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Development of the Emotional Brain

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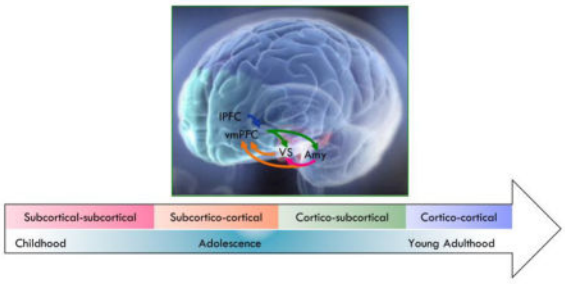
Abstract

In this article, we highlight the importance of dynamic reorganization of neural circuitry during adolescence, as it relates to the development of emotion reactivity and regulation. We offer a neurobiological account of hierarchical, circuit-based changes that coincide with emotional development during this time. Recent imaging studies suggest that the development of the emotional brain involves a cascade of changes in limbic and cognitive control circuitry. These changes are particularly pronounced during adolescence, when the demand for self regulation across a variety of emotional and social situations may be greatest. We propose that hierarchical changes in circuitry, from subcortico-subcortical to subcortico-cortical to cortico-subcortical and finally to cortico-cortical, may underlie the gradual changes in emotion reactivity and regulation throughout adolescence into young adulthood, with changes at each level being necessary for the instantiation of changes at the next level.

Graphical abstract



Keywords

Adolescence; development; emotion; limbic; prefrontal cortex

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Introduction

A rapidly evolving literature on the development of the emotional brain seeks to account for dynamic changes in emotional behavior, particularly during adolescence [1]. This developmental phase is a time when the incidence of many mental disorders involving emotion dysregulation peaks [2]. Although individuals differ substantially in the capacity to regulate emotions, adolescence is thought to be a sensitive period of development when this ability may be especially vulnerable to influences of the social and emotional environment. This review article focuses on two key questions. How do dynamic changes in neural circuitry help to explain changes in emotion reactivity and regulation during the transition into and out of adolescence? When does the capacity for emotion regulation reach adult levels of functioning and does this vary across emotional contexts?

Neurobiological Models of Adolescence

Several models of adolescence have been proposed to explain the neurobiology underlying heightened fluctuations in emotions and diminished emotional control during this time. Specifically, adolescent behaviors have been attributed to two competing brain systems. Dichotomous frameworks typically emphasize competing cognitive control and emotive systems (e.g., [3,4]). According to these dual systems accounts, behavior breaks down when emotional systems win out over less mature cognitive control systems. Empirical evidence for this model emphasizes value and often pitches reward versus control systems [5]. These models have been effective in simplifying and conveying complex scientific findings to the lay public and in informing policies relevant to the protection and treatment of youth [6]. However, this heuristic account of brain development may not fully capture the complexities and temporal time course of emotionally driven behaviors [7].

The imbalance model, unlike dual systems accounts of adolescence [4,8], emphasizes a circuit-based account of the complex and nonlinear ways in which emotion reactivity and regulation change with age [1]. Emotionally driven behaviors are complex and rely on a number of interconnected circuits from subcortical to cortical. Temporal differences in the fine-tuning of each of these circuits with age and experience could impact the functioning and development of these interacting circuits [7]. According to the imbalance model, changes in behavior during adolescence coincide with a series of developmental changes across multiple systems with the regional fine-tuning of connections within subcortical limbic circuits, then between cortical prefrontal and limbic circuits and subsequently between corticocortical circuits ([7], see Figure 1). Thus, the most prominent difference between dual systems and imbalance models is in how one would approach the study of brain mechanisms. Rather than simply contrasting specific systems against one another as discrete regions, the focus is on how connections from subcortical to cortical circuits change and lead to different forms of behavior gradually emerging across development from early to mid to late adolescence.

Viewing developmental findings through a circuit lens is not only faithful to the organization of the underlying biological systems and to knowledge gained from elegant nonhuman studies, but it readily accommodates key findings demonstrating how the interactive effects of emotive signals on cognitive control continuously and gradually change over development

[7]. This approach also highlights the profound differences between the developed brain and the developing brain [9]. The dual systems model fits a model of individual differences [10] to development and while an effective heuristic, it may limit our ability to measure and test subtle developmental progressions in behavior that parallel continued hierarchical development of distributed brain networks from childhood, throughout adolescence and into young adulthood.

Evidence in support of hierarchical developmental changes in the brain comes from post mortem studies showing selective stabilization and regional elimination of excitatory synaptic connections in prefrontal cortex before sensorimotor cortex [11]. These processes have been suggested to alter the balance between excitatory and inhibitory neural connections within these regions [1]. Human neuroimaging studies have shown corresponding patterns of regional brain changes across development [12] with functional connectivity studies [13,14] suggesting refinement of local subcortical circuits precedes refinement of distal cortical ones. Regional increases in white matter [15] are thought to occur through myelination of axons, influencing conduction of electrical impulses across the brain and transport of cargoes essential for neurotransmission, cell metabolism, and survival [2]. The regional changes in synaptic morphology, dendritic arborization, cortical cell firing, and availability of neurochemicals and their receptors during adolescence have been posited to lead to transient imbalances in functional brain circuitry that impact behavior [1].

Figure 1 provides a simplified illustration of hierarchical changes from subcortical to cortical circuits during childhood, adolescence and adulthood that correspond with behavioral changes reported in the developmental literature. The notion of temporally defined cascading events of this nature across the brain parallels psychological theories of developmental cascades in behavior [16] and provide a plausible mechanistic account for observed nonlinear changes in behavior with age. Specifically, these developmental cascades could serve a critical function in stimulating neurodevelopment. For example, robust subcortical signaling could provide the key functional inputs to provoke strengthening of descending cortical projections. Subsequently, the capacity for top-down control of cortico-subcortical circuits may be dependent in part on the functional development of subcortical circuits as part of a dynamic cascade [7].

This view is consistent with Thelen's notion of development as hierarchical [17]. Accordingly, each phase of development builds on the preceding one. Thus, heightened functionality and connectivity of subcortical circuits may be a necessary precursor for signaling top-down cortical control circuitry which is then a necessary precursor for cortico-cortical interactions for complex interactions among cognitive and affective processes.

This perspective highlights the importance of considering interconnections among brain regions rather than relying on a single brain region in isolation to assign function or computation. By focusing on circuit-based changes with age, we may better understand why certain emotive behaviors emerge at different time points in development [18] and how they impact cognitive control continuously over the course of development.

How do developmental changes in neural circuits relate to changes in emotion reactivity and regulation?

Each of the circuits identified in the graphical abstract has been implicated in emotional processes in adults. At the subcortical level are the amygdala and ventral striatum. The ventral striatum, a region implicated in learning and prediction of positive outcomes, receives inputs from the basolateral amygdala. The amygdala is important in learning the emotional significance of cues in the environment, and can facilitate ventral striatum activity through its direct inputs from the basolateral nucleus [19], leading to motivated action [20]. The medial prefrontal cortex has been implicated in fear and emotion regulation. This region has dense projections to the intercalated (inhibitory) cells in the amygdala and to the GABAergic medium spiny neurons in the ventral striatum (VS) that modulate emotive behaviors [21]. Finally, cortico-cortical connections include pathways between lateral prefrontal cortex, implicated in higher cognitive functions, and medial prefrontal regions, involved in emotion and social interactions [22]. These connections may serve as an interface between cognitive and emotional processes. We illustrate how hierarchical fine-tuning with development and experience of these circuits, from subcortical to cortical, provides a potential mechanism for dynamic changes in emotional reactivity and regulation in the sections below.

Subcortico-subcortical connectivity and emotional reactivity

Most developmental human imaging studies of the emotional brain have focused on the amygdala and ventral striatum in isolation, attributing negative affect to the amygdala and positive affect to ventral striatum. However, rodent work has shown that different populations of amygdala neurons respond preferentially to either or both unexpected rewards and punishments [23], reflecting the role of the amygdala in valence non-specific emotional processes and behaviors [24]. Optogenetic studies further suggest a role of amygdala-accumbens interactions in motivated action [20]. Thus, developmental changes in subcortical circuits before cortico-subcortical circuits could lead to an unchecked subcortical system resulting in emotional cue-driven impulsivity. Consistent with this hypothesis is evidence from human developmental imaging studies showing impulsivity to emotional cues regardless of valence (positive or negative) or value (rewarding) in early adolescence [25,26] and activation of these two regions [25,27].

Heller et al. [28] recently tested whether developmental changes in amygdala – ventral striatum connectivity might help to explain heightened reactivity and impulsivity to emotional cues during early adolescence. He utilized task-based fMRI from a cross-sectional sample of over 150 children, adolescents and adults, who performed a go/no-go task to emotional faces. The prediction was that amygdala-ventral striatum connectivity would be associated with greater cue-driven impulsivity. The results of this study are depicted in Figure 1. Functional connectivity between the amygdala and ventral striatum was associated with greater impulsive actions towards emotional cues regardless of valence, controlling for impulsivity to nonvalenced cues.

Subcortico-cortical connectivity and conflicting emotions

The association between subcortical connectivity and impulsive responses to emotional cues decreased linearly with age. So how might the circuitry be changing from early adolescence to later adolescence? A collection of recent optogenetic studies by Tye and colleagues provide novel insights from adult mice that may inform our developmental findings. They [29,30] showed parsing of reward and aversion in basolateral amygdala microcircuits. Specifically, they provided evidence of valence coding in the basolateral amygdala, that could bias motivated action to appetitive cues via projections to the accumbens and to aversive cues via projections to the central nucleus of the amygdala. How these basolateral amygdala projectors come to respond preferentially to positive and negative valenced cues remains unknown since neither the central nucleus nor accumbens projects directly to the basolateral amygdala [31]. One possible developmental explanation consistent with our hierarchical account, involves amygdala inputs to the prefrontal cortex. In fact, Tye and colleagues have gone on to show that these amygdala-prefrontal inputs guide behavior amid conflicting cues of reward and punishment [32] to resolve conflicting actions. Thus, development of subcortical microcircuits between the amygdala and ventral striatum may be necessary for the instantiation of subsequent amygdala-prefrontal circuit development.

To test this hierarchical view of circuit development, Heller and colleagues (2016) went onto examine the association between amygdala-prefrontal connectivity on emotional cue-driven impulsivity with age. They found that increased medial prefrontal-amygdala connectivity was associated with better cognitive control to emotional cues, and this cortical-subcortical connectivity mediated the association between amygdala-ventral striatum connectivity and emotional cognitive control (Figure 2). These findings suggest a dissociation in how subcortical-subcortical and cortical-subcortical connectivity differentially impact emotion reactivity and regulation to cues in the environment with age.

Cortico-subcortical connectivity and emotion regulation

Previous work suggests that development of top-down modulation of the subcortical output via cortical projections could diminish emotive and reflexive actions. The majority of human imaging research on the emotional brain has focused on this ventromedial frontoamygdala connectivity (e.g. [33,34]). In contrast to subcortical changes, activity in ventromedial prefrontal cortex and its connectivity, show more protracted changes with age [18,35]. Tract tracing in rodents shows that ascending projections from subcortical to cortical regions, specifically from the amygdala to the prefrontal cortex, emerge earlier than descending projections from the prefrontal cortex to the amygdala [36,37]. These dynamic circuit-based changes during adolescence [38–40] reflect the importance of subcortical signaling of prefrontal regions before development of top-down prefrontal connections. Human imaging studies show that functional coupling between prefrontal and limbic subcortical regions (e.g., amygdala) shifts from positive to negative from childhood to adulthood [35]. This shift in connectivity has been associated with decreasing subcortical activity to emotional cues (e.g., [35,41]) and is consistent with the rodent studies showing earlier emergence of ascending projections (i.e., from amygdala to ventromedial prefrontal cortex; vmPFC) relative to descending connections (i.e., from vmPFC to the amygdala) [36,37].

These changes in brain circuitry are consistent with resting-state functional connectivity studies showing refinement of local circuits prior to distal connections [13], and task-based functional connectivity studies showing local subcortical coupling preceding enhanced prefrontal cortico-subcortical coupling [28]. Robust subcortical signaling early in development may provide essential functional inputs to instantiate the strengthening of reciprocal cortical projections. Together these findings in humans and rodents corroborate the role of descending PFC-limbic projections in emotional and behavioral regulation [35,42–44].

Cortico-cortical connectivity and cognitive control under emotional influences

Evidence in the domain of emotion reappraisal further highlights the importance of cortical modulation of neural circuitry related to self-control. While development of medial prefrontal circuitry has been implicated in emotion regulation, lateral prefrontal circuitry important for redirection of attention, has been implicated in cognitive reappraisal of emotion [25,26,45]. Recent evidence suggests that the lateral PFC plays a significant role in the development of these abilities [46], mediating the association between increasing age and diminished amygdala responses to emotionally evocative stimuli. This association is stronger for individuals with greater inverse coupling between the vmPFC and amygdala. This developmental pattern suggests that shifts in vmPFC-amygdala connectivity may be a prerequisite for effective modulation by lateral prefrontal circuitry. Together, the findings provide support for a hierarchical framework for how vmPFC and ventrolateral PFC may work in concert to enhance emotion regulation and reappraisal and how age-related improvements in cognitive regulation are instantiated in the developing brain.

When does emotional development reach adult levels of functioning?

Typically, studies on cognitive and emotion regulation during adolescence have focused on the ages of 13 to 17 given that by18, individuals begin taking on societal-based adults roles (e.g., voting, marrying, military service). However, legal definitions of adulthood in the United States vary substantially by specific policy and by state. Though the age of majority is typically 18 and the legal age for purchasing alcohol is 21, the minimum age for criminal prosecution is 14 or younger in most states. Thus the question of when an adolescent reaches adult-like cognitive capacity in emotionally arousing situations has important social and legal policy implications [18,47].

Recently, Cohen and colleagues [18] attempted to address this question by examining cognitive control under emotionally arousing conditions across development. They compared cognitive control under neutral and emotional conditions in teens (13–17), young adults (18–21) and adults (22–25) using an emotional go/nogo task that dissociated emotional valence from general arousal. Specifically, they assessed the impact of both brief and prolonged emotional states, and of both positive and negative valence, on cognitive task performance. Emotional facial expressions (smiling, fearful, neutral) were used to assess the effects of brief emotional triggers on cognitive control. Prolonged emotional states involved the anticipation of a negative event (loud aversive noise), positive event (winning up to $100), or no event occurring when the computer screen background turned yellow, purple or

blue. These emotional events were unpredictable in an attempt to elicit sustained states of anticipation and did not relate to the individual's performance. Teens showed diminished cognitive control relative to adults under both negative and positive emotional states. Like teens, young adults showed diminished performance relative to adults over 21, but only in the context of negatively valenced arousal.

This behavioral pattern was paralleled by enhanced ventromedial prefrontal activity associated with emotional regulation and diminished lateral prefrontal activity implicated in cognitive control in the teens and young adults. These results suggest that cognitive control remains susceptible to negative emotional influences into young adulthood as lateral and ventromedial prefrontal circuitries continue to develop. Further evidence of emotional arousal leading to less "mature" patterns of functional connectivity, relative to non-arousing states, has been reported by Rudolph and colleagues [48]. Together the neuroimaging findings suggest a dynamic and hierarchical course of development from subcortico-subcortical changes associated with emotional reactivity to cortico-subcortical changes implicated in emotion regulation to cortico-cortical changes associated with regulation of emotionally-driven attention and reappraisal [7].

Conclusions

There is currently a shift in the neurodevelopmental literature from simple dichotomies to circuit-based accounts of emotional development that may enhance a mechanistic understanding for changes in self regulation from childhood to young adulthood. These studies suggest that the development of the emotional brain, especially during adolescence, involves a cascade of changes in connections from subcortical to cortical circuits. Our neurodevelopmental account of these changes suggests that the instantiation of circuit changes is dependent on the preceding ones. First, increases in functional connectivity between the amygdala and ventral striatum correspond to increases in impulsive action toward emotional cues. Subsequent decreases in this subcortical connectivity are associated with diminished reactivity to emotional cues, and changes in medial PFC-amygdala functional connectivity mediate this association. By late adolescence "maturity" of medial PFC-amygdala connectivity with the shift from positive to negative vmPFC-amygdala connectivity appears to be a prerequisite for cognitive regulation of emotions via cortico-cortical projections. This shift may be a potential prerequisite for subsequent effective modulation of emotion (e.g., redirection of attention and reappraisal) by lateral prefrontal circuitry.

Together, the findings suggest that hierarchical changes in circuit connectivity appear to be critical for the continuous development of regulatory processes in emotionally charged situations from late childhood to young adulthood. These findings have important implications for legal and social policies relevant to both the protection and treatment of youth and suggest a need for rethinking specific ways in which we meet the needs of young people as they transition across these development stages and into adult societal roles [47].

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Highlights

- Adolescence is a period of increased reactivity to emotional and social cues
- Subcortical limbic connectivity is associated with cue-driven impulsivity
- A shift in frontoamygdala connectivity occurs around the transition into adolescence
- Prefrontal cortico-cortical regulation of emotion is reliant on frontoamygdala connectivity
- Hierarchical circuit-based changes underlying emotion regulation extend into the 20s

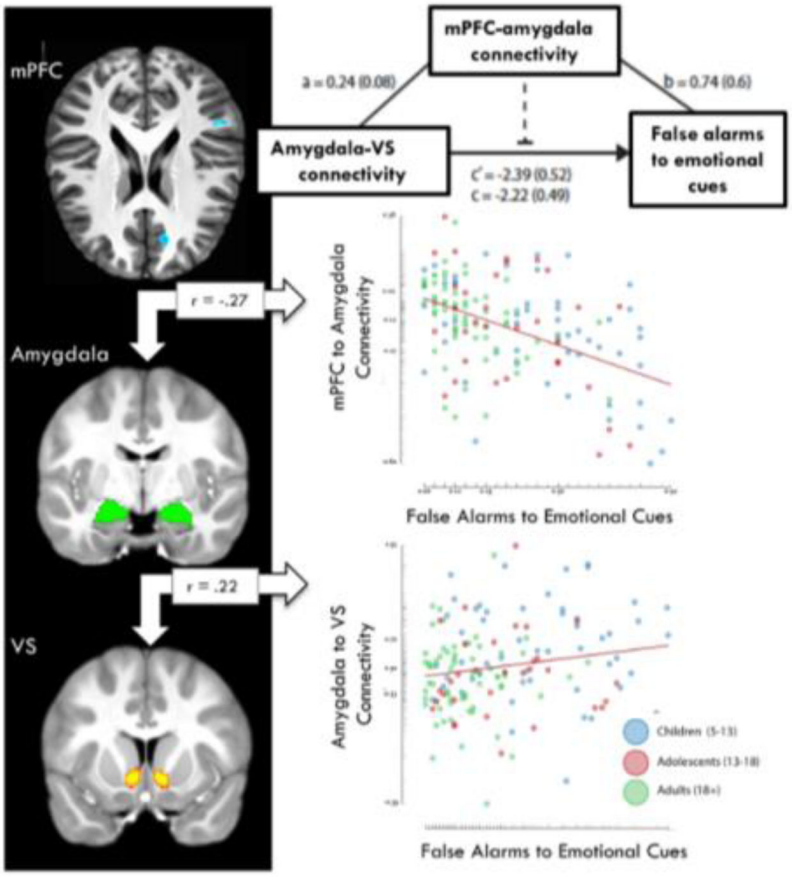

Figure 1. Illustration of hierarchical changes in brain circuitry from subcortical to cortical with age

Regional changes in connectivity from childhood to adolescence to adulthood are indicated by the colors of pink (subcortico-subcortical), orange (subcortico-cortical), green (cortico-subcortical) and blue (cortico-cortical). Ventromedial prefrontal cortex, vmPFC; lateral prefrontal cortex, lPFC; ventral striatum, VS; amygdala, Amy.

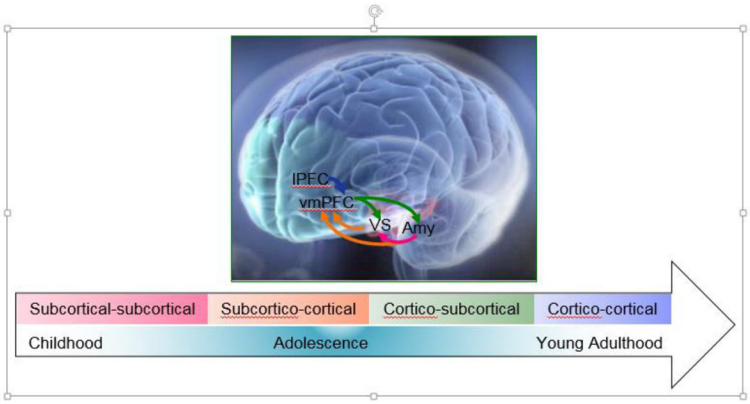

Figure 2. A model of how cortical-subcortical connectivity between the medial PFC and amygdala mediates the relationship between subcortical-subcortical connectivity and emotional cue-reactivity

Subcortical-subcortical connectivity is associated with more false alarms to emotional cues whereas greater cortical-subcortical (medial PFC-amygdala) connectivity is associated with fewer false alarms. Ventromedial prefrontal cortex, vmPFC; ventral striatum, VS.