

64 The Amygdala: Relations to Biologically Relevant Learning and Development

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ABSTRACT The amygdala plays a critical role in learning about cues in the environment that predict biologically relevant outcomes and informing our behavioral responses in anticipation of these outcomes. Consistent with classic principles of learning theory, the amygdala is particularly responsive to uncertainty, which enhances learning. Much of the extant research on the human amygdala has employed facial expressions to elucidate its contributions to emotional learning. In addition to their role in nonverbal communication, facial expressions can be considered conditioned stimuli based on their reinforcement history in prior social situations. Through interactions between the amygdala and prefrontal cortex (PFC), bottom-up and top-down processing shape this social learning. Stronger amygdala-prefrontal connectivity begets better behavioral outcomes, and disrupted cross-talk between these regions underlies emotion dysregulation in healthy and clinical populations. Moreover, the amygdala and its connections with PFC undergo dynamic changes throughout development, which likely contribute to developmental changes in emotional behavior. Given the neurodevelopmental nature of many disorders and the widespread implication of amygdala-prefrontal circuitry in psychopathology, understanding how the amygdala changes in typical development and possible disruptions in biologically relevant learning are both fundamental to treating psychopathology. The following chapter will detail how the amygdala contributes to biologically relevant learning and gives rise to individual differences in emotional behavior, as well as how these processes change with development and risk for psychopathology.

The amygdala and biologically relevant learning

The amygdala plays a central role in learning about biologically relevant events, which can signal the relative safety or danger of a given environment. In the framework of classical conditioning, the amygdala responds to biologically relevant events that require no previous learning (i.e., unconditioned stimuli, or USs, that are inherently emotionally salient, such as a shock), as well as the events that predict these biologically relevant events (i.e., conditioned stimuli, or CSs, which begin as neutral but take on emotional salience through conditioning). This form of learning depends on the amygdala in both humans and nonhuman animals (see LeDoux, 1996). While nonhuman animal studies still comprise the majority of our knowledge about amygdala

contributions to biologically relevant learning during classical conditioning (see Davis & Whalen, 2001), neuroimaging studies have documented a largely similar role for the human amygdala. For example, functional neuroimaging studies have demonstrated contributions of the amygdala during classical conditioning paradigms with a variety of CS-US contingencies, including colored squares predicting electric shock (LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998).

These findings demonstrate in a clear manner that the human amygdala is involved in learning about environmental cues that predict biologically relevant outcomes as well as informing behavioral responses in anticipation of these outcomes (LeDoux & Schiller, 2009). Research in humans has extended this initial work to show that the amygdala might function in a more general manner, facilitating all kinds of biologically relevant learning. For example, the amygdala is responsive to both aversive and appetitive CSs (Paton, Belova, Morrison, & Salzman, 2006). Data such as these fit well with attentional hypotheses (Kapp, Whalen, Supple, & Pascoe, 1992) and seminal work demonstrating a critical role for the amygdala in associative changes observed in appetitive reward paradigms in the rat (Gallagher & Holland, 1994). That is, amygdala activation to a tone that predicts shock is but a part of an affective information-processing system that directs our attention to important events in the environment. The amygdala functions as an orienting subsystem for the rest of the brain, which allows us to respond appropriately to those events (Davis & Whalen, 2001; Gallagher & Holland, 1994). In alerting other systems at times when it would be advantageous to gather information (i.e., learn), the amygdala supports adaptive functions that cross the categorical boundaries of constructs such as motivation, emotion, vigilance, attention, and cognition.

THE ROLE OF UNCERTAINTY IN BIOLOGICALLY RELEVANT LEARNING Derived from principles of learning theory, the idea that there is more to learn in the face of uncertainty is fundamental to how the amygdala

responds and orients the rest of the brain to the environment. The Rescorla-Wagner model is based on the notion that an increase in the associative value of a CS will be greatest (i.e., learning is most likely) on trials when the individual finds the occurrence of the US to be surprising (Rescorla & Wagner, 1972). Together with the magnitude of the US, the predictive value of the CS dictates the degree of surprise created by the US. The predictive value of the CS increases quickly in early conditioning trials, when the organism makes new associations, but decreases during late trials (see Bouton, 2007). A related but separate model of classical conditioning, the Pearce-Hall model, focuses on the amount of attention to the CS that is recruited by the degree of surprise created by the US on the preceding trial (Pearce & Hall, 1980). Interestingly, this model has helped to guide research on the influence of amygdala activity on attention. Particularly relevant is work establishing a role for the central nucleus of the amygdala in enhancing CS associability when expectations are violated (Holland & Gallagher, 1999) and in nonspecific attention or arousal observed in the service of learning (Kapp et al., 1992). Recent work has extended these principles to the human amygdala by testing a hybrid model positing that the degree of surprise to the US (i.e., prediction errors) drives learning, but that associability of the CS affects learning rates. Specifically, a reversal-learning task revealed a functional dissociation of amygdala subregions during associative learning, such that a more dorsal portion of the human amygdala (where the central nucleus resides) was more sensitive to immediate surprise at the time of the US, whereas the ventral portion was more sensitive to associability at the time of the CS (Boll, Gamer, Gluth, Finsterbusch, & Büchel, 2013). Taken together, these studies highlight the contributions of the amygdala in processing uncertainty that is fundamental to learning.

FACIAL EXPRESSIONS AS CONDITIONED STIMULI
Humans have a great deal of experience with facial expressions of emotion (Somerville & Whalen, 2006) and have learned that they predict important outcomes. Facial expressions play a crucial role in nonverbal communication. Not only do they communicate the internal state of the expressor, but they also convey important information about the immediate environment. Thus, information gleaned from facial expressions of emotion can be used to guide future behavior. When conceptualized in this manner, facial expressions are conditioned stimuli. That is, they are environmental cues that have been associated with important outcomes in the past. When they are encountered, we use their past reinforcement history to predict what will happen next.

Indeed, human neuroimaging research shows that presentations of static pictures of facial expressions engage neural systems similar to those engaged during associative learning tasks, including the amygdala. Like associative learning, responses to facial expressions can be implicit (Whalen et al., 1998). In humans, patients with selective amygdala lesions displayed deficits in processing the facial expression of fear (Adolphs, Tranel, Damasio, & Damasio, 1995), leading to numerous neuroimaging studies using presentations of fearful faces to probe amygdala function. These studies have shown that the amygdala is particularly responsive to fearful faces compared to other expressions, including angry, happy, and neutral faces (e.g., Breiter et al., 1996; Morris et al., 1996). Consistent with the importance of uncertainty in learning, since the amygdala responds more to fearful faces than angry faces, which embody a direct threat, one function of the amygdala may be to augment cortical function to assist in the resolution of predictive uncertainty (Whalen et al., 2001). That is, the inherent ambiguity of fearful faces, in that they predict the increased probability of threat without providing information about its nature or location, leads to greater activation of the amygdala.

Given that the amygdala plays a major role in the resolution of predictive uncertainty associated with fearful faces, surprised faces provide a particularly important comparison expression. Indeed, surprise may be the second-most compromised expression in patients with selective amygdala damage, following fear (Adolphs, Tranel, Damasio, & Damasio, 1994). Fearful and surprised faces have common features (e.g., eye-widening), and both expressions indicate the detection of a significant but *unknown* eliciting event. Consistent with this logic, the amygdala shows robust activation to surprised faces (Kim et al., 2004). Further, neural responses to surprised expressions show a greater resistance to extinction, presumably due to their inconsistent reinforcement history. Likening facial expressions of emotion to conditioned stimuli allows us to draw parallels between two seemingly distinct avenues of research: those that characterize the neural processes associated with learning about stimuli that predict biologically relevant outcomes (i.e., Pavlovian conditioning) and those that characterize reactions to stimuli that have acquired similar predictive value through our experiences in the social world (i.e., facial expressions of emotion) (Davis, Johnstone, Mazzulla, Oler, & Whalen, 2010).

Amygdala-prefrontal connectivity

Bottom-up and top-down connections between the amygdala and medial PFC (mPFC) are fundamental to

emotional behavior. While attention to salient stimuli can be biased through bottom-up processes driven by the amygdala, this reactivity is thought to be modulated through top-down cognitive control by the mPFC (Ochsner, Bunge, Gross, & Gabrieli, 2002). Competition between these bottom-up and top-down processes is highlighted in behavioral phenomena such as emotion regulation, fear conditioning, and extinction (Bishop, 2007; Quirk & Beer, 2006). While numerous studies have assessed the separate contributions of the amygdala and mPFC to top-down and bottom-up interactions in emotion, respectively, more recent studies suggest that the structural and functional connectivity between these two regions is a better predictor of behavioral outcomes than the activity of either region alone (Banks, Eddy, Angstadt, Nathan, & Phan, 2007; Kim, Gee, Loucks, Davis, & Whalen, 2011; Pezawas et al., 2005). Stronger coupling between the amygdala and the mPFC begets better behavioral outcomes in terms of effective emotion regulation and lower anxiety.

AMYGDALA-PREFRONTAL STRUCTURAL CONNECTIVITY Data from nonhuman primate brains have revealed strong bidirectional anatomical connections between the amygdala and mPFC. A heavy projection of afferent fibers to the amygdala originates in the mPFC (including orbitofrontal cortex and ventral anterior cingulate cortex; Aggleton, Burton, & Passingham, 1980; Leichnetz & Astruc, 1976). There is also a heavy projection from a posterior but dorsal portion of mPFC to the amygdala (Pandya, van Hoesen, & Mesulam, 1981). Reciprocally, the amygdala sends efferent projections to these same ventral and dorsal mPFC regions (Amaral & Price, 1984; Barbas & de Olmos, 1990; Carmichael & Price, 1995; Ghashghaei & Barbas, 2002), and to a slightly more rostral portion of the mPFC (Ghashghaei, Hilgetag, & Barbas, 2007). The mPFC regulates activity of the amygdala through input to the basolateral nuclei of the amygdala and the intercalated cells, which regulate inputs from the basolateral nuclei to the central nucleus and thus inhibit amygdala output (Harris & Westbrook, 1998; Milad & Quirk, 2002).

The majority of our knowledge about structural connections in this circuitry is based on the literature of nonhuman animal studies due to the invasive nature of lesion and tracing studies, which are difficult to employ in humans. However, a number of studies using noninvasive methods such as diffusion tensor imaging have identified an amygdala-prefrontal axonal pathway in the human, with a specific focus on amygdala connectivity with the dorsal and ventral regions of the mPFC (Crosson et al., 2005; Johansen-Berg et al., 2008; Kim & Whalen, 2009). These regions may be analogous to

the dorsal and ventral prefrontal regions identified in the previous studies of connectivity in nonhuman primates.

AMYGDALA-PREFRONTAL FUNCTIONAL CONNECTIVITY AT REST While structural connectivity characterizes the neuroanatomical architecture of amygdala-prefrontal circuitry, functional connectivity measures provide information about the moment-to-moment interactions between the amygdala and mPFC in response to particular stimuli or at rest. Based on the extensive anatomical connections between the amygdala and mPFC shown in human and nonhuman primates, a number of investigations have used functional connectivity to assess the strength of amygdala-mPFC coupling and its relationship with behavioral outcomes. Resting-state functional MRI provides unique information about the intrinsic connections between brain regions in the absence of explicit task instructions and has been shown to index the functional integrity and maintenance of network connections (Biswal, Yetkin, Haughton, & Hyde, 1995). Resting-state maps have revealed distinct patterns of connectivity for each of the human amygdala subdivisions (Roy et al., 2009). At rest, the amygdala was positively coupled with ventral regions and negatively coupled with dorsal regions. Amygdala coupling at rest can be used to predict individual differences. For example, the amygdala was positively coupled with ventromedial prefrontal cortex (vmPFC) in participants reporting lower levels of anxiety, but not in subjects reporting higher levels of anxiety (Kim et al., 2011; figure 64.1). In future examinations, resting-state connectivity may be used to predict amygdala-prefrontal activation or how well someone regulates their emotional responses when challenged with a particular task.

AMYGDALA-PREFRONTAL FUNCTIONAL CONNECTIVITY PREDICTING ADAPTIVE BEHAVIOR The majority of examinations of amygdala functional connectivity have been conducted during explicit tasks, with findings demonstrating the central role of amygdala-prefrontal interactions for behaviors such as emotion regulation, extinction, and resolving ambiguity. Emotion regulation is a classic example of how top-down and bottom-up processes compete and interact to produce optimal (or counterproductive) behavioral outcomes. For example, one's instinctive reaction to a frightening scene in a horror movie may include an urge to scream or run out of the room. Normally, this bottom-up reaction is controlled by a top-down intervention (e.g., reminding oneself that this is only a movie). Recent findings suggest that the degree of efficient crosstalk

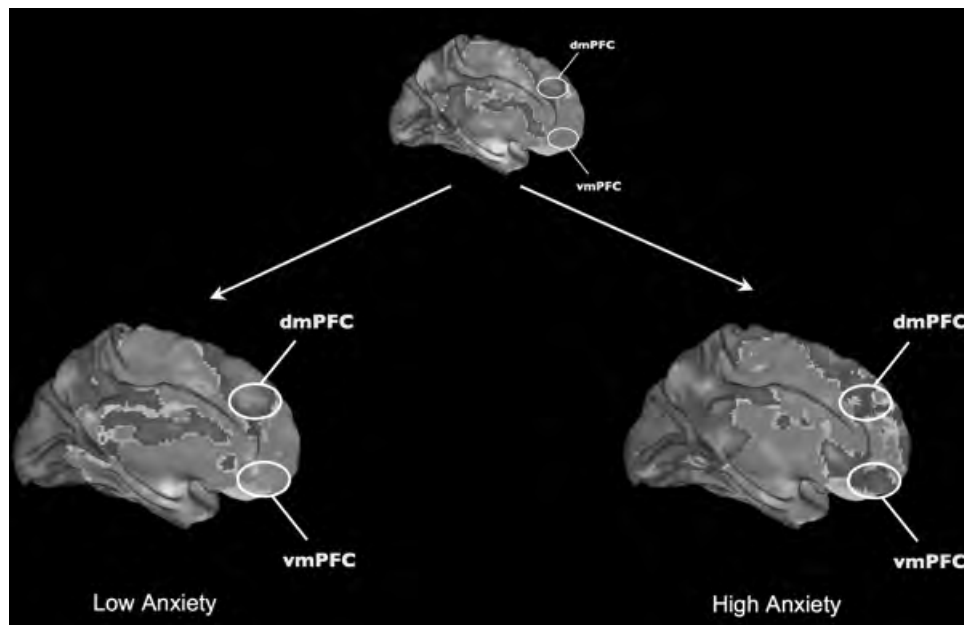


FIGURE 64.1 Amygdala-prefrontal functional connectivity at rest. While all subjects show that amygdala activity is positively correlated with vmPFC activity and negatively correlated with dorsomedial PFC activity at rest, highly anxious subjects show

a reverse pattern in the vmPFC compared to low anxious subjects. (Adapted from Kim et al., 2011.) (See color plate 53.)

between the amygdala and the PFC corresponds to one's ability to regulate one's emotions in this way.

In a study of emotion regulation, functional connectivity between the amygdala and mPFC increased during reappraisal, and the strength of this connectivity was associated with participants' self-report of how effective they were at regulating their emotions (Banks et al., 2007). A selective increase in the functional coupling of the amygdala with the vmPFC and dorsolateral PFC during emotion regulation has also been reported (Erk et al., 2010). Similarly, numerous studies have demonstrated increased prefrontal activity and concomitant decreased amygdala activity during successful emotion regulation (e.g., Ochsner et al., 2002; Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008), highlighting the importance of amygdala-prefrontal interactions in successful top-down control of emotion. Supporting the idea that stronger amygdala-prefrontal connectivity begets better emotion regulation, stronger amygdala-mPFC functional coupling has also been associated with greater amygdala habituation (Hare et al., 2008) and lower anxiety (e.g., Gee et al., 2013; Pezawas et al., 2005). Although correlational measures cannot inform the directional nature of regional influences, negative (inverse) amygdala-prefrontal coupling has been theorized to reflect top-down regulation.

Functional interactions between the amygdala and mPFC also support the extinction of fear conditioning,

which involves the suppression of a previously learned pairing between a CS and US (Quirk, 2002; Rescorla, 2001). The inhibition of CS-US associations depends critically on top-down regulatory input from the mPFC to the basolateral amygdala (Milad & Quirk, 2002). For example, in rodents, electric stimulation of the mPFC resulted in the inhibition of conditioned responses. In humans, increased vmPFC activation and structural volume have been associated with successful extinction (Hartley, Fischl, & Phelps, 2011; Phelps, Delgado, Nearing, & LeDoux, 2004). These results suggest that emotion regulation and extinction rely on overlapping neural mechanisms (Delgado, Nearing, LeDoux, & Phelps, 2008), consistent with the fact that both processes involve reevaluating biologically relevant stimuli (Quirk & Beer, 2006). These structural and functional findings highlight the importance of amygdala-mPFC interactions for the regulation and inhibition necessary for extinction learning and memory.

Amygdala-prefrontal interactions further support the resolution of ambiguity in our environment. Unlike fearful faces, surprised faces do not predict the valence of an unknown eliciting event such that they can be subjectively interpreted as either positive or negative (Neta, Norris, & Whalen, 2009). Individual differences in valence judgments of surprised faces correspond to distinct patterns of brain activity involving the amygdala and vmPFC (Kim, Somerville, Johnstone, Alexander, &

Whalen, 2003). Specifically, lower amygdala and greater vmPFC activity were observed during positive interpretations, with the opposite pattern to negative interpretations. Here, the vmPFC plays a theorized role in resolving the emotional ambiguity of surprised faces, similar to its role in top-down regulatory input to the amygdala during fear extinction or emotion regulation (Quirk & Beer, 2006). Indeed, greater vmPFC activity predicts both (1) more positive ratings of surprise (Kim et al., 2003) and (2) more positive interpretations of an extinguished tone (i.e., tone now predicts no shock; Oler, Quirk, & Whalen, 2009). Amygdala reactivity to surprised faces can also be modulated by context. When surprised faces were paired with positive or negative sentences that provided a clear resolution to the ambiguity of the face, greater amygdala, weaker vmPFC, and greater ventrolateral PFC activity were observed in response to faces in negative contexts (Kim et al., 2004). Taken together, these studies suggest that emotionally ambiguous stimuli incite competition between top-down and bottom-up processes, with the balance of activity in this circuitry reflecting the resolution of ambiguity.

Though various forms of top-down control depend critically on the amygdala and PFC, the extent to which different emotional processes rely on the same regions of PFC is less clear. While extinction specifically involves the ventromedial region of PFC, emotion regulation paradigms highlight the role of ventral and dorsal lateral PFC, in addition to vmPFC, in regulating amygdala reactivity (Erk et al., 2010; Wager et al., 2008). Specifically, mPFC may mediate the top-down effects of lateral PFC on the amygdala (Delgado et al., 2008; Lieberman et al., 2007). When comparing specific types of emotion regulation, suppression and reappraisal strategies were both characterized by decreased activity of the amygdala and increased activity of the PFC—usually including both medial and lateral PFC (Ochsner & Gross, 2005). These same regions also support more automatic, incidental forms of emotion regulation such as affect labeling (Hariri, Bookheimer, & Mazziotta, 2000; Lieberman et al., 2007). These findings provide functional and structural evidence for shared neural mechanisms during different types of top-down control of amygdala reactivity.

AMYGDALA-PREFRONTAL CONNECTIVITY AND PSYCHOPATHOLOGY An emphasis on amygdala-prefrontal interactions is particularly relevant to clinical studies, as impaired interaction between bottom-up and top-down processes is believed to be a hallmark of many psychiatric disorders (Davis & Whalen, 2001). As detailed earlier in this chapter, individual differences in

normative anxiety relate to the strength of amygdala activity and its connections with mPFC (e.g., Hare et al., 2008; Pezawas et al., 2005). Not surprisingly, pathological anxiety in psychiatric disorders is marked by disruption in this circuitry, particularly an imbalance between hyperactivity of the amygdala and hypoactivity of the PFC (e.g., Shin et al., 2005). While atypical amygdala-prefrontal circuitry is a classic neurobiological model for anxiety disorders, disturbances in amygdala-prefrontal function have now been implicated in a range of psychopathology including depression, bipolar disorder, schizophrenia, borderline personality disorder, psychopathy, and attention-deficit/hyperactivity disorder (e.g., Blair, 2008; Foland et al., 2008; Taylor et al., 2012). Future research is needed to understand how abnormal amygdala-prefrontal interactions contribute to psychopathology. For example, it may be the case that a failure of top-down regulatory control allows bottom-up responses to disrupt typical functioning. Alternatively, initial bottom-up reactions might be so exaggerated that they override the normally functioning top-down control system (LeDoux, 1996). Given the prominent role of amygdala-prefrontal circuitry in typical and atypical behavior, future research in this domain will be critical for informing the etiology of psychiatric disorders, understanding the nature and timing of their onset, and developing novel treatments.

Developmental trajectories of amygdala circuitry

Typical development is marked by dramatic changes in emotional behavior and regulation (e.g., Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Tottenham, Hare, & Casey, 2011). Moreover, given the neurodevelopmental nature of many psychiatric disorders and the increase in risk for psychopathology in adolescence (Pine, Cohen, Gurley, Brook, & Ma, 1998), research on the healthy maturation of amygdala circuitry can elucidate how neurodevelopmental processes may go awry in patients who develop disorders characterized by amygdala abnormalities (Gee et al., 2012).

AMYGDALA DEVELOPMENT IN CHILDHOOD AND ADOLESCENCE Consistent with behavioral changes in emotional learning across development, relevant networks in the brain change significantly across the course of typical development (reviewed in Somerville, Fani, & McClure-Tone, 2011). Structurally, the amygdala is a rapidly developing region (reviewed in Tottenham & Sheridan, 2009). The fastest rate of structural volume growth in the amygdala occurs within the first two postnatal weeks and stabilizes by eight months old in nonhuman primates (Payne, Machado, Bliwise, &

Bachevalier, 2010). In humans, the basic neuroanatomical architecture of the amygdala is present at birth (Humphrey, 1968; Ulfig, Setzer, & Bohl, 2003). Longitudinal examination in humans has demonstrated continued structural development of the amygdala through two years of age, and evidence suggests that structural growth is complete by age four in girls but shows a modest but significant linear increase beyond childhood in boys (Giedd et al., 1996; Gilmore et al., 2012). Taken together, these studies suggest that the amygdala undergoes early structural development.

However, functionally, the amygdala displays protracted changes throughout development. The amygdala shows functionality early in life, since it responds to emotional stimuli in childhood (Baird et al., 1999; Thomas et al., 2001). Though children show reliable amygdala signal to facial expressions of emotion, evidence suggests that patterns of amygdala activation to distinct expressions may differ between children and adults. For example, whereas adults show greater amygdala activation to fearful than neutral faces (Whalen et al., 2001), distinctive patterns of amygdala activation have been observed in youth, with some evidence that children display greater activation to neutral than fearful faces (Thomas et al., 2001; Tottenham, Hare, Millner, et al., 2011). However, other studies have found similar patterns of differential amygdala response to sad and disgusted faces in children, as seen in adults (e.g., Lobaugh, Gibson, & Taylor, 2006). Thus, the extent to which the amygdala responds to facial expressions uniquely in children remains unclear.

Evidence suggests that significant changes in amygdala function occur from early childhood throughout adolescence; however, findings on the direction of change in amygdala activation across development differ depending on task design and age groups studied. To date, studies comparing amygdala activation to facial expressions of emotion across children, adolescents, and adults have demonstrated important functional changes across the life span (Gee et al., 2013; Hare et al., 2008). During the presentation of fearful faces, a linear decrease in amygdala activation was observed from 4 through 22 years of age, such that amygdala reactivity was highest in childhood and decreased with age (Gee et al., 2013). When activation was collapsed across facial expressions (fearful, happy, and calm), amygdala reactivity was higher in adolescence compared with children and adults (Hare et al., 2008). Though fewer investigations have examined amygdala function during childhood, studies directly comparing adolescents with adults have shown decreases in amygdala activation from adolescence to adulthood (Gee et al., 2013; Guyer et al., 2008; Hare et al., 2008; Monk

et al., 2003). Recent research has also shown changes in amygdala function related to puberty. Consistent with a decrease in amygdala activation with development, amygdala activation was higher in prepubertal and early pubertal adolescents compared with mid- and late-pubertal adolescents (Forbes, Phillips, Silk, Ryan, & Dahl, 2011). In addition, amygdala function related more strongly to pubertal stage at age 13 than at age 10, though there were no significant differences in activation at these ages (Moore et al., 2012). Future research will aid in characterizing the trajectory of amygdala function across a broader developmental period, as well as clarifying how the observation of linear or nonlinear developmental trajectories may depend on factors such as task.

DEVELOPMENT OF AMYGDALA-PREFRONTAL CONNECTIVITY

Given the fundamental role of amygdala-prefrontal interactions for effective emotion regulation, fear conditioning, and extinction learning, it is critical to investigate how connections between the amygdala and mPFC emerge. Rodent models indicate key changes in amygdala-prefrontal connectivity during adolescence (Cunningham, Bhattacharyya, & Benes, 2002; Kim & Richardson, 2009). While less is known about the development of amygdala connectivity in humans, prior work has demonstrated that the strength of amygdala-mPFC functional connectivity was associated with amygdala habituation in adolescents, suggesting a functional role of connectivity in adolescence similar to that in adulthood (Hare et al., 2008). In addition, prior research has shown that the strength of amygdala-prefrontal effective connectivity increases with age (Perlman & Pelphrey, 2011). To characterize changes in connectivity during typical development, a recent study examined amygdala-mPFC functional connectivity to fearful faces from early childhood through early adulthood. Findings revealed a developmental switch in the valence of connectivity, such that the amygdala and mPFC were positively coupled in early childhood and became negatively coupled across development (Gee et al., 2013). Specifically, amygdala-mPFC coupling switched from an immature phenotype (positive coupling) to a mature phenotype (negative coupling) during the transition to adolescence (figure 64.2).

Moreover, connectivity became more strongly negative with age, replicating studies of amygdala-mPFC coupling in adults (e.g., Hare et al., 2008; Kim et al., 2003). In this study, the developmental switch in amygdala-mPFC functional connectivity mediated the relationship between age and a developmentally normative decrease in separation anxiety. Given the role of mPFC in regulating amygdala reactivity, evidence of stronger

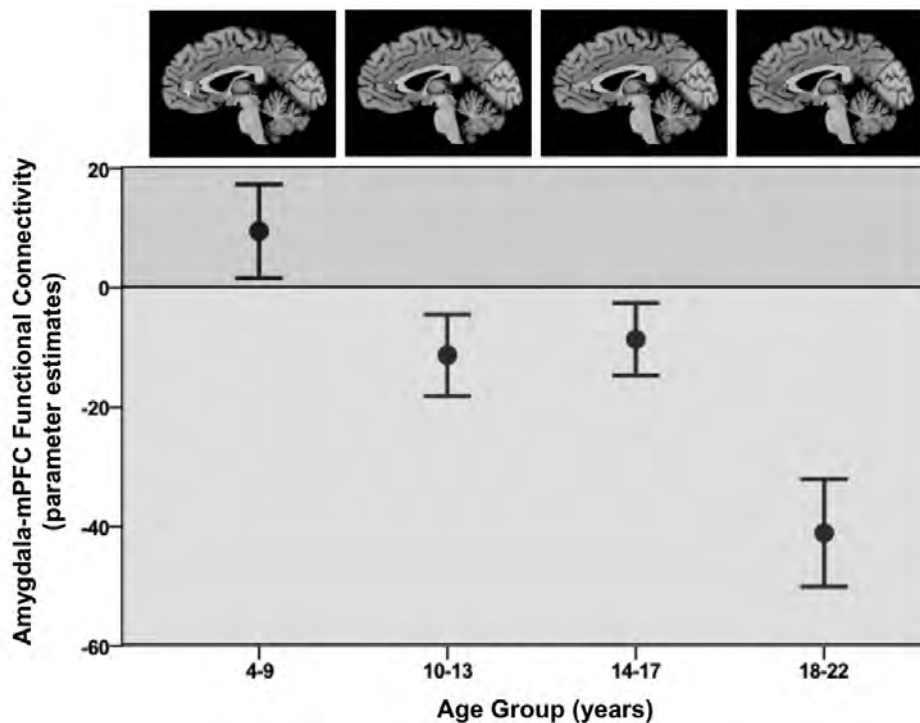


FIGURE 64.2 Development of amygdala-prefrontal functional connectivity. A developmental switch from positive to negative functional connectivity between the amygdala and

mPFC was observed during the transition from childhood to adolescence. (Adapted from Gee et al., 2013.) (See color plate 54.)

negative coupling and reduced amygdala reactivity with age may provide a neurobiological basis for developmental improvements in emotion regulation.

Conclusion

Emotion, whether typical or in the context of psychopathology, can be conceived as a constant interplay between an organism's reactions to biologically relevant stimuli (bottom-up processing) and its attempts to modulate these responses (top-down processing). A wealth of animal and human studies demonstrate the central role of the amygdala and its connections with PFC in these processes. Across the life span, amygdala function and connectivity undergo dynamic changes, which likely support changes in learning and social behavior that are fundamental to development. For example, learning about the relative safety or danger of a given environment plays a critical role in key developmental transitions, such as when the organism leaves the nest or enters adolescence. Moreover, it is through amygdala contributions in development that faces take on predictive value through experiences in the social world, building the reinforcement history that gives rise to individual differences in neural and behavioral responses. While these neurodevelopmental changes

facilitate adaptive behavior such as stronger emotion regulation, changes in amygdala-prefrontal circuitry may also render individuals vulnerable in certain stages of development or with risk for psychopathology. The coming decades will be an exciting time for research on affective neuroscience, as we better understand how the amygdala interacts with a broader brain circuitry to give rise to what we currently call emotion. This line of research will play a critical role in detailing how amygdala circuitry facilitates adaptive behavior, contributes to developmental changes, and influences risk for psychopathology.

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