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Social Scaffolding of Human Amygdala-mPFC Circuit Development

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Abstract

Strong evidence indicates that reciprocal connections between the amygdala and medial prefrontal cortex (mPFC) support fundamental aspects of emotional behavior in adulthood. However, this circuitry is slow to develop in humans, exhibiting immaturity in childhood. The argument is made that the development of this circuitry in humans is intimately associated with caregiving, such that parental availability during childhood provides important and enduring scaffolding of neuroaffective processes that ultimately form of the nature of the adult phenotype.

Keywords

Amygdala; child development; sensitive periods; parents; emotion

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Adverse caregiving early in life is a major risk factor for mental illness later in life (Heim & Nemeroff, 2001). The mental illnesses most associated with early life caregiving adversity include those whose root problems involve difficulty with emotion regulation. These links suggest strongly that early caregiving influences adult outcomes by acting proximally on the neurobiology of emotion regulation. In this review, the influences of early caregiving will be discussed as they relate to developmental changes in core circuitry of emotion regulation processes, namely the amygdala and the medial prefrontal cortex.

The neurobiology of emotion has been extensively and best characterized at the level of the amygdala and its connections with the medial prefrontal cortex (mPFC). Amygdala nuclei rest subcortically and mediate emotional learning, increasing attention to and arousal for emotionally relevant stimuli (Davis & Whalen, 2001). In adulthood, these nuclei are bidirectionally coupled with the mPFC to provide tight regulation over emotional behaviors (Banks, Eddy, Angstadt, Nathan, & Phan, 2007; Motzkin, Philippi, Wolf, Baskaya, & Koenigs, 2015; Phelps, Delgado, Nearing, & LeDoux, 2004). As will be discussed in more detail below, evidence suggests that the amygdala is an earlier developing structure relative to the prefrontal cortex, which may not show mature functioning until late adolescence or early adulthood. This late development of the circuitry raises the question of how emotion regulation is accomplished prior to neuromaturity. This paper posits that during development

of amygdala-mPFC circuitry, the parental stimulus provides significant scaffolding of neuroaffective processing in ways that both support emotion regulation in the child and has enduring effects of adult functioning.

Human research has shown that early caregiving adversity influences brain development, and there is a disproportionate influence on affective systems (Cohen, Tottenham, & Casey, 2013; Davidson & McEwen, 2012; Gianaros et al., 2008; Tottenham & Sheridan, 2010). For example, adults who report a history of early maltreatment (abuse, neglect) exhibit exaggerated amygdala reactivity in response to emotional or stressful stimuli (Banihashemi, Sheu, Midei, & Gianaros, 2014; Dannlowski et al., 2013), which corresponds to greater emotional responding at the level of behavior. At the same time, there is a relative lack of prefrontal connectivity in adults reporting childhood adversity suggesting less regulatory tone over the amygdala (Burghy et al., 2012), including during effortful attempts to regulate emotions (e.g., cognitively reappraising emotionally distressing images) (Kim et al., 2013). Findings like these suggest that one significant outcome of early caregiving adversity is diminished prefrontal regulation of the amygdala.

These studies are examples of some of the best evidence to date showing that early caregiving adversity produces enduring effects in affective neurocircuitry that last into adulthood in humans. One large challenge to these conclusions lies in the reliance on retrospective reporting, which might increase the risk of apocryphal reports (Maughan & Rutter, 1997). Perhaps a greater challenge is the limited ability to make claims about the developmental timing of events (infancy vs childhood vs adolescence) – without this information, the temporal resolution for identifying sensitive periods is blurred. Compounding this challenge is the fact that for most individuals who experience adversity early in life, the odds of experiencing future adverse events are unfortunately high. Thus it cannot be ascertained whether the early event, the later events, or the accumulation of adverse events over a lifetime (Evans & Kim, 2007; Sameroff, 2000) caused the adult outcome.

Knowledge about timing is important because with this information, we can search for correlations between timing of the event and developmental changes in underlying neurocircuitry. The coincidence between an environmental event and development of a particular circuit is a critical step in developing a neurobiologically plausible mechanistic model of early environmental influences that can be empirically tested. Animal models provide an opportunity to consider timing factors given the great control over the timing and administration of parental care (Moriceau, Raineke, Holman, Holman, & Sullivan, 2009; Sanchez et al., 2005). This control is usually not available in human studies.

At the heart of much research examining the coincidence of environmental agents and neurodevelopment is the concept of sensitive periods for brain development. A priming or “readiness” of a particular neural system may be referred to as a sensitive period. A sensitive period is a period in development during which certain capacities are readily shaped or altered by particular experiences (Knudsen, 2004). These special periods allow for developmentally-unique moments for learning that endures, which scaffolds the maturation of brain function and behavioral output.

For the past 14 years, I have been working on research projects studying a group of children and adolescents who have a unique caregiving history. This group of children and adolescents were born outside of the United States and spent the majority of their infancy in institutional care (e.g., orphanages) and thus experienced significant and extreme parental deprivation as a result of institutional care. At some point, which differs across individuals, children were adopted by families in the United States via international adoption. Families that adopt internationally are, in research terms, a special group of families; because international adoption often requires that parents travel to the country of adoption and stay for some extended time, the families typically have the financial means to adopt internationally. They tend to be a highly educated group of parents (Balding, Feng, & Atashband, 2015; Hellerstedt et al., 2008); and most importantly for child outcome, they clearly have a great desire to provide care since international adoption requires significant effort. It is this desire to provide care that has been most closely linked to optimal child outcomes (Hodges & Tizard, 1989). This naturally occurring developmental timeline – that is, early caregiving adversity followed by family enrichment – allows for asking questions about early caregiving experiences in a temporally defined manner, which unlike in tightly controlled animal studies, is rare in human research. As described by Gunnar and colleagues (M.R. Gunnar, Bruce, & Grotevant, 2000), institutional care – even in the best of circumstances – is a suboptimal caregiving situation. The caregivers are staff, who rotate shifts and who are responsible for the care of a high number of infants and children. There are, of course a huge number of unknowns when working with this population – prenatal records are unavailable and preadoption records are not always reliable. There is also wide variation in the quality of care from country to country and from orphanage to orphanage; e.g., the wretched conditions described in some orphanages is not representative of all institutional care facilities. However, there is one important constant across all institutional care settings, which is the lack of a stable caregiver, the most potent stressor for a developing infant.

At the time of adoption, many children exhibit a number of developmental delays including motor, cognitive, and emotional; however, because of the family environments into which previously-institutionalized (PI) children and adolescents are adopted, they often show remarkable rebound. The rate of developmental improvement is notable such that across many domains of behavior, PI children begin to more closely resemble children without a history of caregiving adversity (Nelson et al., 2007; Rutter, 1998).

In many cases however, catch-up is incomplete. In particular, socio-emotional behaviors often exhibit lingering effects despite the enriched environment of the adoptive home. While there is large heterogeneity in outcome, with some children thriving, one of the most common concerns that adoptive parents report is heightened emotional reactivity and difficulty with self and emotion regulation (Casey et al., 2009; Malter Cohen et al., 2013; Merz & McCall, 2010; Wiik et al., 2011). For example, at the group level, PI youth exhibit heightened trait anxiety and increased depressive symptoms, particularly in adolescence (Goff et al., 2013). On laboratory tests, PI youth are more likely to show behavioral interference from highly arousing emotional stimuli (Tottenham et al., 2010) and increased behavioral freezing in response to fear eliciting stimuli (Stellern, Esposito, Mliner, Pears, & Gunnar, 2014).

At the neural level, these behaviors have been paralleled by differences in amygdala and medial prefrontal cortex development (Gee, Gabard-Durnam, et al., 2013; Tottenham, Hare, Millner, et al., 2011; Tottenham et al., 2010). Specifically, on average, PI youth have exhibited larger amygdala volumes (Mehta et al., 2009; Tottenham et al., 2010) (though see Hanson et al., 2014; Hodel et al., 2015) and heightened amygdala reactivity in response to emotional stimuli, like fearful faces (Gee, Gabard-Durnam, et al., 2013; Tottenham, Hare, Millner, et al., 2011) relative to peers without a history of institutional caregiving. There is some evidence that the age at which children were removed from institutional care is important in that larger amygdala volumes were observed in children adopted at a later age (after their first birthday; Tottenham et al., 2010). Earlier reports using PET scanning have shown that the pattern of resting glucose metabolism in medial temporal structures including the amygdala was lower in children adopted from Romanian orphanages (whose duration in institutional care ranged from 16 to 90 months) compared to the activity of controls (the nonepileptic hemisphere of children with a history of epilepsy) (Chugani et al., 2001). It is not possible to obtain basal activity of the amygdala using fMRI, but with the PET and fMRI data taken together, these findings may suggest that the amygdala hyperactivity in PI youth may be specifically elicited by emotional events in the environment.

The amygdala phenotypes described are consistent with a large non-human animal literature showing that premature separations from the parent (i.e., mothers in the case of rats) is causally related to premature development of amygdala structure (Ono et al., 2008) and function (Moriceau & Sullivan, 2006) as well as increased anxiety (Ono et al., 2008) and premature fear-learning (Moriceau & Sullivan, 2006). These effects on the amygdala have been shown to be mediated by the stress hormone corticosterone (Moriceau & Sullivan, 2004), the end-product of the hypothalamic-pituitary-adrenal (HPA) axis. Notably, dysregulation of the HPA axis in PI youths have also been documented (Gee, Gabard-Durnam, et al., 2013; M. R. Gunnar, Frenn, Wewerka, & Van Ryzin, 2009; Koss, Hostinar, Donzella, & Gunnar, 2014; Wismer Fries, Shirtcliff, & Pollak, 2008) across laboratories. However, there is evidence that these cortisol phenotypes were improved upon adoption (for earlier adoption) relative to institutional care (McLaughlin et al., 2015).

Animal studies that have examined the effects of premature separation from the parent have also shown evidence that amygdala-mPFC circuitry is atypical in part because the early separations act to accelerate development of this circuit. For example, separation from the mother has been followed by premature myelination of amygdala neurons (Ono et al., 2008), earlier engagement of amygdala function during fear learning (Moriceau & Sullivan, 2006), more adult-like retention of fear memories (Callaghan & Richardson, 2012b; Cowan, Callaghan, & Richardson, 2013), and adult-like fear extinction learning, suggesting that the mPFC becomes engaged at a premature age following maternal separation (Callaghan & Richardson, 2012a; Cowan et al., 2013). These amygdala-mPFC differences following maternal separation have been interpreted as ontogenetic adaptations (Callaghan, Sullivan, Howell, & Tottenham, 2014; Callaghan & Tottenham, 2015) that occur in response to environmental signals that the mother is unavailable. Viewed in this way, development may proceed with a reprioritization towards neural circuitry that will aid in independent navigation of the safety and danger of the environment (i.e., survival). In our laboratory, we have examined functional connectivity in the amygdala-mPFC circuitry following early

institutional care and observed that children with a history of institutional caregiving similarly show a more “adult-like” pattern of connectivity between the amygdala and mPFC relative to children without a history of institutional care (Gee et al., 2013). Current thinking is that early caregiving adversity may act to accelerate the closure of a developmental sensitive period for amygdala-mPFC circuitry. This difference in connectivity in the PI children may be a developmental adaptation that helps meet the immediate needs of regulating highly reactive amygdala nuclei. The current framework is based on the idea that early chronic absence of parental availability results in early and high amygdala reactivity. This reactivity may initiate earlier development of connections with the mPFC. Moreover, this adaptation seems to benefit children such that those PI youth who exhibit the “adult-like” functional connectivity exhibit lower trait anxiety than those that do not (Gee et al., 2013). However, structural connectivity using diffusion tensor imaging has identified reduced white matter integrity in tracts that run between the amygdala and prefrontal cortex in previously-institutionalized children (Bick et al., 2015; Govindan, Behen, Helder, Makki, & Chugani, 2009) suggesting that functional and structural connectivity follow different developmental trajectories following early adversity.

Across laboratories, researchers have shown that early parental absence is associated with age-atypical emotional behaviors. Moreover, for decades, researchers and theorists of varying orientations (including ethological/attachment theories, parenting styles, family systems) have discussed the profound influence of parental availability on emotional behaviors and development (Baumrind, 1966; Bowen, 1966b; Bowlby, 1982; Gewirtz, Baer, & Roth, 1958; Hofer, 1994a). The goal of this paper is to address the question: if parental availability is so important for emotional development, what exactly is parental availability doing on a moment-to-moment basis to scaffold affective neurobiology in enduring ways? Can we develop a testable neurobehavioral model that characterizes parental influence on emotional development?

To develop such a model, it is useful to first characterize what is known about human amygdala development and its connections with mPFC. These data have been collected in a standard laboratory manner such that parents were not allowed in the scanner room. In general, fMRI studies show that the amygdala is highly reactive to emotional stimuli. For example, in response to fear faces (Gee et al., 2013) or other highly arousing negative images (Decety, Michalska, & Kinzler, 2012; Silvers, Shu, Hubbard, Weber, & Ochsner, 2014; Swartz, Carrasco, Wiggins, Thomason, & Monk, 2014; Vink, Derks, Hoogendam, Hillegers, & Kahn, 2014) children show a very strong amygdala response that typically exceeds that of older participants (adolescents and adults). (Importantly, not all studies have shown high amygdala reactivity in childhood. In Hare et al. (2008), amygdala response in children was lower than adolescents'. It is unclear why these differences exist. One possibility is that the nature of the stimuli or task used to elicit amygdala reactivity in children matters. This is an important matter for future research to clarify). This strong amygdala responding to negatively valenced stimuli is paralleled by immature functional and structural connectivity with the mPFC. Functional anisotropy measures (diffusion tensor imaging) of the uncinate fasciculus, a primary structural connection between the amygdala and prefrontal cortex, shows low structural integrity of white matter relative to adult levels (Lebel et al., 2012; Swartz et al., 2014). Functional connectivity, which measures the degree

to which two regions correlate in time, has also been shown to exhibit immature coupling between the amygdala and the mPFC during childhood (Decety et al., 2012; Gabard-Durnam et al., 2014; Gee, Humphreys, et al., 2013; Perlman & Pelphrey, 2011). For example, in our laboratory, we have observed that unlike adults and adolescents who show strong amygdala-mPFC functional connectivity, children (under the age of 10 years old) either show an absence of stable connectivity (during resting state (Gabard-Durnam et al., 2014)) or a child-unique connectivity pattern that suggests the nature of communication between the amygdala and mPFC is yet immature and perhaps not exhibiting the regulatory relationship it does in the adult (Gee, Humphreys, et al., 2013). Taken together, these data show that childhood (prior to adolescence) is characterized by heightened amygdala reactivity without the addition of mature top-down control from prefrontal inputs (see Figure 2).

In the absence of a mature amygdala-mPFC circuit, how is emotional regulation accomplished in young ages? The rodent work of Myron Hofer is probably some of the most relevant when addressing this question. Hofer and his team were able to show that the parent (mother in rodents) is a primary regulator of offspring physiology and homeostasis (Hofer, 1994b). This work in addition to the pioneering research of Seymour Levine (e.g., Levine & Mody, 2003) (and his many students) was critical in laying the ground work for future ideas centered on conceptualizing infant brain development in the context of parental milieu. These research studies were performed in developing rodents, which are phylogenetically quite distant from humans. However, when considered in the context of developmental needs of an altricial or semi-altricial animal, there are many parallels to be drawn between species that might lend important insight.

Indeed, for decades it has been appreciated that parental availability is a potent modulator of child emotional behaviors (in particular fear/anxiety). Across various scientific perspectives (including ethological/attachment theories, parenting styles, family systems; (Baumrind, 1966; Bowen, 1966a; Bowlby, 1982; Gewirtz et al., 1958; Hofer, 1994a; Kernberg, 1972) researchers have noted the special relationship between parent and child and the regulatory influence this relationship has on children's emotionality. For the last century, these effects have been documented and empirically tested at the behavioral level.

One of the most fundamental things that parents do to influence children's emotionality is be physically close. Physical proximity of the parent signals to the child that the parent is available (either for physical or psychological assistance), which exerts profound (and sometimes inconspicuous) effects on children's reactivity and emotional learning. Physical presence and availability of the parent increases children's likelihood of entering a novel (Sorce & Emde, 1981) or threatening situation (e.g., new school), decreases nighttime fears (Simard, Nielsen, Tremblay, Boivin, & Montplaisir, 2008), inhibits acquisition of new fears (Egliston & Rapee, 2007) and buffers against elevations in stress hormones during childhood (Hostinar, Johnson, & Gunnar, 2015; Kertes et al., 2009). These effects are so strong that even availability of the parent through a phone call is effective (Seltzer, Prosski, Ziegler, & Pollak, 2012). Despite its critical function, the neural mechanisms of parental buffering effects on children's emotional development have not yet been described.

Parental buffering of amygdala reactivity

Our laboratory has begun addressing the question of how parents influence emotional development by first considering the nature of the scanning environment during a typical MRI testing session. We noted that during scanning, children are not with their parents. Perhaps if we could provide access to a parental stimulus, amygdala function would change in a state-like manner during childhood. Specifically, we examined whether providing children and adolescents with some access to a parental stimulus would buffer against the high amygdala reactivity that is typically observed (Gee, Humphreys, et al., 2013). In rodents, empirical examination of the effects of parental (i.e., maternal) cues might come in the form of an odor cue (Sullivan – see this issue), which during a sensitive period in development acts to dampen amygdala engagement during fear learning. Odor is the primary sensory modality in developing rat, and thus an odor cue is a potent stimulus to represent the mother. For humans, the visual modality is a primary route for emotional information, and thus we provided pictures of a parent's face to healthy children and adolescents during fMRI scanning. The contrasting conditioning involved presenting pictures of someone else's parent (a stranger). The hypothesis that we tested was that availability of a parental cue would act to dampen amygdala reactivity. However, the effect would be developmentally transient such that the attenuating effect of the parental cue on amygdala reactivity would only be observed during childhood and not during adolescence. This hypothesis was generated by the developmentally unique phenotypes of the amygdala-mPFC circuit that has been observed across laboratories.

The results supported the buffering hypothesis, and indeed children showed lower amygdala response when presented with their own parent's images (Gee et al., 2014). Adolescents did not show this effect and amygdala responding did not differ between their own parent and someone else's. The dampening of amygdala response by the parental cue in children was noteworthy given the high amygdala response that is typically observed in children. A similar result has been documented in clinically anxious children and adolescence when their mothers were physically near them in the scanner (Conner et al., 2012). Although we observed this amygdala dampening across all children, the magnitude of the amygdala buffering effect was associated with attachment representations such that children whose amygdala decreased the most in response to a parental cue were more likely to report that they would tend to turn to their parent (as opposed to another individual) in times of duress. These findings suggest that the strength of amygdala buffering was associated with the strength of the parent-child relationship, but on average, all children showed some degree of buffering by parental stimuli. We interpreted this finding as being parallel to rodent studies showing a developmentally transient maternal buffering effect on amygdala engagement.

Functional connectivity analyses showed that presentation of a parental cue also strengthened (negative) correlations between the amygdala and the mPFC. This effect was specific to the parental cue and developmentally specific during childhood. The analysis used a voxel-wise approach, which means that the effect of the parent on amygdala connectivity was specific to the mPFC since other regions did not show parental modulation in amygdala connectivity. Examination of parental buffering effects on emotional behaviors of developing rhesus monkeys have shown that the mPFC is critical for the buffering effect

to occur (Rilling et al., 2001). If the amygdala dampening by parental cue was indeed evidence of parental buffering at the neural level, what we might have been observing in children during fMRI scanning is a phasic increase in top-down communication between the mPFC and amygdala caused by presentation of the parental cue.

We observed parental effects at the level of behavior as well (Gee et al., 2015). Out of the scanner, children and adolescents performed an emotional face go/nogo task (Tottenham, Hare, & Casey, 2011), which assesses behavioral-regulation under different affective conditions. Participants responded (via button press) as quickly as they could to facial stimuli (e.g., neutral faces) that were serially repeated to build up a prepotent tendency to respond. Infrequently, a negative (e.g., fear) or a positive (e.g., happy) face was presented. Prior to the task subjects were instructed to only press to the neutral faces. Thus, a button press to the emotional faces would be a false alarm error. False alarm error rate that was greater to fear faces than happy faces was interpreted as an error in affective behavior regulation (Johnson & Tottenham, 2015). Children and adolescents performed this task twice, once sitting next to their parent and once sitting next to a friendly female experimenter in counterbalanced order. Both the parent and the experimenter were instructed to not interact with the subject, but to busy themselves with paperwork. As anticipated, children performed worse on this measure than adolescents, but importantly, their false alarm rate for fear faces (i.e., their affective behavior regulation) improved significantly when seated next to their parents. Moreover, it improved most for children who showed the largest parental buffering effects on the amygdala during fMRI scanning. These brain-behavior associations suggest to us that during childhood, the parent is effective in phasically modulating affective behavior by influencing amygdala-mPFC. When the parent is not available, amygdala activity increases, and when the parent becomes available again, amygdala activity decreases again. The difference between children and adolescents' responding suggests that the window during which parents can exert these effects may close as children transition into adolescence.

Proposed Neurobiological Model of Parental Influence

Based on evidence from rodents, non-human primates, and human studies that include lesion, imaging, and endocrine methods, we have reasonable evidence to begin building a neurobiological model of parental influence on emotional development. This model is in its earliest stages but is testable, and the predictions that it generates will allow for future modification.

Figure 4 illustrates the working model. During childhood, amygdala and associated emotional behaviors may be under direct control of parental availability. (NOTE: This control may extend downward into toddlerhood and infancy but the youngest ages tested with our fMRI data collection thus far has been 4-year-olds. However, the findings of amygdala hyperexcitability in children with a history of parental deprivation in infancy coupled with evidence of amygdala modulation by mother's voice in sleeping infants (Dehaene-Lambertz et al., 2010) would support the hypothesis that parents modulate amygdala development throughout early development). This responsiveness to the parent is the result of a proposed sensitive period prior to adolescence, including childhood (and

possibly earlier) and associated heightened plasticity of the amygdala and connections with the mPFC. During the sensitive period, routine parental availability and non-availability phasically influence amygdala and associated behaviors (green up and down arrows). The proposed mechanism involves interactions at the level of hormones, neural activity, and behavior. When the parent is temporarily unavailable, cortisol levels are elevated. This elevation will be associated with heightened amygdala reactivity to emotional events in the environment, which increases emotional reactivity at the level of behavior. However, when the parent becomes available, cortisol is buffered at the same time that connectivity between the mPFC and amygdala increases. Together, these two factors result in a decrease in amygdala reactivity and associated emotional reactivity. This phasic modulation is predicted to be important in the “toning” of the amygdala-mPFC circuit to respond independently at older ages, once the system becomes more stable. Note that the model allows for periodic parental absence (e.g., parents go to work and children go to school). In fact this cycle of presence and absence is key to the toning process, and may be akin to models of “stress inoculation” proposed by others (e.g., Parker, Buckmaster, Sundlass, Schatzberg, & Lyons, 2006), where a bit of exposure to phasic stress is helpful for toning of the system in maturity. The opportunity for parental availability to influence this circuitry is hypothesized to end with the increasing independence from the parent in adolescence. At this point the circuitry will operate in a way that reflects the toning that occurred during childhood.

This working model provides one possible mechanism explaining individual differences in amygdala-mPFC functioning and emotional dysregulation in adults with a history of early caregiving adversity. As can be seen by the red arrow, we propose that parental neglect/deprivation (and perhaps other forms of insecure parenting) may eliminate the opportunity for affect related neurobiology to be phasically modulated; thus, amygdala and emotional reactivity will not be routinely buffered and the system will stabilize in a way that results in emotional dysregulation.

This model is only a working model; it is yet incomplete, and there is much work to be done. For example, the model does not currently include infancy and toddlerhood. Surely parents provide significant scaffolding of affective neurobiology at these younger ages. The nature of the scaffolding might be similar to what the model proposes in childhood, in which case the proposed sensitive period would be extended down to infancy. Indeed, the effects of parental deprivation described in this paper were the results of deprivation experienced in infancy and toddlerhood. Alternatively, the effects may be different at very younger ages in which case the model would have to be significantly accommodated. Those data are difficult to obtain given the technical challenges of collecting fMRI data from awake infants and toddlers. Nonetheless, a testable working model can be useful for making future progress in characterizing the neurobiological mechanisms of emotional scaffolding by parents.

Conclusions

As discussed elsewhere (Tottenham, 2012, 2014) since the parent is external to the developing child yet so critical for the progression of normal emotional development, qualifies parental availability as a species-expected stimulus. Therefore, it seems necessary to appreciate brain development in the context of parental presence versus absence to

acquire a complete understanding of human amygdala-mPFC development. This manuscript began with a focus on amygdala-mPFC phenotypes of children and adolescents with a history of institutional caregiving, but the ramifications of parental influences extends beyond this group to many other individuals experiencing various forms of caregiving adversity. Moreover, understanding how parents scaffold affective neurobiology provides a fuller mechanistic understanding of brain development in all humans.

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More "Child-Like"

Figure 1.

Amygdala-mPFC connectivity across children and adolescents as a function of early caregiving. Two independent groups of typically raised children exhibit positive correlations between amygdala and mPFC, which then switches for adolescents, who show a more adult-like negative correlation. Children in the previously institutionalized group show a connectivity pattern that more closely resembles the adolescents. Adapted from Gee et al., 2013.

Figure 2. Schematic of human amygdala-mPFC functional development from childhood through young adulthood. Developmentally-unique period is emphasized with orange stars.

Figure 3. Parents decrease amygdala reactivity (A), & strengthen amygdala-mPFC functional connectivity (B) in children. Adapted from Gee et al., 2014.

Figure 4.

Working model of parental influence on emotional development. Parents may have their largest effects in modulating amygdala activity and functional development prior to adolescence. Importantly, there is little data on amygdala functional reactivity in humans prior to early childhood; thus although the x-axis begins in childhood, we would predict that parental influence on amygdala development extends downward into infancy.