family contexts. *NeuroImage*, *124*, 989-996. 10.1016/j.neuroimage.2015.09.063

McLoyd, V. c., Dodge, K A., & Lansford, J. E. (2005). *The cultural context of physically disciplining children.* In V. C. McLoyd, N. E. Hill, & K. A. Dodge (Eds), African A men'can family life: Ecological and cultural diversity (pp. 245-263). New York: Guilford Press.

Mehta, M. A., Golembo, N. I., Nosarti, C., Colvert, E., Mota, A., Williams, S. C., ... & Sonuga-Barke, E. J. (2009). Amygdala, hippocampal and corpus callosum size following severe early institutional deprivation: The English and Romanian Adoptees study pilot. *Journal of Child Psychology and Psychiatry*, *50*, 943-951. 10.1111/j.1469-7610.2009.02084.x

Mehta, M. A., Gore-Langton, E., Golembo, N., Colvert, E., Williams, S. C., & Sonuga-Barke, E. (2010). Hyporesponsive reward anticipation in the basal ganglia following severe institutional deprivation early in life. *Journal of Cognitive Neuroscience*, *22*, 2316-2325. 10.1162/jocn.2009.21394

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: A network model of insula function. *Brain Structure and Function*, *214*, 655-667. 10.1007/s00429-010-0262-0

Milgrom, J., Newnham, C., Anderson, P. J., Doyle, L. W., Gemmill, A. W., Lee, K., ... & Inder, T. (2010). Early sensitivity training for parents of preterm infants: Impact on the developing brain. *Pediatric Research, 67*, 330-335. 10.1203/PDR.0b013e3181cb8e2f

Miller, J. G., Vrtička, P., Cui, X., Shrestha, S., Hosseini, S. H., Baker, J. M., & Reiss, A. L. (2019). Inter-brain synchrony in mother-child dyads during cooperation: An fNIRS hyperscanning study. *Neuropsychologia*, *124*, 117-124. 10.1016/j.neuropsychologia.2018.12.021

Mills, K. L., Goddings, A. L., Herting, M. M., Meuwese, R., Blakemore, S. J., Crone, E. A., ... & Tamnes, C. K. (2016). Structural brain development between childhood and adulthood: Convergence across four longitudinal samples. *Neuroimage*, *141*, 273-281. 10.1016/j.neuroimage.2016.07.044

Mills, K. L., Lalonde, F., Clasen, L. S., Giedd, J. N., & Blakemore, S. J. (2014). Developmental changes in the structure of the social brain in late childhood and adolescence. *Social Cognitive and Affective Neuroscience, 9*, 123-131. 10.1093/scan/nss113

Morgan, J. K., Shaw, D. S., & Forbes, E. E. (2014). Maternal depression and warmth during childhood predict age 20 neural response to reward. *Journal of the American Academy of Child & Adolescent Psychiatry*, *53*, 108-117. 10.1016/j.jaac.2013.10.003

McCrory, E. J., Gerin, M. I., & Viding, E. (2017). Annual research review: Childhood maltreatment, latent vulnerability and the shift to preventative psychiatry–the

contribution of functional brain imaging. *Journal of Child Psychology and Psychiatry*, *58*, 338-357. 10.1111/jcpp.12713

McLaughlin, K. A., Sheridan, M. A., & Lambert, H. K. (2014a). Childhood adversity and neural development: Deprivation and threat as distinct dimensions of early experience. *Neuroscience & Biobehavioral Reviews*, *47*, 578-591. 10.1177/0963721416655883

McLaughlin, K. A., Sheridan, M. A., Winter, W., Fox, N. A., Zeanah, C. H., & Nelson, C. A. (2014b). Widespread reductions in cortical thickness following severe early-life deprivation: A neurodevelopmental pathway to attention-deficit/hyperactivity disorder. *Biological Psychiatry*, *76*, 629-638. 10.1016/j.biopsych.2013.08.016

Nusslock, R., & Miller, G. E. (2016). Early-life adversity and physical and emotional health across the lifespan: A neuroimmune network hypothesis. *Biological Psychiatry*, *80*, 23-32. 10.1016/j.biopsych.2015.05.017

Pechtel, P., Lyons-Ruth, K., Anderson, C. M., & Teicher, M. H. (2014). Sensitive periods of amygdala development: The role of maltreatment in preadolescence. *Neuroimage*, *97*, 236-244. 10.1016/j.neuroimage.2014.04.025

Phelps, E. A., & LeDoux, J. E. (2005). Contributions of the amygdala to emotion processing: From animal models to human behavior. *Neuron, 48*, 175-187. 10.1016/j.neuron.2005.09.025

Plomin, R., DeFries, J.C., McClearn, G.E., & McGuffin, P. (2008) *Behavioral genetics.* New York: Worth Publishers.

Plotsky, P. M., & Meaney, M. J. (1993). Early, postnatal experience alters hypothalamic corticotropin-releasing factor (CRF) mRNA, median eminence CRF content and stress-

induced release in adult rats. *Molecular Brain Research*, *18*, 195-200. 10.1016/0169-328X(93)90189-V

Pozzi, E., Simmons, J. G., Bousman, C. A., Vijayakumar, N., Bray, K. O., Dandash, O., . . .Whittle, S. L. (2019). The influence of maternal parenting style on the neural correlates of emotion processing in children. *Journal of the American Academy of Child & Adolescent Psychiatry*. Advance online publication. 10.1016/j.jaac.2019.01.018

Qu, Y., Fuligni, A. J., Galvan, A., & Telzer, E. H. (2015). Buffering effect of positive parent–child relationships on adolescent risk taking: A longitudinal neuroimaging investigation. *Developmental Cognitive Neuroscience*, *15*, 26-34. 10.1016/j.dcn.2015.08.005

Qu, Y., Fuligni, A. J., Galván, A., Lieberman, M. D., & Telzer, E. H. (2016). Links between parental depression and longitudinal changes in youths' neural sensitivity to rewards. *Social Cognitive and Affective Neuroscience, 11*, 1262-1271. 10.1093/scan/nsw035

Qu, Y., Jorgensen, N.A., & Telzer, E.H. (in press). A call for greater attention to culture in the study of brain and development. *Perspectives on Psychological Science.*

Rao, H., Betancourt, L., Giannetta, J. M., Brodsky, N. L., Korczykowski, M., Avants, B. B., ... & Farah, M. J. (2010). Early parental care is important for hippocampal maturation: Evidence from brain morphology in humans. *Neuroimage*, *49*, 1144-1150. 10.1016/j.neuroimage.2009.07.003

Reindl, V., Gerloff, C., Scharke, W., & Konrad, K. (2018). Brain-to-brain synchrony in parent-child dyads and the relationship with emotion regulation revealed by fNIRS-based hyperscanning. *NeuroImage*, *178*, 493-502. 10.1016/j.neuroimage.2018.05.060

Rifkin-Graboi, A., Kong, L., Sim, L. W., Sanmugam, S., Broekman, B. F., Chen, H., . . .Qiu, A.

(2015). Maternal sensitivity, infant limbic structure volume and functional connectivity: A preliminary study. *Translational Psychiatry*, *5*(10), e668. 10.1038/tp.2015.133

Romund, L., Raufelder, D., Flemming, E., Lorenz, R. C., Pelz, P., Gleich, T., ... & Beck, A. (2016). Maternal parenting behavior and emotion processing in adolescents—An fMRI study. *Biological Psychology*, *120*, 120-125. 10.1016/j.biopsycho.2016.09.003

Rougé-Pont, F., Deroche, V., Moal, M. L., & Piazza, P. V. (1998). Individual differences in stress-induced dopamine release in the nucleus accumbens are influenced by corticosterone. *European Journal of Neuroscience*, *10*, 3903-3907. 10.1046/j.1460-9568.1998.00438.x

Rudolph, K. D., Davis, M. M., Modi, H. H., Fowler, C., Kim, Y., & Telzer, E. H. (2018). Differential susceptibility to parenting in adolescent girls: Moderation by neural sensitivity to social cues. *Journal of Research on Adolescence, 30*, 177-191. 10.1111/jora.12458

Sanchez, M.M., Ladd, C.O., & Plotsky, P.M. (2001). Early adverse experience as a developmental risk factor for later psychophathology: Evidence from rodent and primate models. *Development & Psychopathology, 13*, 419– 449. 10.1017/S0954579401003029

Schneider, S., Brassen, S., Bromberg, U., Banaschewski, T., Conrod, P., Flor, H., ... & Nees, F. (2012). Maternal interpersonal affiliation is associated with adolescents' brain structure and reward processing. *Translational Psychiatry*, *2*, e182. 10.1038/tp.2012.113

Schriber, R. A., Anbari, Z., Robins, R. W., Conger, R. D., Hastings, P. D., & Guyer, A. E. (2017). Hippocampal volume as an amplifier of the effect of social context on adolescent depression. *Clinical Psychological Science*, *5*, 632-649. 0.1177/2167702617699277

Schriber, R. A., & Guyer, A. E. (2016). Adolescent neurobiological susceptibility to social

context. *Developmental Cognitive Neuroscience*, *19*, 1-18. /10.1016/j.dcn.2015.12.009

Sequeira, S. L., Butterfield, R. D., Silk, J. S., Forbes, E. E., & Ladouceur, C. D. (2019). Neural activation to parental praise interacts with social context to predict adolescent depressive symptoms. *Frontiers in Behavioral Neuroscience, 13*, e222. 0.3389/fnbeh.2019.00222

Tan, P. Z., Oppenheimer, C. W., Ladouceur, C. D., Butterfield, R. D., & Silk, J. S. (2020). A review of associations between parental emotion socialization behaviors and the neural substrates of emotional reactivity and regulation in youth. *Developmental Psychology*, *56*, 516-527. 10.1037/dev0000893

Tan, P. Z., Lee, K. H., Dahl, R. E., Nelson, E. E., Stroud, L. J., Siegle, G. J., ... & Silk, J. S. (2014). Associations between maternal negative affect and adolescent's neural response to peer evaluation. *Developmental Cognitive Neuroscience, 8*, 28-39. 10.1016/j.dcn.2014.01.006

Teicher, M. H., Anderson, C. M., & Polcari, A. (2012). Childhood maltreatment is associated with reduced volume in the hippocampal subfields CA3, dentate gyrus, and subiculum. *Proceedings of the National Academy of Sciences*, *109*, 563-572. 10.1073/pnas.1115396109

Teicher, M. H., & Samson, J. A. (2016). Annual research review: Enduring neurobiological effects of childhood abuse and neglect. *Journal of Child Psychology and Psychiatry*, *57*, 241-266. 10.1111/jcpp.12507

Teicher, M. H., Samson, J. A., Anderson, C. M., & Ohashi, K. (2016). The effects of childhood maltreatment on brain structure, function and connectivity. *Nature Reviews Neuroscience*, *17*, 652-666. 10.1038/nrn.2016.111

Telzer, E.H., Masten, C.L., Berkman, E.T., Lieberman, M.D., & Fuligni, A.J. (2010). Gaining while giving: An fMRI study of the rewards of family assistance among White and Latino youth. *Social Neuroscience, 5*, 508-518. 10.1080/17470911003687913

Telzer, E.H., Fuligni, A.J., Lieberman, M.D, & Gálvan, A. (2013). Ventral striatum activation to prosocial rewards predicts longitudinal declines in adolescent risk taking. *Developmental Cognitive Neuroscience, 3*, 45-52. 10.1016/j.dcn.2012.08.004

Thijssen, S., Muetzel, R. L., Bakermans-Kranenburg, M. J., Jaddoe, V. W., Tiemeier, H., Verhulst, F. C., ... & Van Ijzendoorn, M. H. (2017). Insensitive parenting may accelerate the development of the amygdala–medial prefrontal cortex circuit. *Development and Psychopathology*, *29*, 505-518. 10.1017/S0954579417000141

Tottenham, N., Hare, T. A., Quinn, B. T., McCarry, T. W., Nurse, M., Gilhooly, T., ... & Thomas, K. M. (2010). Prolonged institutional rearing is associated with atypically large amygdala volume and difficulties in emotion regulation. *Developmental Science*, *13*, 46-61. 10.1073/pnas.1323014111

Tottenham, N., & Sheridan, M. A. (2010). A review of adversity, the amygdala and the hippocampus: A consideration of developmental timing. *Frontiers in Human Neuroscience*, *3*, 68. 10.3389/neuro.09.068.2009

Turpyn, C. C., Poon, J. A., Ross, C. E., Thompson, J. C., & Chaplin, T. M. (2018). Associations between parent emotional arousal and regulation and adolescents' affective brain response. *Social Development*, *27*, 3-18. 10.1111/sode.12263

Whittle, S., Simmons, J. G., Dennison, M., Vijayakumar, N., Schwartz, O., Yap, M. B., ... & Allen, N. B. (2014). Positive parenting predicts the development of adolescent brain

structure: A longitudinal study. *Developmental Cognitive Neuroscience*, *8*, 7-17. 10.1016/j.dcn.2013.10.006

Whittle, S., Yap, M. B., Yücel, M., Sheeber, L., Simmons, J. G., Pantelis, C., & Allen, N. B. (2009). Maternal responses to adolescent positive affect are associated with adolescents' reward neuroanatomy. *Social Cognitive and Affective Neuroscience*, *4*, 247-256.

Whittle, S., Vijayakumar, N., Dennison, M., Schwartz, O., Simmons, J. G., Sheeber, L., & Allen, N. B. (2016). Observed measures of negative parenting predict brain development during adolescence. *PloS One*, *11*, e0147774.

Whittle, S., Yap, M. B., Sheeber, L., Dudgeon, P., Yücel, M., Pantelis, C., ... & Allen, N. B. (2011). Hippocampal volume and sensitivity to maternal aggressive behavior: A prospective study of adolescent depressive symptoms. *Development and Psychopathology*, *23*, 115-129. 10.1093/scan/nsp012

Valiente, C., Lemery-Chalfant, K., & Reiser, M. (2007). Pathways to problem behaviors: Chaotic homes, parent and child effortful control, and parenting. *Social Development*, *16*, 249-267. 10.1111/j.1467-9507.2007.00383.x

Vijayakumar, N., Mills, K. L., Alexander-Bloch, A., Tamnes, C. K., & Whittle, S. (2018). Structural brain development: A review of methodological approaches and best practices. *Developmental Cognitive Neuroscience*, *33*, 129-148. 10.1016/j.dcn.2017.11.008

Yap, M. B., Whittle, S., Yücel, M., Sheeber, L., Pantelis, C., Simmons, J. G., & Allen, N. B. (2008). Interaction of parenting experiences and brain structure in the prediction of depressive symptoms in adolescents. *Archives of General Psychiatry*, *65*, 1377-1385. 10.1001/archpsyc.65.12.1377

Table 1

Neuroimaging modalities commonly used in the study of parenting and brain development

Modality	**Activity Measured/Description**	**Advantages (+)/ Disadvantages (-)**
Structural magnetic resonance imaging (sMRI)	Anatomical volume and cortical thickness of soft tissue: grey and white matter	• High spatial resolution (+) • No temporal information regarding cognitive processes (-) • Nonportable (-)
Task-based functional magnetic resonance imaging (fMRI)	Metabolic activity (blood oxygen level dependent [BOLD] signal) during task engagement to assess specific cognitive processes	• High spatial resolution (+) • Low temporal resolution (-) • Nonportable (-)
Resting state functional magnetic resonance imaging (rsfMRI)	Metabolic activity (BOLD signal) during rest to identify intrinsic networks	• High spatial resolution (+) • Low temporal resolution (-) • Nonportable (-)
Electroencephalogram (EEG)	Electric potentials from neuronal activity during tasks or rest	• High temporal resolution (+) • Low spatial resolution (-) • Less susceptible to movement, thus used with younger samples (e.g., infants) (+)
Functional near-infrared spectroscopy (fNIRS)	Metabolic changes in hemoglobin concentrations	• High temporal resolution (+) • Low spatial resolution (-) • Portable, thus often used in parent-child shared task activity (i.e., studies of neural synchrony) (+)

Figure 1

Proposed Model of Caregiving Influences on Youth Brain Development