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A time of change: Behavioral and neural correlates of adolescent sensitivity to appetitive and aversive environmental cues

Leah H. Somerville, PhD, **Rebecca M. Jones, MS**, and **BJ Casey, PhD**
Sackler Institute for Developmental Psychobiology, Weill Cornell Medical College, New York, NY USA

Abstract

Adolescence is a developmental period that entails substantial changes in affective and incentive-seeking behavior relative to both childhood and adulthood, including a heightened propensity to engage in risky behaviors and experience persistent negative and labile mood states. This review discusses the emotional and incentive-driven behavioral changes in adolescents and their associated neural mechanisms, focusing on the dynamic interactions between the amygdala, ventral striatum, and prefrontal cortex. Common behavioral changes during adolescence may be associated with a heightened responsiveness to incentives and emotional cues while the capacity to effectively engage in cognitive and emotion regulation is still relatively immature. We highlight empirical work in humans and animals that addresses the interactions between these neural systems in adolescents relative to children and adults, and propose a neurobiological model that may account for the nonlinear changes in adolescent behavior. Finally, we discuss other influences that may contribute to exaggerated reward and emotion processing associated with adolescence, including hormonal fluctuations and the role of the social environment.

Keywords

Adolescence; brain; development; fMRI; emotion; reward; cognitive control; connectivity; peers; risk; function; amygdala; nucleus accumbens; prefrontal cortex

Introduction

The description of adolescence as “a developmental period rife with change” may be an understatement for those of us who think back to our own experiences during this time of life, or who observe teens today (Hall, 1904). Adolescence can be defined as the phase of gradual transition between childhood and adulthood, which is overlapping yet conceptually distinct from the physical changes marking puberty and physical maturation (Ernst, Pine, & Hardin, 2006; Spear, 2000). In recent years, researchers from a broad spectrum of scientific disciplines have shown significant interest in this period of the lifespan due to its intense physical, behavioral, social, and neurological changes, and the alarming health statistics associated with this time of life.

Address correspondence to: Leah Somerville, PhD, 1300 York Avenue, Box 140, New York, NY 10065, Phone: (212) 746 5830, Fax: (212) 746 5755, lhs2003@med.cornell.edu.

Beyond the intellectual interest in this period as a psychological snapshot in time, research examining adolescent behavior and its associated neural changes is particularly relevant to adolescent health. In adolescence, there is a heightened propensity to engage in risky behaviors that can lead to negative outcomes, including substance abuse, unprotected sex, inflicting harm on others, injuries, and death. According to the 2007 Youth Risk Behavior Survey (YRBS, Eaton, et al., 2008) the four leading causes of death that account for 72% of adolescent mortality – motor vehicle accidents, unintentional injuries, homicide, and suicide - are preventable. Such statistics suggest that these fatalities may be attributed, in part, to poor choices or risky actions (e.g., accidents, injuries) and/or heightened emotionality (e.g., suicide) underscoring the importance of understanding the biological basis of emotional and incentive-seeking behavior of adolescents, the focus of the present review.

Storm and stress? Affective changes during adolescence

Adolescence has been considered, almost by definition, as a period of heightened stress (Spear, 2000) due to the array of transitions being experienced concomitantly, including physical maturation, drive for independence, increased salience of social and peer interaction, and brain development (Blakemore, 2008; Casey, Getz, & Galvan, 2008; Casey, Jones, & Hare, 2008). Although new-found independence and social engagement can be stimulating and challenging in a positive way, it may also lead to feelings of being overwhelmed by change, which has historically led some researchers to characterize adolescence as ridden with ‘storm and stress’ (Hall, 1904). The controversial ‘storm and stress’ viewpoint is bolstered by reports that the onset of many psychiatric illnesses increases sharply from childhood to adolescence (Compas, Orosan, & Grant, 1993), with the lifetime risk for the emergence of mental illness peaking at 14 years of age (Kessler, et al., 2005). Although a full discussion of clinical adolescent populations is of inherent interest to this topic, it is outside the scope of the present review and we refer the reader to existing articles that address these issues in greater detail (Paus, Keshavan, & Giedd, 2008; Steinberg, 2005).

In terms of the typical range of emotions, certain classes of emotional states- particularly negative emotional states- show a peak in prevalence during adolescence (Compas, Hinden, & Gerhardt, 1995; Petersen, et al., 1993; Rutter, et al., 1976). Most recently, YRBS results showed that in the prior year, more than one in four adolescents (27.3%) had experienced significant symptoms of depression for at least two weeks, to the point that it interfered with their everyday functioning (Eaton, et al., 2008). Experiencing frequent negative affect is particularly common during the early adolescent years, more so in females than males (Larson, Moneta, Richards, & Wilson, 2002), and in addition to sad mood, also manifests itself in anxiety (Abe & Suzuki, 1986), self-consciousness, and low self-esteem (Simmons, Rosenberg, & Rosenberg, 1973; Thornburg & Jones, 1982). Feeling sad, depressed, or hopeless may be associated with the heightened rates of affective disorders, attempted and completed suicide, and addiction also observed during adolescence (Pine, Cohen, & Brook, 2001; Silveri, Tzilos, Pimentel, & Yurgelun-Todd, 2004; Steinberg, 2005, Mościcki, 2001). These statistics underscore the need to understand the physiological basis of these emotional states changes in adolescents.

Finally, adolescents’ negative emotional states are not only frequent but their emotional responses also tend to be more intense, variable and subject to extremes relative to adults (Arnett, 1999; Buchanan, Eccles, & Becker, 1992; Eccles, et al., 1989; Simmons & Blyth, 1987). Larson and colleagues (2002) performed a cross-sectional beeper study that sampled the momentary affect experienced by early adolescents several times per day for a week, and then retested those individuals approximately three years later, after they had transitioned into late adolescence. Results indicated that early adolescents, defined here as fifth to eighth graders, experienced substantially greater short-term variability in affective state relative to what the same individuals experienced in ninth to twelfth grades (Larson, et al., 2002). This study and others suggest that adolescent emotional states tend to be more labile than children and adults, and this appears to be particularly true during the early adolescent years.

The work just described paints a relatively bleak picture, suggesting that adolescence is doomed to be a very negative time of life. However, it is important to note that most adolescents are actually not miserable, and negotiate this potentially difficult period with relative ease and without lasting problems (Steinberg, 2008). We believe that a bias in available data may contribute to this discrepancy – while many studies ask adolescents to report on their negative emotions, very few ask about positive emotions which may also be elevated during this time (see Ernst et al., 2005). Consequentially, a more current view of adolescent affect is not deterministic with regard to experiencing ‘storm and stress’, but contends that being an adolescent may be a risk factor for experiencing intense negative emotional states (Arnett, 1999).

Adolescent incentive-driven behavior

In the previous section, we have asserted that adolescents frequently experience negative and volatile emotions. However, the period of adolescence is also marked by a nonlinear enhancement in risk-taking behavior, characterized by approaching pleasurable experiences without appropriate reverence to their associated potentially negative consequences. Several classes of epidemiological data support this conceptualization of adolescent behavior. In particular, adolescents engage in significantly more risky driving, illicit drug use, criminal acts and unsafe sexual behavior than children and adults (National Research Council, 2007; Substance Abuse and Mental Health Services Administration, 2007; Eaton et al., 2008). These health statistics suggest that adolescents are risk-takers, but environmental influences such as reduced parental supervision and increased access to risk-enabling situations could also explain the increase in risk-taking between childhood and adolescence.

Empirical work measuring risk-taking in controlled environments has largely supported the notion that adolescents show disproportionate risk-taking in the absence of differential environmental demands. Cauffman and colleagues (2009) used the Iowa Gambling Task to test participants varying in age from pre-adolescence (10 years old) to adulthood (up to 30 years old). Using this task, approach- and avoidance-based decision-making was calculated separately by quantifying participants’ ability to use experimenter feedback to learn to approach ‘good’ decks of cards (positive feedback) and avoid ‘bad’ decks (negative feedback). They found that levels of approach toward potential reward took on a curvilinear function, with the maximal sensitivity to positive feedback occurring during the adolescent years. In contrast, use of negative feedback to avoid negative outcomes strengthened with age in a linear fashion, not showing full maturity until the adult years. These findings suggest that adolescents may have a disproportionate approach orientation, paired with an immature avoidance orientation, which may explain the nonlinear boost in risk-taking behavior. These findings are consistent with the results of Figner and colleagues (2009), who employed the Columbia Card Task, a risky decision-making task with ‘hot’, or affectively driven, and ‘cold’, deliberative decision making contexts. They observed that in the ‘hot’ condition, adolescents showed an increase in risk-taking relative to adults. Recently, this sample has been extended to individuals as young as 10 years of age, with findings indicating that pre-adolescents display a level of risk-taking comparable to adults, and less than adolescents (Figner, Mackinlay, Wilkening, & Weber, 2009). These experiments lend support to the notion that adolescents are disproportionately motivated to approach potential rewards, particularly in contexts with heightened arousal or salience.

Why do adolescents display greater propensity for risk taking? Although the answer is complex and addressed by another article in this volume (see article by Doremus-Fitzwater, Verlinskaya, & Spear), risky behaviors observed in adolescence are likely related to an enhanced motivation to seek out incentives and new experiences. This drive may be mediated by a greater salience of rewarding stimuli during this age relative to children or adults (Steinberg, 2008)- in other words, a sensitization to reward (Casey, Getz, et al., 2008; Casey, Jones, et al., 2008; Fareri, Martin, & Delgado, 2008). This interpretation is consistent with the behavioral findings just described, a documented enhancement of sensation seeking in adolescents relative to children and adults (Zuckerman, Eysenck, & Eysenck, 1978), enhanced reported positive affect following the receipt of a monetary reward (Ernst et al. 2005), and neurobiological evidence which will be discussed in the forthcoming sections. Interestingly, rodents also show enhanced novelty and sensation seeking during their period of adolescence, suggesting that reward-seeking behavior is governed by primitive biological mechanisms (Adriani, Chiarotti, & Laviola, 1998; Laviola, Macri, Morley-Fletcher, & Adriani, 2003).

In humans, this tendency paired with an immature “self-regulatory competence” leads to heightened risk for poor choice behavior (Steinberg, 2004). When placed in an emotionally salient situation, enhanced sensitivity to positive environmental cues biases adolescent behavior toward approaching incentives, even when that choice may be suboptimal or risky (Casey, Jones, et al., 2008). Importantly, risky behavior cannot be explained by a deficiency in comprehending the potential consequences of these actions (Reyna & Farley, 2006). Adolescents are cognitively able to appreciate the objective riskiness of their behaviors, yet in the moment these warnings are not heeded, perhaps due to a variety of influences including peers, environmental context, or internal emotional state (Gardener & Steinberg, 2005; Steinberg, 2005), leading environmental cues to ‘win’ over cognitive control in emotionally charged circumstances. This conceptualization proposes that disproportionate sensitivity to salient environmental cues can partially account for the nonlinear increase in risky reward-seeking behavior during this stage of development.

Although at first glance, risky adolescent behavior may appear inconsistent with adolescents’ frequent experience of negative mood states, these tendencies need not be mutually exclusive (Bogin, 1994; Spear, 2000). Indeed, negative and extreme emotional behavior paired with increased risk-taking may facilitate evolutionarily appropriate behavior (Casey, Jones, et al., 2008; Spear, 2000). Risk-taking and novelty seeking can be viewed as faciliatory to some of the primary goals of adolescence in societal structures in which individuals must leave their home territory – “testing out” one’s independence, generating sufficient motivation to explore new environments, and developing bonds with non-family members (including potential mates). A propensity to generate reactive and extreme emotions may complement this process of striving for independence. Labile and negative emotions may signal a heightened state of vigilance toward threat and safety cues, which may serve a greater importance when engaging in risk. As such, the combination of emotionality and incentive seeking may have come about for good reason, but in present society serves less of an adaptive purpose.

Synthesizing a model of adolescent behavior change

Based on the behavioral work just described, we have observed three main themes characterizing unique aspects of adolescent behavior, relative to behavior of children and adults. First, adolescents appear to show heightened sensitivity to salient environmental cues. Behaviorally, this idea is supported by epidemiological reports of adolescent risk-taking behavior, and empirical work showing exaggerated responses to both positive and negative environmental cues in adolescents relative to children and adults. What may seem like a mildly annoying or hurtful event to adults may constitute an intense emotional trigger in adolescents leading to strong negative affect. Similarly, an environmental cue signaling a potential source of hedonic pleasure may drive incentive seeking behavior to a greater extent than in children or adults due to a heightened sensitivity to potential rewards.

A second theme in the characterization of adolescent behavior is that adolescents are often unable to exert behavioral control in the face of environmentally salient cues, leading to risky and potentially dangerous choice behaviors. In particular, adolescents are able to comprehend and reason the outcomes of suboptimal decisions. Yet, in the right context, be it with peers or in a certain mood state, adolescents approach salient environmental cues even when it is disadvantageous or potentially dangerous. In terms of controlling negative affect, a lack of prefrontal control may lead to deficient emotional regulation abilities, resulting in affective responses left ‘unchecked’ and resulting in highly emotional output.

Lastly, although adolescents tend to show heightened affective responsiveness and incentive-based behavior changes, these responses are highly subject to individual differences. It is easy to forget that many adolescents make rational decisions, and have no problem regulating their emotions. However, we believe that adolescence is a time of life that is, consistent with more current views on ‘storm and stress’ (Arnett, 1999), a risk factor for heightened emotionality. This stage of life, combined with predisposing factors such as individual differences in trait anxiety or mood, or state contextual factors such as the stability of family or peer relations, may constitute a compounded source of risk for experiencing intense emotional states observed during adolescence.

Toward a neurobiological model of adolescent behavior

We have developed a biological model that characterizes brain changes underlying the patterns of adolescent behavior that takes into account the nonlinearity of emotional and incentive seeking behaviors that are unique to this period (Casey, Getz, et al., 2008; Casey, Jones, & Hare, 2008). This empirically driven model posits an imbalance between the relative structural and functional maturity of brain systems critical to emotional and incentive based behavior (e.g., subcortical limbic regions including the amygdala and ventral striatum) as compared to brain systems mediating cognitive and impulse control (e.g., the prefrontal cortex), see Figure 1. A relative maturity of limbic structures compared to a still immature prefrontal signaling, to account for the biased emotional and incentive-based behavior that is typical of adolescence. This is in contrast with the periods of childhood, where both brain systems are relatively immature, and adulthood, when both brain systems are relatively mature – and in both cases, more balanced in their influence over behavior. The following section will discuss empirical research outlining the development, structure, and function of limbic and prefrontal control brain systems and their interaction, as well as how imbalanced engagement of these systems can lead to the emotional and reward-seeking behaviors associated with adolescence.

We will focus primarily on three interacting brain systems whose dynamic functions are critical to adolescent emotional, incentive, and cognitive control behaviors. The amygdaloid complex, a cluster of nuclei situated in the medial temporal lobe, plays a critical role in processing information of biological significance (Aggleton, 2000; Davis & Whalen, 2001; LeDoux, 2000), including emotionally evocative stimuli, potential threats, and cues depicting the emotional states of others. A second critical player in this circuitry is the ventral striatum, a portion of the basal ganglia that contains the nucleus accumbens (NAcc). The NAcc contributes to decision-making behavior by signaling the anticipation and attainment of rewards, and serves to influence motivated behavior via connections with the prefrontal cortex (Cardinal, Parkinson, Hall, & Everitt, 2002; Delgado, 2007; Schultz, 2006). Finally, the prefrontal cortex has been implicated in wide-serving cognitive functions including the implementation of cognitive control, regulation of emotion, rational decision-making and complex cognition (Casey, Galvan, & Hare, 2005; Miller & Cohen, 2001; Ochsner & Gross, 2005). It is an imbalance between the relative maturity of the amygdala and NAcc, relative to the PFC, that we believe gives rise to the tendency toward disproportionately emotional and reward-sensitive behavior in adolescence.

Assessing differential relative maturity of limbic and prefrontal regions

Outside of the functional neuroimaging literature, there is evidence to suggest a differential relative maturity of subcortical limbic brain structures as compared to prefrontal regions, which may be most pronounced during adolescence. Evidence for the continued pruning of prefrontal cortical synapses well into development has been established in both nonhuman primates and humans (Rakic, Bourgeois, Eckenhoff, Zecevic, & Goldman-Rakic, 1986; Huttenlocher, 1997), with greater regional differentiation found in the human brain (Huttenlocher, 1997) such that cortical sensory and subcortical areas undergo dynamic synaptic pruning earlier than higher-order association areas. This conceptualization of cortical development is consistent with anatomical MRI work demonstrating protracted pruning of gray matter in higher-order prefrontal areas that continues through adolescence (e.g., Giedd et al., 1999) relative to subcortical regions. This amygdala and nucleus accumbens also show anatomical changes during this time of life but to a lesser degree. In an anatomical MRI experiment, gray matter measurements of the nucleus accumbens were not predicted by age, unlike prefrontal regions that were strongly negatively predicted by age (Sowell et al., 2002). In terms of amygdala maturation, the volumetric analyses of the human amygdala showed a substantially reduced slope of change magnitude relative to cortical areas in 4–18 year olds (Giedd et al., 1996). Taken together, these findings suggest a protracted developmental timecourse of the prefrontal cortex relative to these limbic subcortical regions.

Our model is similar to other models of adolescent brain development (Nelson, Leibenluft, McClure, & Pine, 2005; Steinberg, 2008). However, the present model differs in that it attempts to account for adolescent changes in the processing of both appetitive and aversive cues, and emphasizes the dynamic interplay between subcortical and cortical brain systems across development. Finally, the current model integrates findings from children, adolescents and adults in order to account for the nonlinear nature of adolescent behavior change, and incorporates the important role of individual differences in modulating behavioral and brain responsivity.

Brain mechanisms of enhanced sensitivity to salient environmental cues

Functional neuroimaging techniques allow for the noninvasive measurement of regional brain activity while subjects perform tasks aimed at isolating psychological processes of interest. In affective neuroscience, researchers have used neuroimaging techniques to identify a network of brain regions that appear to be particularly responsive to appetitive and aversive stimuli, including the amygdala, ventral striatum, midbrain nuclei, and medial and lateral prefrontal cortices (Adolphs, 2002; Kober et al., 2008). One can then look across a developmental trajectory to determine how the recruitment of emotion- and incentive- sensitive brain regions changes as a function of development, behavior, and individual differences.

Several neuroimaging experiments have examined the nature of subcortical responsivity to aversive and appetitive environmental cues during adolescence. Early work on this topic documented that adolescents showed a reliable amygdala response to facial expressions of emotion, including fearful faces (Baird et al., 1999). Subsequent experiments including an adult comparison group reported that adolescents elicited a greater amygdala response magnitude to negatively valenced facial expressions relative to adults (Guyer et al., 2008a; Monk et al., 2003). However, it should be noted that this effect has not always been observed, as Thomas and colleagues (2001) documented an increase in amygdala response to neutral relative to fearful facial expressions in a pre-adolescent sample, the opposite effect of what was observed in adults. In addition, there is some evidence that the amygdala response in adolescents may be valence-independent, as adolescents also show enhanced amygdala activity to happy relative to neutral facial expressions (Williams, et al., 2006), consistent with what is observed in adults (Somerville et al., 2004).

Most recently, research has focused on tracking changes in neural responses to emotional cues during the transition into, during, and out of adolescence (Casey, Tottenham, Liston, & Durston, 2005) in order to detect nonlinear effects during this period of life. By testing individuals ranging in age from middle childhood to adulthood, it was observed that the response magnitude of the amygdala was significantly larger in adolescents compared to both children children and adults, who showed comparable amygdala recruitment in response to facial expressions of emotion (Hare et al., 2008, see Figure 2A). These studies and others have led to the interim conclusion that adolescents show an exaggeration in amygdala responsivity to emotional facial expressions relative to children and adults (Somerville, Fani, & McClure-Tone, in press). However, these patterns are not thought to be specific to facial expressions, as other negative cues such as the omission of a large monetary reward has been shown to generate disproportionately large amygdala responses in adolescents relative to adults as well (Ernst, et al., 2005).

Functional neuroimaging techniques also have examined the neural underpinnings of adolescents' enhanced sensitivity to appetitive cues by using variations on incentive-related decision tasks, where subjects' behavioral choices determined the win or loss of money and/or magnitude of reward. These experiments have focused on the activity of the ventral striatum, which is sensitive to reward anticipation and learning in both the human (Delgado, Nystrom, Fissell, Noll, & Fiez, 2000; Knutson, Adams, Fong, & Hommer, 2001; O'Doherty, Deichmann, Critchley, & Dolan, 2002) and animal (Schultz, Dayan, & Montague, 1997). May and colleagues (2004) tested adolescent participants during a gambling task in which they could win or lose money on each trial, probing neural activity to the processing of reward outcomes. When comparing win to loss trials, adolescent participants recruited similar brain regions to what had been shown previously using the same task in adults (Delgado, et al., 2000), including heightened activity in the ventral striatum. Interestingly, the ventral striatal timecourse of the reward response was temporally extended in adolescents compared to adults (Fareri, et al., 2008),suggesting a temporal exaggeration in striatal recruitment to rewards. Using another gambling task, Ernst and colleagues (2005) measured neural activity and subjective affective responses to the wins and losses during fMRI scanning. Relative to adults, adolescents reported an exaggeration in subjective happiness experienced when winning large rewards, and these large reward trials elicited exaggerated neural responses within the NAcc. Taken together, these two experiments lend support to the notion that adolescents show a heightened sensitivity to the receipt of incentives, both in terms of behavior and ventral striatal responses (cf Bjork, et al., 2004).

A study from our laboratory assessed changes in the neural response to appetitive cues in participants of various ages to examine neural response changes to incentives during the transition into and out of adolescence. Galvan and colleagues (2006) reported on neural responses in children, adolescents, and adults during a reward learning paradigm paying out small, medium, and large monetary incentives. In adolescents and adults, the NAcc showed linearly increasing activity as a function of reward outcome, with larger reward magnitudes eliciting greater NAcc activity (see Figure 2B). Children showed a less coordinated NAcc response, with no difference in activity across low, medium, and high reward magnitude conditions. However, in the NAcc, adolescents showed an exaggeration in this magnitude-based response, with a significant boost in response to large monetary rewards relative to children and adults. This biological hypersensitivity to reward in dolescents has been demonstrated in several additional studies (Ernst et al., 2005; May et al., 2004) and suggests a relative functional maturity in adolescent NAcc response as compared with children, with overall patterns of response mimicking that of adults, but in an exaggerated fashion.

Brain mechanisms of reduced top-down control over responses to salient cues in adolescents

Another important change in brain structure occurs within tracts of white matter, bundles of myelinated axons that transport neural signals between brain regions (Cascio, et al., 2007). In contrast to gray matter, white matter pathways appear to increase in size, density, and organization throughout adolescence and well into adulthood (Schmithorst, Wilke, Dardzinski, & Holland, 2002; Snook, Paulson, Roy, Phillips, & Beaulieu, 2005). Of particular interest is the structural integrity of white matter tracts between subcortical brain regions and the prefrontal cortex, as these pathways may mediate cross-communication between subcortical emotion- and incentive-driven regions and prefrontal control regions (Hare & Casey, 2005; O#x00027;Doherty, 2004; Pessoa, 2008; Phelps, 2006).

A growing body of work is accumulating to suggest that the structural integrity of subcortical-cortical white matter pathways regardless of age is related to behavior and personality characteristics pertinent to reward and emotion processing. Kim and Whalen (2008) have recently shown that the strength of connectivity between the amygdala and the ventromedial prefrontal cortex predicts fewer symptoms of anxiety in healthy adult subjects, consistent with previous reports identifying a similar amygdala-PFC pathway (Johansen-Berg et al., 2008). Perhaps the link between structure and personality would explain individual differences in these behaviors during adolescence, where white matter maturity appears to be intermediate and variable across individuals.

Using a developmental sample, Liston and colleagues (2006) reported that several white matter tracts showed continued maturation across adolescence, including tracts between the ventral prefrontal cortex and striatum. Of the tracts examined, only the maturity of a ventral frontostriatal pathway predicted better impulse control, measured by effort in performance on a go-no-go task (Liston, et al., 2006). Taken together, these studies offer intriguing evidence that subcortical-cortical white matter pathways continue to undergo structural change throughout adolescence and that the efficiency of cognitive control is, in part, dependent on the maturity of frontostriatal connections. This may be consequential to the ability to control impulses in the face of potential rewards. Future studies relating properties of white matter tracts to personality traits and cognitive abilities within developmental samples may allow greater understanding of the role of top-down and bottom-up connections in emotional and incentive-driven behavior.

The studies discussed in the previous section suggest that adolescents may show a “hyper-reactivity” to salient environmental cues. A more comprehensive picture of adolescent emotional development takes into account the interaction between affective and control systems in the brain when required to suppress, ignore, or inhibit responses to emotional cues. Cognitive control can be defined as the ability to sustain goal-directed cognition in the face of extraneous information, and its development and neural substrates are discussed at length in another article in this volume (Luna et al, this issue). However, cognitive control is also relevant to emotional and incentive processing, because it is particularly difficult for youth to maintain cognitive control in the face of emotionally charged or incentive-laden distractors (Eigsti et al., 2006). When healthy adult participants are asked to consciously suppress their affective responses to salient environmental cues, enhanced activity is often observed in ventrolateral and medial prefrontal cortices (Ochsner & Gross, 2005; Urry et al., 2006). Counterproductive recruitment of the ventromedial prefrontal cortex may serve as a neural predictor for psychiatric illnesses such as clinical depression (Johnstone et al., 2007), the incidence of which is elevated during adolescence. The interplay between emotional and cognitive systems is at the crux of our model, and we assert that adolescents display a functionally imbalanced pattern of neural activity that may be related to behavioral deficits in successfully inhibiting emotional responses.

More functional neuroimaging studies are needed to elucidate the interaction between emotional and controlled processing in adolescence, but initial studies have provided important insight into these interactions. A study by Monk and colleagues (2003) compared neural activity of adolescent and adult participants while they viewed fearful and neutral facial expressions of emotion. While viewing the faces, participants engaged in passive viewing or were asked to shift focus away from the face stimuli and instead rate their own emotional state. The emotional state rating was thought to necessitate shift in focus away from the facial stimuli, calling for an enhancement in controlled processes in the presence of emotion cues. Adults recruited the ventrolateral prefrontal cortex, localized to the inferior frontal gyrus to a greater extent than adolescents during trials requiring this attentional shift, when fearful faces were presented. The authors interpreted this finding as reflecting adults' ability to recruit lateral prefrontal regions to disengage from external emotional cues in order to focus on internal goals, while adolescents recruited this system less efficiently. The observation of a lateral prefrontal locus of activation is interesting and may reflect important differences between this paradigm and those presented in latter sections. For example, in this experiment, activity was not correlated with any behavioral index of disengagement, implying that adolescents may be making use of different psychological strategies to complete the task at hand relative to adults. It will be important for future work to include behaviorally matched samples as well as those with modified performance across ages (presumably indexing the psychological process at hand) to further enable the interpretation of cross-developmental effects (as in Schlaggar et al., 2002).

Hare and colleagues (2008) additionally tested for associations between subcortical limbic and frontal regions implicated in cognitive control. Functional connectivity analyses identified a region of the ventral prefrontal cortex whose recruitment predicted the downregulation of the amygdala and less slowing of reaction times over the course of the experiment. When examining this relationship across development, adolescents under-recruited the ventral prefrontal cortex relative to adults. In other words, this study drew a linkage between under-recruitment of the ventral prefrontal cortex, exaggeration of the amygdala and slowed performance – and this pattern was characteristic of adolescents. In sum, these findings suggest that a limbic-cortical functional network mediates the ability to exert control in the face of emotion, with adolescents showing relatively greater limbic and differential prefrontal recruitment. This functional imbalance results in less efficiency in performing a goal-directed action in the presence of emotional cues.

Paralleling these results in the domain of incentive processing, Galvan also reported differential recruitment of the orbitofrontal cortex (OFC) in a sample including children, adolescent, and adult participants. The OFC is a subregion of the prefrontal cortex that has been shown in adults to represent reward contingencies and exert inhibitory control over risky reward-related impulses (Daw, O#x00027;Doherty, Dayan, Seymour, & Dolan, 2006; Galvan, et al., 2005; see Rolls, 2000 for a review). Galvan and colleagues reported that in adolescents, the OFC increased in response to the receipt of monetary reward (Galvan et al., 2006), similar to that observed in prior reports (May et al., 2004). In addition, adolescents showed spatially diffuse patterns of OFC activity that were more similar to children than adults, in contrast to the extent of activity in the NAcc, that in adolescents was comparable to that of adults. The spatially diffuse activity in the OFC reported by Galvan and colleagues relative to the NAcc serves as a functional marker of brain immaturity (Durston, et al., 2006), providing additional evidence to a functional immaturity of the prefrontal cortex during the adolescent years relative to the earlier and more focal pattern of NAcc activity observed during this age.

In conclusion, subcortical systems critical to reward processing, including the ventral striatum and amygdala, show hyperactive responses to emotion and reward eliciting cues relative to both children and adults. The exaggerated neural responses in these regions lend support to the model proposed earlier, whereby limbic and striatal signals are disproportionately large during the adolescent years. In contrast with the peaking of subcortical emotional and incentive-relevant brain responses, activity in the prefrontal cortex shows a very different trajectory of development. Our model theorizes that the prefrontal cortex undergoes a late-onset linear maturation with age, which is supported by structural and functional data just described. Work to date largely supports the notion that the prefrontal cortex continues to function at immature levels during the adolescent years, and exerts less regulatory control over subcortical regions relative to adults. The hyper-active upregulation of subcortical responses to salient environmental cues, paired with an immature regulatory system, may be responsible for changes in adolescent behavior, and can account for the nonlinear peak in incentive-seeking and emotional behavior often observed in adolescents.

Individual differences bias the responsivity of a subcortical-cortical network

The experiments just described suggest that adolescents tend to show enhanced subcortical responsivity to environmentally salient cues, as well as diminished prefrontal responses in contexts requiring cognitive control. However, simple observation of the raw data points representing the amygdala response in Figure 2A, and nucleus accumbens response depicted in Figure 2B, clearly shows there is substantial individual variability in these responses. In our conceptualization, adolescence in and of itself is a risk factor for the functional ‘imbalance’ discussed previously, but other individual difference factors may also serve as powerful mediators of subcortical-cortical responsivity (See Figure 3). Such individual differences may take form in stable personality traits, differences in neurotransmitter profiles, biologically governed changes in hormones or other effects of puberty, and the social context, such as one’s social status among peers.

The importance of individual differences as a predictor of ‘imbalance’ in subcortical-cortical networks has been demonstrated in numerous experimental contexts, including in some of the experiments described previously. Hare and colleagues (2008) showed that a substantial proportion of variability in the amygdala response to negative stimuli was accounted for by individual differences in trait anxiety irrespective of age, which is consistent with reports in adults indicating that anxiety induces a bias toward limbic hyperresponding (Etkin et al., 2004; Somerville et al., 2004; Stein et al., 2007). In terms of incentive processing, Galvan and colleagues demonstrated that across ages, a substantial proportion of variance in ventral striatal responses to the anticipation of a large reward was predicted by real-life probability of engaging in risky behavior (Galvan et al., 2007). These studies offer initial evidence that individual difference variables, which are often not measured, may play an important role in biasing neural responses to affective and incentive-related cues in adolescents, and in the final sections we will examine some other additional sources of variability that may also modulate these effects. Discussion of other individual difference variables, including variability of neurotransmitter properties across development (particularly for the dopaminergic system) can be found in another article in this volume (Wahlstrom et al., this issue).

The role of gonadal hormones on affective and incentive processing in the adolescent brain

One potential source of influence in ‘imbalanced’ subcortical-cortical responding is individual differences in pubertal hormone levels. During adolescence there is a significant increase in circulating gonadal hormones, which ultimately leads to the process of sexual maturation (Spear, 2000). Gonadal hormone effects on the brain have been conceptualized into either “organizational” mechanisms whereby sex hormones cause permanent changes to neural systems which in turn influence behavior, or “activational” mechanisms whereby sex hormones only influence acute changes and the effects are reversible once the steroids are removed (Cooke et al., 1998). A perspective that is becoming more common is that the acute effects of sex hormones during adolescence may sensitize neural circuits to hormone activation, which in turn allows for the development and maturation of social and sexual behaviors (Romeo, Richardson & Sisk, 2002; Sisk & Zehr, 2005; Steinberg, 2008). In other words, adolescence may be a sensitive period for gonadal hormones to induce organizational effects, which drive social and reproductive behaviors – and potentially, emotional and incentive-seeking behaviors on a larger scale.

Sexual dimorphisms have been reported in both global changes in brain structure (Giedd et al., 1997) as well as differing trajectories for maturation of the amygdala and striatum (Caviness et al., 1996; Giedd et al., 1997, Schumann et al., 2004). Thus, shifts in hormonal levels may be consequential to brain development during this time of life and its associated behavioral changes. In boys (ages 8 – 15yrs), higher basal levels of testosterone correlated with increases in volume in the amygdala (Neufang et al., 2009). This recent finding suggests that gonadal hormones may have activational effects on regions that were shown to be responsive to emotionally salient information. Because adolescence is a time when hormones levels are heightened (Norjavaara et al., 1996), it is possible that these hormones serve as an important individual difference measure in mediating emotion and incentive-seeking behavioral and neural responses in adolescents.

Studies in adolescents also show a link between changes in hormones and social behaviors. In adolescent boys, lower levels of testosterone and testosterone levels that decreased more slowly during the day had greater levels of anxiety, depression and attention problems irrespective of pubertal development, while in adolescent girls, steeper declines in testosterone during the day correlated with greater disruptive behavior (Granger et al., 2003). In adolescent boys and girls, acute increases in gonadal hormones correlated with greater affiliations with risk-taking peers (Vermeersh et al., 2008a; Vermeersh et al 2008b) and higher social dominance (Schaal et al., 1996) suggesting that the social environment and gonadal hormones may interact to predict individual differences in incentive and social behaviors.

While there may be a link between fluctuating hormones influencing behavior it is also important to consider the role of gonadal receptor genes, which act to mediate circulating gonadal hormones. A recent study (Perrin et al., 2008) showed variability in white matter volume in adolescent boys was mediated not only by testosterone levels but by a genetic polymorphism in the androgen receptor (AR) gene, such that boys with the short AR gene with higher testosterone levels had a greater increase in white matter volume than those with the long AR gene. This suggests the important role of genetics in understanding the activational and organization effects of hormones.

The influence of peers on affective and incentive processing in the adolescent brain

Relations with peers takes on a heightened importance in adolescence (Steinberg, 2005), rendering it a potential source for mediating changes in affective and incentive behavior. On one hand, adolescents as a group may show enhanced sensitivity to social cues, particularly those generated by peers, as compared to adults and children. Additionally, individual differences in sensitivity to peers may be particularly relevant in biasing adolescent behavior.

Recent studies have attempted to understand the influence of peers on biasing behavioral and neural responses to affectively relevant cues. Grosbras et al. (2007) reported adolescents who were highly resistant to peer influence had less right dorsal premotor cortex and left dorsolateral prefrontal cortex activity while watching angry hand movements and facial expressions, versus those with lower resistance to peer influence. This suggested that individuals who are particularly sensitive to peer pressure may have an increase in motor preparation to angry movements and may engage more attention when viewing emotionally salient information. Guyer et al. (2008b) reported that female adolescents who interacted with high and low interest peers in a virtual chat room task had greater activity in the nucleus accumbens, hypothalamus, hippocampus and insula to high versus low interest peers. All of these regions, besides the insula, had age-related increases in activity suggesting a hyperresponding in reward-sensitive regions to socially desirable peers. These findings implicate the reward systems discussed earlier as potentially mediating the enhanced salience of social interactions during adolescence.

Both of these studies have attempted to elucidate the neural basis of peer influence on affective processing, yet are limited in their ability to inform neural responses during actual social interactions. In other words, during the experiments just discussed, participants do not believe they are actually interacting with peers. Work in adults has attempted to mimic real-life social interactions inside of the fMRI scanner and measure neural responses to ostensible social inclusion and exclusion (Eisenberger et al., 2003; Somerville et al., 2006). Work is presently underway to develop paradigms in which adolescents are simulating or experiencing real social exchanges, and it will be of interest to assess the contribution of brain regions in reward and affective networks in mediating social behavior and monitoring the outcomes of peer interactions.

Caveats and limitations

The research just described, primarily conducted in just the past five years, has made remarkable strides in characterizing the nature of emotion and reward responding in the adolescent brain. However, it should be pointed out that the number of experiments on this topic is still relatively few and caution should be taken in drawing unequivocal conclusions from them. More studies with larger samples sizes are called for to fully elucidate the nature of limbic-striatal-prefrontal interactions and their relation to adolescent behavior. In addition, testing children, adolescents, and adult subjects in a single experiment is critical for identifying nonlinear changes, because adolescents are expected to differ from both groups. This is rarely tested within a single experiment.

In terms of striatal and limbic functioning in adolescents, evidence has converged nicely in support of the idea that both systems show an exaggerated response profile in adolescents. To understand adolescent reward and emotional behavior, prefrontal control mechanisms must be taken into account, but relatively few experiments have assessed the role of the prefrontal cortex in mediating these behaviors. In addition, many experiments have discussed prefrontal responses with relative imprecision in terms of which particular area within the prefrontal cortex was active and discussing it within the context of its associated literature. The prefrontal cortex is a large area of the brain with heterogeneous subregions varying in function, architecture, inputs and outputs. Future work, both in adults and adolescents, will likely allow for greater understanding of prefrontal subdivisions and their relation to limbic and striatal function across development.

Conclusions

Relative to adults and children, adolescents engage in disproportionately risky behaviors, which can lead to a wide variety of negative outcomes including substance abuse, unprotected sex, injuries, and suicide. Many of these behaviors are at least in part mediated by incentive and emotional responding, be it inappropriate appetitive behavior leading to risky approach of potential rewards, or the outcome of experiencing extreme negative affect such as self-harm and suicide. Emotional and incentive-related behaviors are intimately linked to these risks, and understanding the role of developing brain systems in mediating these behaviors is of inherent importance to adolescent health.

Human structural and functional imaging studies have begun to shed light on the complex changes occurring in the brain at this time of life, and their relationship to adolescent behavior. At this point, it appears that the differential trajectories of subcortical limbic and reward-sensitive regions in the striatum, relative to late-maturing control regions in the prefrontal cortex, may lead to adolescent behavioral changes characterized by enhanced sensitivity to environmental cues without appropriate behavioral inhibition. A host of individual differences also appear to be critical for predicting heightened risk for this behavioral profile, which are just beginning to be explored empirically. Relatively mature emotional and reward systems left unchecked by prefrontal control systems may be the key neural ‘imbalance’ that leads to the nonlinear, unique behavioral profile of adolescents. It is hoped that continued work in this field will improve our understanding of this fascinating and complex time of life.

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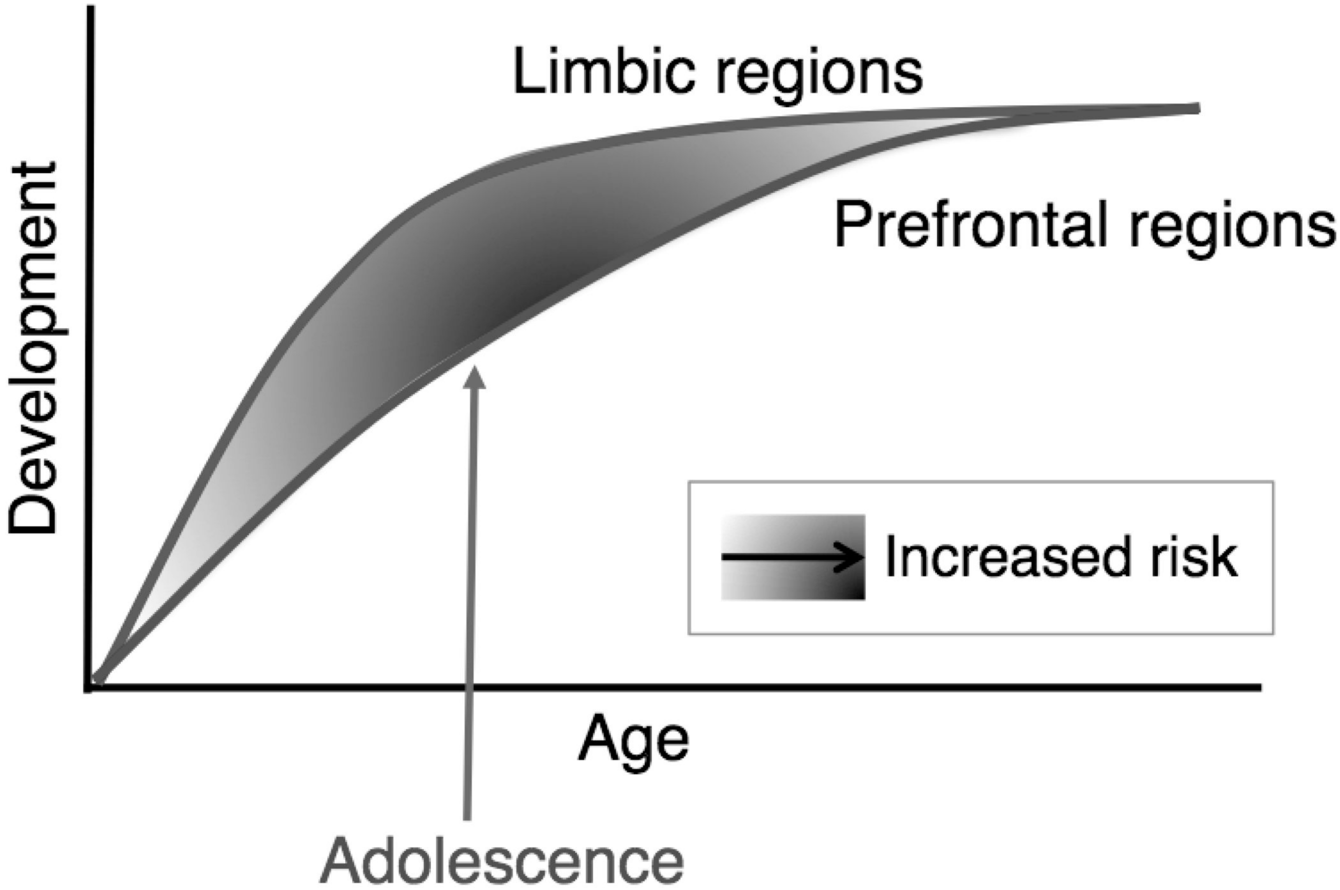

Figure 1.
Model for enhanced affective and incentive-based behavior in adolescence. Early maturation of subcortical regions such as the amygdala and ventral striatum (red line), combined with late maturation of prefrontal cortical regions (blue line), predicts a nonlinear enhancement in affectively-driven behavior during adolescence.

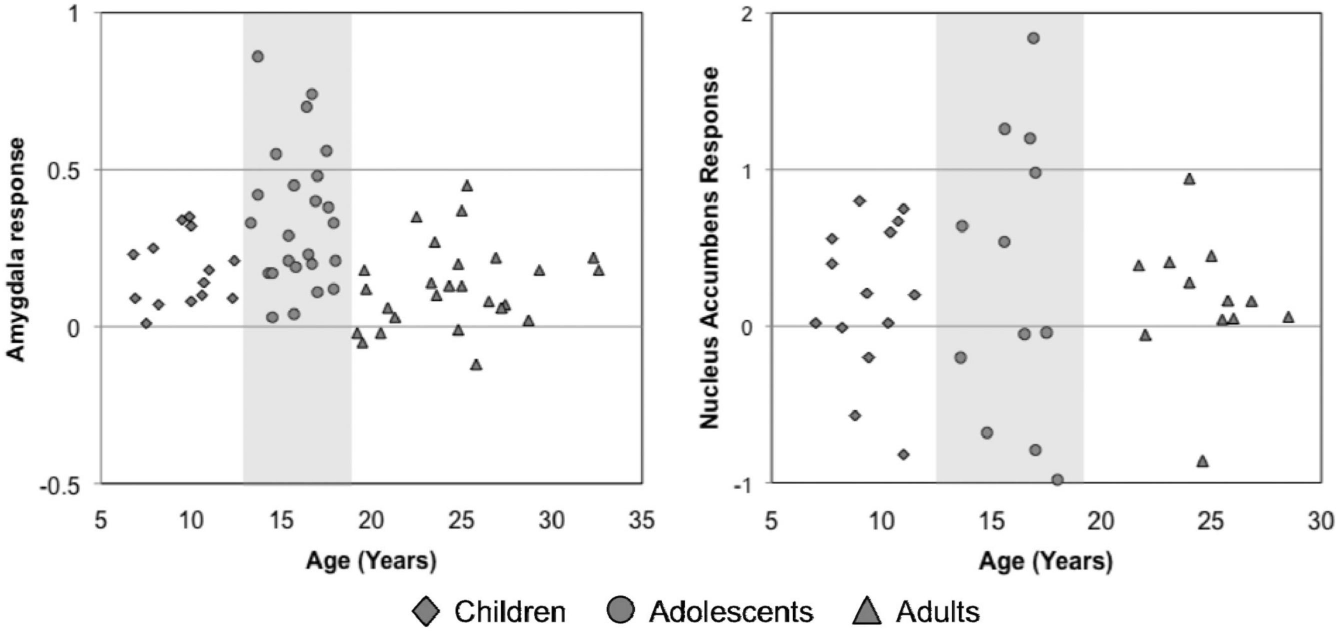

Figure 2.

(A) Amygdala response to facial expressions of emotion was significantly greater in adolescents than children or adults. Adapted from Hare et al., 2008, *Biological Psychiatry*. (B) Nucleus accumbens response to receiving a large monetary reward was significantly greater in adolescents than in children or adults. Adapted from Galvan et al., 2007, *Developmental Science*.

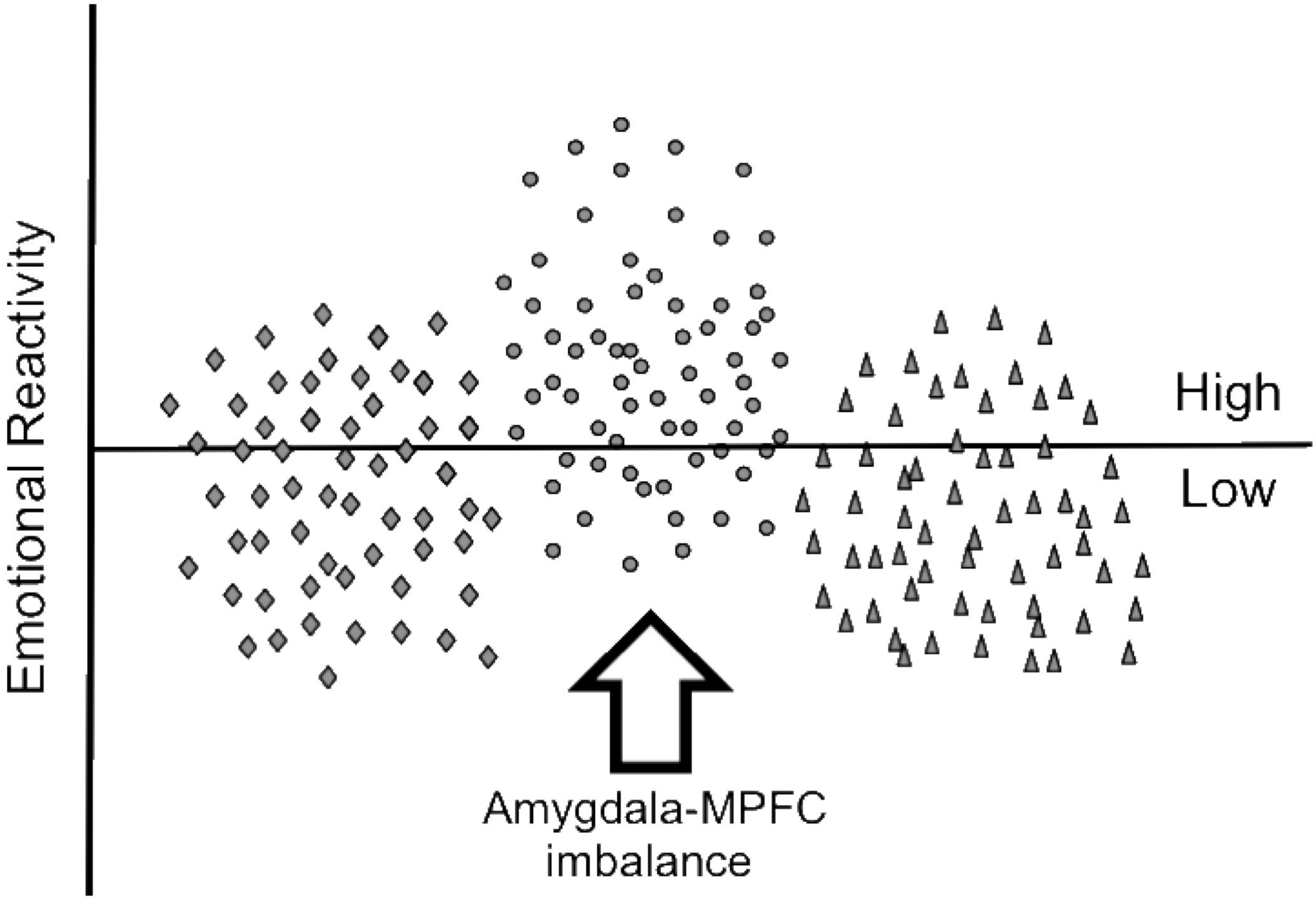

Figure 3.

Schematic representation of age and individual differences as compound risk factors for predicting highly emotional and risky behavior in adolescents.