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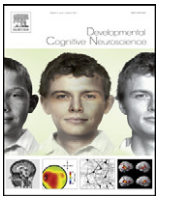

Review

Rewards, aversions and affect in adolescence: Emerging convergences across laboratory animal and human data

Linda Patia Spear*

Department of Psychology and Center for Development and Behavioral Neuroscience, Binghamton University, Binghamton, NY 12902-6000, USA

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ABSTRACT

The adolescent transition is associated with increases in reward- and sensation-seeking, peer-directed social interactions, and risk-taking, with exploratory use of alcohol and other drugs often beginning at this time. These age-related behaviors may have biological roots embedded in the evolutionary past, with similar adolescent-typical characteristics evident across a variety of mammalian species. Drawing across human behavioral and fMRI data and studies conducting in laboratory animals, this review examines processing of rewards, aversions, and affect in adolescence. Evidence for both hyper- and hypo-reactivity during adolescence in the processing of rewards is reviewed, along with possible contributors to these differences. Indications of sometimes heightened reward reactivity during adolescence are contrasted with frequent attenuations in adolescent sensitivity to aversive stimuli. At the same time, adolescents appear particularly prone to becoming emotionally aroused, especially in social contexts. Emerging evidence hints that exaggerated adolescent reactivity in reward and affective systems may be promoted in part by unusual strong cross-reactivity between these systems during adolescence. Such age-related propensities may promote adolescent risk taking, especially in social and exciting contexts, and contribute to adolescent-typical propensities to attach greater benefit and less cost to risky behaviors such as alcohol and drug use than individuals at other ages.

Contents

* Tel.: +1 607 777 2825; fax: +1 607 777 6418.
E-mail address: Lspear@binghamton.edu

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Adolescents often differ from children and adults in the ways they interact with and react to stimuli in their environment. Their social orientation shifts, with marked elevations in the importance of and time spent interacting socially with peers (e.g., Hartup and Stevens, 1997; Brown, 2004). With the hormonal and physiological changes associated with puberty and the processes of sexual maturation, romantic and sociosexual interests begin to emerge (see Forbes and Dahl, 2010). Adolescents often pursue new and exciting stimuli and situations (i.e., novelty- and sensation-seeking) more avidly than younger and older individuals (see Steinberg, 2007, for review). The adolescent period is also characterized by increases in consumption of palatable substances (not withstanding the dieting often seen in female youth in cultures where the media promotes thinness), along with an associated growth spurt (Post and Kemper, 1993). It is during adolescence that individuals typically first initiate use of alcohol and other drugs, with some exploratory use of alcohol being normative by 14 years or so in the United States (Johnston et al., 2009).

Adolescent-associated alterations in social behavior, increases in risk-taking, and elevations in drug use appear to be conserved evolutionarily, with organisms undergoing the transition from dependence to independence across a variety of mammalian species generally showing seemingly similar basic behavioral attributes as outlined above as well as relatively comparable pubertal and other physiological changes (see Spear, 2000, for review). For instance, even in a simple rodent model, adolescent rats exhibit transient age-related increases in peer-directed social interactions, novelty-seeking/risk taking, and consummatory behaviors, and voluntarily consume 2–3 fold more ethanol than their adult counterparts (see Spear, 2000, 2007; Doremus et al., 2005, for review). Such age-associated behavioral commonalities are thought to have been maintained over evolutionary history because of their overall adaptive significance, with for instance the adolescent focus on peer-directed social behavior and elevations in risk-taking postulated to facilitate the transition to maturity as well as to encourage emigration as a strategy for avoiding inbreeding depression (see Steinberg and Belsky, 1996; Spear, 2000, for review and discussion).

Such an evolutionary view suggests that adolescent-typical increases in risk-taking, exploratory drug use and other age-related behaviors are influenced in part by biology persisting from our evolutionary past. Indeed, rapid progress is being made both in studies with laboratory animals and with human adolescents showing age-related alterations in motivational, affective and cognitive control systems that influence the processing of and responding to rewards, with relevant data and theories proliferating rapidly. Among the influential theories that have emerged is that of the Casey group (e.g., Casey and Jones, 2010) suggesting that adolescent-typical increases in risky behaviors and propensity for substance abuse are related to "tension between early emerging 'bottom-up' systems that express exaggerated reactivity to motivational stimuli and later maturing 'top-down' cognitive control regions" (p. 1197)—systems that are exemplified by the striatum and prefrontal cortex (PFC), respectively. With time and the maturation of top-down control, early maturing striatal systems are thought to gradually lose their "competitive edge", resulting in the gradual emergence of behaviors more typical of the adult. Similar themes have emerged with other groups, with adolescence, for instance, characterized as a time of hypersensitive striatal approach systems that outweigh underdeveloped PFC regulatory systems (Fareri et al., 2008) or of more influential "pro-motivational systems" (largely driven by the dopamine [DA] neurotransmitter system) within a context of immature inhibitory substrates in the PFC (Chambers et al., 2003).

A somewhat different approach was taken by Luciana and colleagues (e.g., Wahlstrom et al., 2010). They suggested that DA "overdose" in the PFC during adolescence results in a bias toward greater input from limbic areas such as the amygdala and weaker input from the PFC into the ventral striatum/nucleus accumbens (nAc), a region critical for processing information about rewards (and to some extent punishments). Other models as well have included a critical limbic component in addition to PFC and ventral striatum/nAc. Perhaps the best-known example is the "triadic model" of Ernst and colleagues (e.g., Ernst et al., 2005a; Ernst and Fudge, 2009) where adolescence was characterized by age-related alterations in activity in three overlapping neural systems: an approach system (exemplified by the ventral striatum) that is more active than in the adult; an avoidance ("harm-avoidant") system (represented in part by the amygdala) that is less active than in the adult: and a modulatory system (ventral and medial PFC [mPFC]) that undergoes protracted development through adolescence. This influential model was one of the first to consider that adolescence might be characterized not only by alterations in approach behavior toward rewarding stimuli, but also by alterations in responsiveness to aversive stimuli as well.

Essentially all theories of adolescent development concur on the importance of delayed maturation of frontal cognitive control regions such as the PFC. There is also emerging consensus that under some circumstances adolescence appears to be characterized by hyperreactive DA/nAc reward-related systems (see Galvan, 2010; Wahlstrom et al., 2010, for excellent reviews), along with compelling evidence for adolescent hyporeactivity in these systems under certain circumstances as well (e.g., Geier and Luna, 2009; Bjork et al., 2010a—reviewed in Doremus-Fitzwater et al., 2010). Fewer theories have keyed in on sensitivity to aversive stimuli, with some suggestions that adolescents are characterized by less sensitive avoidance systems (e.g., Ernst et al., 2005a; Cauffman et al., 2010) contrasting with others presenting adolescents as exhibiting exaggerated responses to both rewarding and aversive stimuli (e.g., Somerville et al., 2010). And, although many researchers include emotional/affective state in their discussions of adolescent neurobehavioral function, there seems little consensus at present as to how affect is viewed as an emergent property and/or critical contributor to adolescent-typical neurobehavioral function.

Drawing on data both from studies in human adolescents and in laboratory animals, material will be reviewed to support the following working hypotheses:

(a) Consistent with the complexity of the DA alterations seen in adolescent forebrain, ventral striatum/nAc reward-relevant systems are not simply early maturing or hyper-reactive, but rather display differential age sensitivities characterized by: (1) often enhanced reactivity when receiving (or preparing to respond for) rewards, but (2) sometimes attenuated sensitivities to cues associated with those rewards. As hypothesized by Luciana and colleagues (Wahlstrom et al., 2010), these changes may be related in part to developmental alterations in DA balance across brain regions (although seemingly not in the direction proposed by Spear, 2000),
(b) Adolescents, conversely, appear generally less sensitive to aversive stimuli – including the aversive properties of rewarding drugs – than do adults, and often respond differently than adults to cues and contexts associated with these stimuli (in ways that could potentially promote fear reinstatement or stress-induced drug seeking).
(c) Adolescents appear particularly prone to becoming emotionally aroused in part because of unusually strong reactivity and cross-reactivity between reward-relevant areas (such as the ventral striatum/nAc) and regions critical for processing arousing, emotionally provoking stimuli (such as the amygdala and insula). As a result, emotional or socially stimulating situations may further exacerbate adolescent propensities toward enhanced responsiveness when receiving (or responding for) rewards but attenuated sensitivities to aversive stimuli, thereby perhaps encouraging adolescents to attach greater benefit but less cost to risky behaviors (including drug use) under these circumstances.

1. Sensitivity to rewards in adolescence

Signs of enhanced responsivity to positive rewards have been reported during adolescence, with sensitivity to rewards often peaking in adolescence at rates higher than that earlier and later. For instance, Steinberg et al. (2009) found that self-reported reward-seeking demonstrated an inverted U-shaped function, peaking at 12–15 years of age at rates higher than seen at younger or older ages. Using a gambling task involving advantageous and disadvantageous decks of cards where reward-seeking was indexed via sensitivity to the positive feedback provided by advantageous decks, reward-seeking was reported to rise to peak beginning at 14–15 years of age, with declines in this measure seen after 21 years (Cauffman et al., 2010). Likewise, an inverted U-shaped developmental function peaking during adolescence was also reported for sensation seeking, with peak levels reached at around 17–18 years of age when defined using a scale with questions such as: "I like to explore strange places" and "I like to do frightening things" (Romer et al., 2010). Even in terms of sweet preferences, individuals tested early in adolescence (from 11 to 15 years of age) were found to be more sensitive to sweet substances than when tested during late adolescence/emerging adulthood (19–25 years) (Desor and Beauchamp, 1987).

Studies conducted in our laboratory and others likewise have found adolescent rats to be more sensitive than their adult counterparts to the rewarding properties of a variety of positively rewarding stimuli. These include food and palatable tastants (Vaidya et al., 2004; Wilmouth and Spear, 2009; Friemel et al., 2010), as well as the rewarding effects of social peers (Douglas et al., 2004) and novelty (Douglas et al., 2003) when indexed via conditioned place preferences (CPP)—i.e., by expressing a preference for a location previously paired with exposure to a novel or social stimulus relative to an equally familiar location not paired with such stimuli. Similar studies have often found adolescent animals to also be more sensitive than their adult counterparts to the rewarding consequences of a variety of drugs, including cocaine (e.g., Brenhouse and Andersen, 2008; Brenhouse et al., 2008), nicotine (e.g., Shram et al., 2006; Torres et al., 2008), and alcohol (e.g., Pautassi et al., 2008), although such age differences are not always apparent (Aberg et al., 2007; Campbell et al., 2000). Adolescent rats are not only more sensitive than adults to the rewarding effects of alcohol, but also to the facilitation of social behavior by alcohol, perhaps enhancing alcohol's rewarding properties further in social contexts (e.g., Varlinskaya and Spear, 2002). Given these notable differences in how adolescents respond behaviorally to rewarding stimuli, it is not surprising that adolescents differ notably from adults in their brain reward neurocircuitry and how they process and respond to rewarding and aversive stimuli.

1.1. Brain reward circuitry in adolescence

Novel and exciting stimuli, as well as alcohol and other drugs used for their rewarding effects, tap into phylogenetically old brain reward circuitry that is critical for seeking out, finding and "consuming" survival-essential natural rewards such as food, water, sexual reproduction and other social rewards. In both basic science studies as well as human imaging work, marked transformations are seen in this reward circuitry during adolescence.

Major components of the reward system that undergo particularly dramatic change during adolescence include projections from DA neurons deep in the base of the brain to subcortical regions including the dorsal and ventral striatum, limbic regions such as the amygdala and hippocampus, as well as the prefrontal cortex (PFC) and other cortical regions (e.g., see Berridge, 2004). A particularly critical node in this reward-related neurocircuitry is the ventral striatum (especially the nAc region located within it), with the nAc thought to contribute to directing behavior toward appropriate goals via integrating affective, contextual, and goal-directed information provided by excitatory (glutaminergic) inputs from the amygdala, hippocampus and portions of the PFC, respectively (e.g., Grace et al., 2007). Competition among these different regions for conveying their interpretations of ongoing activities to the nAc appears controlled in part by DA activity in nAc, with relatively high functional DA levels there inhibiting afferent PFC input to nAc while facilitating information flow from limbic afferents into the region (Goto and Grace, 2008).

Even when considering the mature brain though, controversy still reigns as to how these DA projections, their forebrain targets, interconnecting circuitry, and associated brain regions contribute to different aspects of reward-related processing (e.g., see Baxter and Murray, 2002; Cardinal et al., 2002; Berridge and Kringelbach, 2008). Fundamental questions that are still being discussed include the extent to which reward sensitivity is modulated by DA or non-DA systems (e.g., Gardner, 1999; Robinson and Berridge, 2003), whether reward seeking is a result of less active or hypersensitive DA systems and under what circumstances (e.g., Volkow et al., 2003, 2007; Robinson and Berridge, 2003), and the degree to which the nAc and its DA input contribute to the processing of not only rewarding, but also aversive stimuli (see Carlezon and Thomas, 2009; Matsumoto and Hikosaka, 2009). Some researchers have drawn distinctions between anticipatory/"wanting" vs. consummatory/"liking" of rewards, with the former DA-dependent and the latter largely reflecting non-DA (opiate and cannabinoid) systems (Robinson and Berridge, 2003). These ongoing controversies provide special challenges for assessments of brain reward circuitry and their significance during adolescence.

Marked developmental alterations are seen in the DA system through adolescence and into adulthood, as reviewed recently elsewhere (Ernst et al., 2009; Galvan, 2010; Wahlstrom et al., 2010). For instance, DA firing rates have been reported to rise during adolescence in rats to peak late in adolescence prior to declining thereafter (McCutcheon and Marinelli, 2009). DA concentrations and the density of DA fibers projecting to PFC increase into adolescence (Benes et al., 2000), as do the number of PFC projections to the nAc (Brenhouse et al., 2008). Developmental increases in DA regulation of PFC activity emerge late in adolescence, with critical populations of inhibitory neurons only becoming responsive to activation by the D2 subtype of DA receptors at that time (Tseng and O'Donnell, 2006). The density of DA receptor sites peaks in dorsal striatum early in adolescence in humans and laboratory animals, followed by losses of one-third to almost 50% of these receptors by young adulthood (Seeman et al., 1987; Tarazi and Baldessarini, 2000; Teicher et al., 2003). Similarly timed, but more modest (20–35%) inverted U-shaped developmental rises and declines have been reported in ventral striatum (Andersen, 2002; Tarazi and Baldessarini, 2000; but see also Andersen et al., 2000). In contrast, DA receptor density in PFC does not peak until late adolescence, with pruning of these receptor populations not occurring until young adulthood (Andersen et al., 2000; Weickert et al., 2007). Inverted U-shaped adolescent peaks and later declines are also evident in other reward-critical receptor systems, with for instance cannabinoid receptors peaking during adolescence in dorsal striatum and limbic forebrain and declining thereafter (Rodriguez de Fonseca et al., 1993).

From such studies, it is abundantly clear that DA and other reward-relevant neurocircuitry undergo substantive alterations during adolescence, with not only the losses of up to 50% of the DA receptors in some reward-relevant regions as discussed above, but also marked (2–7 fold) changes in regional levels of DA activity (i.e., "DA tone"—see Andersen, 2002). Yet, it is not straightforward to relate these developmental changes to alterations in reward processing during adolescence. The DA system is highly regulated and it can be challenging to determine which DA alterations are primary versus compensatory, and hence whether a particular change that was observed reflects developmentally enhanced increases or decreases in DA function (see Ernst et al., 2009, for further discussion). For instance, elevated baseline (tonic) levels of DA tone influence how easily the DA system can be acutely activated (phasic activity) (see Goto et al., 2007), and hence the measure chosen to index DA function (e.g., assessment of extracellular, tonic levels of DA via microdialysis vs. estimates of phasic DA release indexed via voltammetry [see Robinson et al., 2011]) can drive the nature of the conclusions reached regarding age-related changes in DA and reward-related functions.

Observed developmental changes often vary regionally and could reflect ontogenetic shifts in the balance of DA activity across brain areas, finding consistent with other evidence for complementarity in DA activity across brain regions (Zigmond et al., 1998). An early hypothesis, though, that DA balance in adolescence is characterized by a predominance of cortical over subcortical DA systems that is further exacerbated by stress (Spear, 2000), failed to take into consideration mounting evidence for "inverted U-shaped" functional influences of DA in PFC, with too little or too much DA activity both leading to impaired PFC function (Arnsten, 2009). Drawing in part on this work and data from individuals with polymorphisms that influence regional levels of DA activity, Luciana and colleagues (e.g., Wahlstrom et al., 2010) have developed a promising alternative hypothesis: that tonic DA levels are sufficiently high during adolescence that DA levels in PFC rise beyond optimal levels, resulting in a PFC DA "overdose" that allows DA activity to predominant in subcortical regions such as the nAc. In work conducted in rats, DA synthesis in PFC was found to be subject to negative feedback regulation early in life, with this synthesis regulation disappearing during adolescence (e.g., Andersen et al., 1997; Dumont et al., 2004)—a loss of feedback control over DA synthesis that could contribute to the vulnerability of the PFC to DA "overdose". Any such shift in DA functional balance could have pronounced consequences on the competition between PFC and limbic regions for control of information within the nAc, given that greater functional levels of DA activity in the nAc shifts information flow toward greater limbic and less PFC influence on the nAC (see Grace et al., 2007, for review). Given the greater stressor sensitivity of the DA projections to PFC than to subcortical terminal regions (e.g., Dunn, 1988), any adolescent DA "overdose" in PFC would seemingly be further exacerbated by stressors, shifting the functional balance toward even greater subcortical DA influences under stressful and arousing conditions (Arnsten, 2009).

1.2. Processing of rewards in adolescence

Evidence is mounting in human fMRI studies that the ventral striatum of the adolescent processes rewarding stimuli differently than do adults, with compelling signs,

however, for both adolescent-associated accentuations as well as attenuations in activity in this region during different stages of reward-related processing (e.g., see Bjork et al., 2010a; Geier et al., 2010). For instance, in an antisaccade visual task requiring inhibition for successful performance, adolescents were found to show attenuated ventral striatal activation relative to adults during cue assessment, overactivity during response preparation, with no age differences evident during reward feedback (Geier et al., 2010). In gambling tasks or other reward receipt situations, although the data are mixed, arguably the strongest evidence is for greater ventral striatum activation among adolescents than adults in response to *reward receipt* (see Galvan, 2010, for review), with some evidence as well for attenuated ventral striatum activation during *reward anticipation* (e.g., see Bjork et al., 2010a). Such data support the possibility that adolescence may be characterized by both underactive and overactive reward systems at different points in the processing of reward-relevant stimuli, as discussed further below (see also Geier and Luna, 2009).

The distinction between reward anticipation vs. reward receipt in the imaging literature in humans is reminiscent of the anticipatory/"wanting" vs. consummatory/"liking" distinctions drawn by Robinson and Berridge (2003). According to this view, "wanting" is thought to reflect incentive salience or desire for the reward (and in the case of addictive drugs, is prone to sensitize with repeated exposures) whereas "liking" reflects the hedonic, affective reaction to rewarding stimuli. Although these two reward components often function similarly in intact adults, Robinson and Berridge (2003) provide converging evidence largely from basic science studies that these systems are mediated via different neural systems and can be dissociated experimentally. And as outlined below, recent (largely behavioral) studies in laboratory animals suggest that these two reward-related distinctions also may be dissociable developmentally, and in ways reminiscent of the reward anticipation versus reward receipt distinction that has emerged as important when characterizing differences between adolescents and adults in the fMRI literature.

1.2.1. Reward anticipation/"wanting"

During *cue assessment* and when *anticipating* a reward, in a number of fMRI studies, human adolescents have been reported to show less activation in the ventral striatum than adults (Bjork et al., 2004; Geier et al., 2010; Bjork et al., 2010a). This ventral striatal underactivation, however, was not seen when adolescents were responding to a cue signaling an uncertain reward possibility (Van Leijenhorst et al., 2010a,b), perhaps reflecting once again the complexities of reward processing. At first blush, any evidence for attenuated ventral striatal responses during cue-induced anticipation among adolescents seems counterintuitive, given the avidity with which many adolescents pursue new sensations and alcohol/drugs. Yet, individuals with attentional-deficit/hyperactivity disorder (Scheres et al., 2007; Ströhle et al., 2008) or a family history of alcoholism (Andrews et al., 2010) likewise exhibit less activation in ventral striatum than control subjects during reward anticipation, with the magnitude of this hypoactivation correlated with impulsivity ratings in both cases. Similar attenuations in ventral striatal responses have been reported during reward anticipation among young smokers relative to age-matched non-smokers, with the magnitude of this ventral striatal response negatively correlated with smoking frequency (Peters et al., 2011). Yet, other types of individual differences linked to increases in risk taking or impulsiveness (e.g., externalizing disorder, Bjork et al., 2010b) are associated with alterations in reward receipt but not reward anticipation (see Section 1.2.2). Work remains to determine the circumstances under which these different ventral striatal responses are linked to specific adolescent behaviors, a point to which we return later.

Studies in laboratory animals to examine anticipatory "wanting" during development have focused nearly exclusively on behavioral responses to reward-predictive cues. In these studies as well, there are clear indications that, at least when using tests of sign-tracking to index "wanting" (Robinson and Berridge, 2003), adolescents frequently exhibit less anticipatory responding than do adults. "Sign-tracking" refers to approach behaviors directed toward a cue that predicts an upcoming, response-independent delivery of a reward (a palatable food pellet). We have found non-deprived adolescents to consistently exhibit notably less sign-tracking than adults (Doremus-Fitzwater and Spear, 2011; Anderson and Spear, 2011; Ung et al., 2010). This marked alteration in sign-tracking behavior to a cue predicting an upcoming reward seen in adolescence is generally evocative of the attenuated adolescent response to reward-predictive cues seen in the human fMRI data.

The attenuation in sign-tracking during adolescence does not appear related in any simple manner to difficulties learning that the cue predicts reward, in that adolescents and adults did not differ in goal-tracking behavior (i.e., approaching during cue presentation the location where the upcoming reward will be delivered) (Anderson and Spear, 2011). A perhaps more likely possibility is that the adolescent attenuation in sign-tracking reflects broader age-associated predispositions in the processing of consequence-predictive cues and contexts, perhaps driven in part by ontogenetic alterations in amygdala/PFC regions and their interactions, as discussed in Section 2.3. Indeed, sign tracking is an amygdala-, anterior cingulate cortex- and nAc DA-dependent behavior (Everitt et al., 1999).

1.2.2. Reward receipt/"liking"

In contrast to the sometimes attenuated fMRI activation seen in the ventral striatum among adolescents when anticipating rewards, adolescents have been reported by a number of groups to show heightened activation of the ventral striatum during *receipt* of rewards relative to younger and/or older individuals (Ernst et al., 2005a; Galvan et al., 2006; Cohen et al., 2010; Van Leijenhorst et al., 2010a,b)—findings supportive of a hyper-responsive striatal reward system (see Galvan, 2010) and reminiscent of the inverted U-shaped developmental curves of reward- and sensation-seeking (Steinberg et al., 2009; Cauffman et al., 2010; Romer et al., 2010) discussed earlier. Such findings are clearly not ubiquitous, however, with some groups finding no evidence of enhanced ventral striatal responses to receipt of rewards during adolescence (Bjork

et al., 2004, 2010a; Holm et al., 2009; Forbes et al., 2010), along with evidence for a post-pubertal decline in striatal reactivity to reward outcome (Forbes et al., 2010). While there is not a sufficient database of studies as yet to disentangle potential contributors to these variable findings, likely suspects include differences across studies in the processing phase(s) during which scans were collected, the nature of the baseline used as well as type of task and response required (if any), and the type, magnitude and frequency of reward (see Galvan, 2010 for an excellent discussion of the complexities of interpreting such fMRI data). Context is also likely important, including whether reward magnitude is varied across trials, the nature and timing of feedback, and whether possible outcomes also include losses or punishment. Indeed, there is evidence to suggest that the relationship between ventral striatal activation and reward magnitude may be exaggerated during adolescence, with human adolescents tending to show weaker responses in the ventral striatum to small rewards (Galvan et al., 2006), but showing more dramatic signal increases (Galvan et al., 2006) or more sustained activation (Delgado et al., 2000) in ventral striatum to rewards of larger magnitude than do adults.

Studies of individual differences in ventral striatal responses to reward receipt have also revealed enhanced ventral striatal reward responses under some (but not all) conditions associated with increased risk-related behaviors. In a study of risky decision making, Galvan et al. (2007) observed that increased nAc activity to rewards correlated with increases in risky behavior during adolescence. Likewise, individuals high on the Behavioral Activation Scale (BAS) (Simon et al., 2009) as well as individuals with externalizing disorders (Bjork et al., 2010b) also were found to exhibit greater increases in ventral striatal activation to reward receipt than those without these characteristics. Further exploration of individual differences along a variety of dimensions may prove useful in disentangling the conditions under which ventral striatal responses to reward anticipation vs. reward receipt are predictive of risk behaviors among youth.

In laboratory animals, studies using voltammetry to assess subsecond, phasic DA release in the ventral striatum of rats have shown that, as in human imaging studies, the nature of the reward can influence age differences in the ventral striatal response to reward. In response to a variety of types of novel sensory (visual, olfactory and auditory) stimuli, adolescent rats were found to exhibit attenuated DA transients in the ventral striatum when compared with adults, whereas they exhibited greater DA release to a highly palatable food reward (Ung et al., 2010; Robinson et al., 2011). Enhanced neural activation to food-related stimuli during adolescence was also seen using expression of the immediate early gene, c-fos to index activation to presentation of a cue associated with access to a palatable food reward, with greater c-fos activation in portions of the nAc in mid- to late-adolescent rats than in adults (Friemel et al., 2010).

Using a variety of behavioral measures thought to reflect hedonic "liking", adolescent rats as well have been found to exhibit greater "liking" responses to rewarding stimuli than adults under a number of circumstances, with adolescent rats exhibiting greater hedonic "liking" than their mature counterparts when indexed via such traditional measures as consumption of sucrose or other highly palatable substances (e.g., Vaidya et al., 2004; Wilmouth and Spear, 2009; Friemel et al., 2010) as well as via taste reactivity to sucrose (Wilmouth and Spear, 2009). Yet, as is becoming a frequent mantra in the complex human imaging and animal literature on adolescent reward sensitivity, signs of enhanced "liking" are not ubiquitous. A major exception in this case is in work using 50 kHz ultrasonic vocalizations (USVs) to index positive affect in rats (Blanchard et al., 1993; Burgdorf et al., 2000), where adolescent rats were found to produce significantly fewer USVs (but more social behavior) during social interactions (Willey et al., 2009).

The overall picture that emerges in these studies of both human and rat adolescents is that depending on the specifics of the rewarding stimulus and other aspects of the testing circumstances, adolescents often show elevated hedonic, "liking" responses to reward receipt relative to adults, while conversely sometimes showing attenuated anticipatory/"wanting" responses to cues predicting those rewards, In almost all cases, however, there are various exceptions to these generalities that may ultimately provide clues leading to the next iteration in our understanding of how adolescents process rewards and reward-relevant stimuli.

2. Adolescent sensitivity to aversive stimuli and punishments

There are substantial data in laboratory animals that adolescents' sensitivity to aversive stimuli is notably attenuated when compared with adults. As we shall see, the data in human adolescents are more limited and the interpretations vary. On the one hand, based in part on the results of fMRI imaging data showing attenuated amygdala responses to aversive outcomes and negative-valenced stimuli during adolescence, Ernst et al. (2005a) suggested in their triadic model that adolescents have a less active amygdala "harm avoidant" system than adults. Although harm avoidance could reflect a number of alterations other than sensitivity to aversive stimuli per se (such as the capacity to inhibit responding to avoid aversive outcomes), this view is generally consistent with the findings to date in laboratory animals.

On the other hand, drawing on data such as declines in average affect from early-to-mid adolescence (approx. 11–16 years) (e.g., Larson et al., 2002) and imaging data showing exaggerated amygdala responses to faces displaying negative emotional states during adolescence (e.g., Monk et al., 2003; Guyer et al., 2008), Somerville and Casey (2010) concluded that human adolescents show "exaggerated responses to both positive and negative environmental cues. . .relative to children and adults" (p. 126). Yet, age differences in overall levels of negative affect may not be necessarily driven by a greater responsiveness to aversive environmental stimuli during adolescence, but rather by other factors. For instance, given associations between life stress and affect (e.g., Larson et al., 2002), increases in negative affect across early adolescence could reflect greater exposure to stressors during this develop-

mental transition (see Spear, 2000, for discussion) rather than an increased sensitivity to aversive stimuli and punishment per se.

2.1. The adolescent brain and aversive stimuli

The neurocircuitry involved in responding to and learning about aversive and noxious stimuli overlaps considerably with areas sensitive to emotional attributions. Indeed, aversive stimuli and punishment are among the stimuli/circumstances/conditions often used to promote negative emotions in experimental studies. Critical areas involved in processing aversive and emotional stimuli and orchestrating appropriate short and/or long-term adaptations to these stimuli include the amygdala, insula, anterior cingulate cortex and portions of the PFC, along with projections throughout the neural axis, including brainstem regions such as the periaqueductal gray and locus coeruleus, the midbrain, and certain hypothalamic regions (e.g., Sandner et al., 1993; Buchel et al., 1998; Nitschke et al., 2006; Schlund et al., 2010).

Several of these regions (e.g., PFC and amygdala) have been the subject of careful ontogenetic study and found to undergo marked neuroanatomical changes during adolescence. In both humans and laboratory animals, the volume of frontal cortex decreases in adolescence whereas the volume of the amygdala increases (e.g., Giedd et al., 1996; Giedd, 2004; Markham et al., 2007). Stereological analyses have revealed declines in the number of neurons within both of these regions between adolescence and adulthood in rats, effects studied in the basolateral nucleus of the amygdala (Rubinow and Juraska, 2009) and seen in ventral (but not dorsal) mPFC (Markham et al., 2007). Evidence for marked changes in connectivity between these regions during adolescence has emerged in elegant neuroanatomical studies. The number of projections from the amygdala to the PFC has been shown to increase through adolescence (Cunningham et al., 2008) whereas developmental declines in PFC projections to the amygdala have been reported, with "approximately half of the neurons projecting to the basal amygdala from the mPFC fully retract(ing) their axons from the basal amygdala between late adolescence and adulthood" (Cressman et al., 2010, p. 2705).

In fMRI studies, adolescents and adults have also been reported to differ in their neural response to aversive and negative-valenced stimuli and outcomes, although many of the experiments that have included both reward as well as loss/punishment trials have focused largely to date on neural responses to rewarding stimuli. One exception is work by Ernst et al. (2005a) where responses to loss or punishment were examined in conditioning situations also used to assess neural responses to rewarding stimuli. Using this approach to explore developmental differences in sensitivity to aversive vs. positively rewarding stimuli, adolescents were found to exhibit less pronounced activation of the amygdala during punishment (response omission) than adults, while also showing greater ventral striatal activation to rewards (Ernst et al., 2005b). In this study, level of ventral striatum recruitment was found to correlate with positive affect to reward receipt only among adolescents, with adults (but not adolescents) showing a correlation between negative emotion and decreased amygdala activation on punishment (reward omission) trials, data consistent with their notion of a relatively delayed development of a "harm-avoidant" system (Ernst et al., 2005a). These findings are reminiscent of other fMRI evidence for earlier maturation of neural responses to positive than negative feedback, with gradual age-related increases in activation to negative feedback/aversive consequences in a variety of cognitive control regions (Crone et al., 2008; van Duijvenvoorde et al., 2008; Gunther Moor et al., 2010; but see also van Leijenhorst et al., 2006). In contrast to the limited number of studies focusing on developmental changes in patterns of neural activation to negative feedback or punishment, there has been considerable emphasis in developmental studies on the sometimes heightened amygdala activation during adolescence to presentation of affect-laden stimuli, often faces displaying negative emotional affect, as reviewed later.

2.2. Adolescent sensitivity to aversive stimuli

Consistent with the notion of adolescents as less "harm avoidant" (e.g., Ernst et al., 2005a), sensitivity to negative feedback as reflected in avoidant behavior displayed in a gambling task has been reported to be low during early-mid adolescence, and to increase gradually with age thereafter (see Steinberg, 2008; Cauffman et al., 2010); this gradual ontogenetic increase in sensitivity to negative outcomes differs notably from the ontogeny of positive reward sensitivity in the same task that, as discussed earlier, was found to exhibit an inverted U-shaped function, peaking from approximately 14 to 21 years at higher levels than seen at younger or older ages (Cauffman et al., 2010). Yet, in other work, adolescents were reported to exhibit greater sensitivity than adults to both positive and aversive outcomes (i.e., rewards and punishments) when indexed by incentive-related alterations in response latency to perform an antisaccade eye movement task, although not in terms of error frequency or accuracy (Jazbec et al., 2006; Hardin et al., 2007). Thus, task conditions and nature of the assessment used are likely to influence the extent to which adolescents exhibit insensitivity to aversive outcomes in adolescence—clearly an important area for further inquiry.

Basic science studies have revealed substantial evidence for attenuated sensitivity to aversive stimuli during adolescence. Adolescent rats, for instance, have often been found to be less sensitive than their adult counterparts to the aversive effects of a variety of drugs when indexed via conditioned taste aversions (CTA)—i.e., learning to avoid a taste previously associated with interoceptive properties of the test drug (e.g., Infurna and Spear, 1979; Schramm-Sapyta et al., 2006, 2010; Torres et al., 2008; Vetter-O'Hagen et al., 2009). These attenuated sensitivities typically emerge at higher doses of the same drugs that adolescents find more rewarding relative to adults—e.g., alcohol, cocaine, amphetamine and nicotine, as reviewed earlier. Many of these converse age-related sensitivities to rewarding and aversive stimuli have been revealed using similar place or taste conditioning procedures (sometimes even within the same study—e.g., see Torres et al., 2008), and hence are unlikely to reflect any potential age differences in capacity to express classical conditioning. These attenuations

in aversive sensitivity during adolescence are also evident with non-drug stimuli (e.g., Schramm-Sapyta et al., 2006; Wilmouth and Spear, 2009). For instance, under the same CTA conditions that revealed adolescent insensitivities to the aversive properties of cocaine, adolescents were also found to be less sensitive to the aversive properties of the non-addictive substance, lithium chloride (Schramm-Sapyta et al., 2006). In a study assessing hedonic sensitivity using a taste reactivity paradigm, adolescents consistently showed less negative taste reactivity to the aversive tastant quinine than adults, while conversely exhibiting adolescent-associated elevations in positive responding to certain concentrations of sucrose (Wilmouth and Spear, 2009).

At least in the case of alcohol, this insensitivity to the aversive effects of alcohol during adolescence extends to a variety of intoxicating effects of alcohol, at least some of which likely contribute to alcohol-related dysphoria. These adolescent alcohol insensitivities include alcohol-induced social impairment, sedation, motor impairment, and even some "hangover" effects (see Spear and Varlinskaya, 2005, for review), although this insensitivity does not extend to the disruption in brain plasticity and memory that also emerges at higher alcohol exposure levels (White and Swartzwelder, 2005). Although ethical concerns against providing alcohol to youth for research purposes largely prohibit the conduct of similar studies in humans, an older study where 8–15 year old boys were given alcohol revealed seemingly similar findings, with Behar et al. (1983) reporting that "little behavioral change was noted clinically, subjectively, or on a validated objective test of intoxication. . ." and that they "were impressed by how little gross behavioral change occurred in the children. . .after a dose of alcohol which had been intoxicating in an adult population" (p. 407). A developmental insensitivity to undesired alcohol effects likely serving as negative feedback cues to moderate intake could contribute to the 2–3 fold greater per episode alcohol intakes seen among adolescents than adults in both humans (SAMHSA survey data, 2006) and laboratory animals (e.g., Doremus et al., 2005). Indeed, among adolescent rats, those that were the least sensitive to alcohol CTA showed the highest levels of alcohol consumption, evidence supporting the suggestion that insensitivity to adverse alcohol consequences may contribute to elevated drinking patterns (Schramm-Sapyta et al., 2010). A decreased sensitivity to intoxicating effects of alcohol is a known genetic risk factor for problematic alcohol involvement (Schuckit, 1994; Green and Grahame, 2008), and may combine with developmental insensitivities and be further exacerbated by a history of repeated alcohol use or stress (Doremus-Fitzwater et al., 2007; Varlinskaya and Spear, 2008). Collectively these alcohol insensitivities may potentially contribute to a pattern of elevated alcohol use during adolescence that places vulnerable youth on a trajectory toward problematic use and dependence (Spear and Varlinskaya, 2005).

2.3. Cues, contexts, and aversions

In a manner somewhat reminiscent of age differences in sensitivity to reward-predictive cues discussed earlier, adolescents differ from adults not only in their relative resistance to aversive stimuli, but also in the way they attribute significance to cues and contexts associated with these stimuli, as well as the longevity of these stimulus associations. For instance, in a classical conditioning paradigm using parameters that support aversions at both ages to a conditioned stimulus (CS) when paired with an aversive (footshock) unconditioned stimulus (US) in a particular context, adolescents have been varyingly reported to exhibit either stronger (Brasser and Spear, 2004; Esmorís-Arranz et al., 2008; see also Barrett et al., 1984) or weaker (Pattwell et al., 2011) aversive (fear) conditioning to the training context than adults—differences perhaps due in part to dissimilarities across studies in salience of the contexts used. Intriguing age differences in cue reinstatement have also been reported. Under circumstances supporting similar fear conditioning to the CS in both adolescents and adults, as well as similar within session extinction of that fear, adolescents showed markedly impaired retention of the extinction, thereby spontaneously reinstating their fear to CS presentation (McCallum et al., 2010; Kim et al., 2011). In tests of cue-induced reinstatement of cocaine seeking, adolescents were found to exhibit attenuated reinstatement relative to adults to cues that had previously been paired with cocaine self-administration (Li and Frantz, 2009; Anker and Carroll, 2010), although only the adolescents showed stress-induced reinstatement of cocaine-seeking (Anker and Carroll, 2010). Thus, adolescents sometimes differ notably from adults in their responding to cues and contexts predicting aversive outcomes—in ways that could perhaps influence their propensity to avoid aversive circumstances, while promoting reinstatement of fear or stress-induced drug-seeking behaviors. These differences seen during adolescence in learning about and extinguishing responding to cues and contexts associated with aversive outcomes perhaps should not be surprising given that critical neural substrates for this conditioning include regions previously discussed as undergoing substantial developmental change during adolescence—i.e., the amygdala and its interconnections with the mPFC, as well as other limbic areas such as the hippocampus (Everitt et al., 1999; Knapska and Maren, 2009; Cressman et al., 2010; Kim et al., 2010; Pattwell et al., 2011).

3. Emotions/affect, processing of rewarding and aversive stimuli, and risk-taking in adolescence

As discussed above, adolescents are often less sensitive than adults to a variety of aversive stimuli, despite complex age differences in attributing cues and contexts to these aversive stimuli. At the same time, adolescents sometimes exhibit greater overall levels of negative affect/emotions than do adults (e.g., see Larson and Lampman-Petraitis, 1989), with some of this negative emotionality seemingly being "intentionally sought and maintained" by adolescents (Riediger et al., 2009, p. 1533), speculated to perhaps help adolescents disengage from unattainable goals, thereby serving a potential adaptive function (Wrosch and Miller, 2009).

Emotional and arousing situations are particularly likely to occur during adolescence (e.g., Larson et al., 2002). Adolescents not only appear more emotional and emotionally reactive than adults, but they are also more likely to have their behavior and decision-making processes influenced by this volatile emotionality. Indeed, although rational decision making reaches adult-typical levels by mid-adolescence (e.g., see Steinberg et al., 2009), adolescents seem particularly prone to have their decision-making influenced by exciting, emotionally charged and/or stressful situations (so called "hot cognitions"—e.g., Arnsten, 1998; Dahl, 2001, 2004; Figner et al., 2009). For instance, using both "hot" and "cold" versions of a risk-taking task (the Columbia Card Task) designed to promote affective vs. deliberative decision making, respectively, adolescents were found to exhibit more risk-taking than adults only under "hot" task conditions (Figner et al., 2009). Social stimuli may be particularly effective means for altering emotional state and subsequent risk-taking behavior, especially among adolescents. One great example is a laboratory study of risk taking conducted by Gardner and Steinberg (2005) where they found that the presence of peers considerably exacerbated risk-taking among adolescents, but not in adults (Gardner and Steinberg, 2005), Indeed, most sensation-seeking and risky behaviors in adolescents occur in social situations (e.g., see Steinberg, 2004, 2008).

Work grounded in studies of personality traits have begun to emphasize that both positive and negative emotional states may trigger "rash" actions and risky behaviors in some individuals—termed "positive urgency" and "negative urgency", respectively. For instance, a laboratory study of positive urgency conducted among college students observed that positive urgency predicted increased risk taking as well as elevations in ethanol consumption after individuals were placed in a positive mood, but not when tested under neutral mood conditions (Cyders et al., 2010). While individual differences in urgency show reasonable stability across time, the incidence of urgency have been suggested to spike in adolescence, with "the normative adolescent experience. . .characterized by developmentally heightened levels of positive and negative urgency" (Cyders and Smith, 2008, p. 22). Thus, whether viewed as prone to exhibit "hot cognitions" or to display elevated "urgency", from several perspectives adolescents appear more likely than adults to exhibit risk-taking in emotional and arousing situations.

3.1. Neural and physiological responses to emotional stimuli during adolescence

As mentioned earlier, emotionally arousing stimuli or situations increase activity in many of the same brain regions involved in rapid and instinctive behavioral responses to arousing, aversive and rewarding stimuli (e.g., Rosen and Levenson, 2009; see also Section 2.1), although the focus to date in developmental studies of emotional processing in brain have largely focused on the amygdala—especially the amygdala response to emotional (often, fearful) faces. In a number of studies, adolescents have been found to exhibit greater amygdalar activation to fearful faces (relative to neutral faces) than adults (Killgore et al., 2001; Monk et al., 2003; Guyer et al., 2008) or than both children and adults (Hare et al., 2008). These findings, however, are not ubiquitous (see Pine et al., 2001; Thomas et al., 2001; McClure et al., 2004; Deeley et al., 2008), perhaps in part due to the transient nature of amygdala activation, as well as to differences across studies in subregions included within amygdala-defined regions of interest, given that the amygdala complex consists of multiple, spatially contiguous subregions with sometimes functionally opposing roles (e.g., see Zald, 2003).

Signs of greater amygdala activation to emotional facial stimuli during adolescence under some test circumstances have been proposed to reflect an increased reactivity of adolescents to the emotional properties of social stimuli (Monk et al., 2003; Nelson et al., 2005; Hare et al., 2008). Indeed, the amygdala has been characterized as one of the important neural substrates for processing components of social information and behavior in both humans and laboratory animals (e.g., Adolphs, 2001; Truitt et al., 2007).

Any bias evident in the adolescent amygdala toward activation by social stimuli could lower the likelihood of adolescents responding effectively to other situational or task demands. For instance, in work using fMRI to examine amygdala activation to emotional faces, Hare et al. (2008) found that increased amygdalar activation to these faces was correlated with slower response times when responding to these stimuli in a go/no-go task, with adolescents overall responding more slowly than adults in this task. Likewise, in an fMRI study using a fearful face perception task, greater amygdala activation was correlated with poorer emotional and social capacities in a group of 8–15 year olds (Killgore and Yurgelun-Todd, 2007). Although such correlations do not necessarily reflect causality, it is nevertheless interesting that elevated activity in amygdala induced by emotional stimuli was associated with poorer affect-relevant performance during development—findings consistent with the notion of "hot cognitions".

Emotional stimuli often activate release of stress hormones (via the hypothalamo–pituitary adrenal axis [HPA]), as well as alter activity in the autonomic nervous system (ANS) with its two components: (a) the sympathetic nervous system (SNS) that facilitates "fight-or-flight" reactions, increasing HR and blood pressure (BP), and shunting blood flow away from digestion to skeletal muscles; and (b) the parasympathetic nervous system (PNS), which slows HR, lowers BP and facilitates rest/recovery. Such ANS-mediated bodily (somatic) reactions are thought not only to reflect emotional reactions, but also to serve as cues for making emotional self-attributions (see Verdejo-García et al., 2006). Although little studied to date, the pubertal/adolescent transition in humans and laboratory animals has generally been reported to be associated with increased ANS and stress hormone reactivity to stressors (e.g., Vazquez, 1998; Walker et al., 2004; Gunnar et al., 2009; Stroud et al., 2009), along with slower post-stress hormonal recovery relative to adults (Romeo and McEwen, 2006). Given high levels of receptors for stress hormones (glucocorticoids) in PFC and limbic regions such as the hippocampus and amygdala, these stress-sensitive regions may provide vulnerable targets for altered maturation by

elevated glucocorticoids when repeatedly exposed to stressors during adolescence; such effects have been suggested to contribute to the propensity for development of psychopathology in vulnerable, prodromal adolescents (see Romeo and McEwen, 2006; Grace, 2007; Walker et al., 2007).

Turning to ANS activation during adolescence, a number of studies have hinted to the provocative possibility that ANS-associated somatic signs may not be as strongly linked to emotional expression (e.g., Quas et al., 2000; Stroud et al., 2009) or to optimizing risky decision-making (e.g., Crone and van der Molen, 2007) during development as in adulthood. For instance, a study examining cardiovascular reactivity to emotional stimuli found no clear association between children's cardiovascular reactivity and their emotional expression, with children that showed greater cardiac reactivity to a needle puncture for blood draw even tending to exhibit *less* behavioral evidence of negative affect and emotional distress to the procedure (Quas et al., 2000). Likewise, the changes in physiological responses to stressors observed by Stroud et al. (2009) during the pubertal transition "were not mirrored by differences in *affective* responses to the stressors" (p. 62). These data raise the speculative but intriguing possibility that, despite increases in ANS emotional reactivity during adolescence, the ability to link these physiological reactions to perceived emotions may develop only slowly and may perhaps even contribute to the enhanced emotional volatility, "hot cognitions" and "urgency" of adolescence.

3.2. Possible cross-reactivity between emotion- and reward-sensitive subcortical regions during adolescence

Adolescents may be particularly prone to becoming emotionally aroused in part because of unusually strong links between subcortical regions critical for processing aversive, arousing and emotion-provoking stimuli (e.g., the amygdala) and systems processing rewarding stimuli such as the nAc/ventral striatum. These two phylogenetically ancient, subcortical systems both show greater reactivity under some circumstances in adolescence than adulthood, with inverted U-shaped developmental patterns characterized by rises in neurobehavioral reactivity to emotional/affective and rewarding stimuli under some circumstances early in adolescence that diminish during late adolescence and in adulthood (e.g., Galvan et al., 2006; Hare et al., 2008; Van Leijenhorst et al., 2010a; Cohen et al., 2010).

While separable to some extent, these emotional/affect and reward systems overlap considerably. They are anatomically interconnected (e.g., see Chambers et al., 2003) and closely functionally interrelated, with for instance socio-emotional stimuli influencing salience of rewarding stimuli (e.g., Thiel et al., 2008, 2009), and the presence or omission of potential or expected rewards often contributing to emotional affect (e.g., see Figner et al., 2009). And, as we have seen, responsiveness within each of these systems emerges early, although it seems somewhat of a misnomer to classify them as "early maturing" in that, as we have seen, they often demonstrate different and sometimes exaggerated patterns of reactivity relative to that seen at maturity. Both of these interrelated systems are also sensitively activated by stress, with stressors tending to increase activation in the ventral striatum, amygdala and other subcortical regions such as the hippocampus, while attenuating functional efficacy within the PFC (Arnsten, 1998; Liston et al., 2009)—regional shifts in activity possibly attributable in part to stress-induced elevations in PFC DA beyond optimal levels, as discussed earlier (Arnsten, 2009).

Activity in emotional/affect and reward systems may be linked during adolescence in at least two ways. On the one hand, adolescent affective systems may be particularly labile to activation by rewarding stimuli (e.g., see Galvan et al., 2006, 2007; Figner et al., 2009), with "a greater behavioral impact of reward on motivational salience" during adolescence than in adulthood (Smith et al., 2011, p. 1701). Indeed, tasks involving rewards appear to be especially arousing during adolescence, with adolescents reported to show particularly marked increases in attention and shorter reaction times under rewarding than less rewarding conditions—a difference that is more prominent than at other ages (Jazbec et al., 2006; Hardin et al., 2007; Cohen et al., 2010; Smith et al., 2011). Likewise, in a lifespan study of adults ranging in age from 18 to 81 years examining relationships between arousal and the relative appetitiveness and aversiveness of stimuli, Keil and Freund (2009) found that the youngest age group examined (18–29 year olds), which included late adolescents, showed greater arousal to pleasant stimuli (appetitive activation) but lower arousal to unpleasant stimuli (aversive activation) than mature (30–59 year old) and older (≥60 year old) adults.

On the other hand, it is also possible that emotional/affect and reward systems may be linked because, under heightened emotional circumstances, adolescent sensitivity to positively valenced rewards or cues predicting those rewards may become even more pronounced. Signs for such a relationship can be seen in the basic science literature. For example, elevations in motivational/emotional arousal induced by mild food deprivation were found to exacerbate extinction responding to a cue previously predicting reward among adolescent rats, whereas no interaction of motivational status and the presence of the reward-predictive cue was seen in adults (Sturman et al., 2010). Isolate housing likewise was found to differentially impact adolescents and adults in a sign-tracking task, with housing animals in social isolation increasing the low incidence of responding toward the reward-predictive cue normally seen in adolescent relative to adult rats (Anderson and Spear, unpublished observations). The stimulation provided by the presence of social peers may be particularly effective in exacerbating adolescent sensitivity to positively valenced rewards, while also perhaps further attenuating their sensitivity to aversive stimuli. For example, the presence of social peers enhances the rewarding properties of cocaine and nicotine among adolescent rats (Thiel et al., 2008, 2009), while further attenuating adolescent sensitivity to aversive effects of alcohol, an effect not seen in adults (Vetter-O'Hagen et al., 2009). In a recent study of human adolescents, even sleep deprivation was found to enhance ventral striatal responding during reward outcomes, while attenuating responding

in insula following losses (Venkatraman et al., 2011). Taken together, these disparate findings provide emerging empirical support for the notion of cross-reactivity between emotional/affect and reward systems that may be particularly prominent during adolescence and that may help trigger the exaggerated reactivity often seen in these systems at this time. Of course, such speculations clearly require further study and exploration of underlying neural mechanisms.

4. Summary and closing comments

Adolescents view rewarding and aversive stimuli differently than do adults. Their neural and behavioral sensitivity to rewards, especially strong rewards, sometimes appears to be heightened, whereas they appear less reactive under other circumstances, especially when responding to cues that predict rewards, and perhaps when receiving relatively weak rewards. Along with these seeming exaggerations in reward reactivity, adolescents are often less sensitive to aversive outcomes and sometimes respond differently than adults to the learning and forgetting of cues and contexts associated with these stimuli. At the same time, they appear particularly prone to becoming emotionally aroused, and to exhibit greater risk-taking, especially under social circumstances. There are hints that reactivity in these reward and emotional/affective systems may be particularly pronounced in adolescence, in part because of unusually strong cross-reactivity between these systems during adolescence. As a result, the adolescent propensity to exhibit accentuated responses to intense, appetitive stimuli but attenuated responsiveness to aversive stimuli may be further intensified in emotional or social situations. Such hedonic shifts could encourage risk-taking, especially when in the presence of peers, for its thrilling and exciting aspects, and may help promote continued engagement in risky activities when prior activities have proved exciting but without catastrophic consequences. Such adolescent-typical shifts toward greater rewarding and attenuated aversive properties seem to extend to alcohol and other drugs as well, and may contribute to the propensity of adolescents to attach greater benefit and less cost to risky behavior such as alcohol and cigarette use than attributed by individuals at other ages (see Millstein and Halpern-Felscher, 2002). Thus, adolescent risk taking may be tethered by biological roots embedded in our evolutionary past that reflect, in part, transient developmental rises in reactivity (and perhaps cross-reactivity) within reward and emotional/affective systems.

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References

Aberg, M., Wade, D., Wall, E., Izenwasser, S., 2007. Effect of MDMA (ecstasy) on activity and cocaine conditioned place preference in adult and adolescent rats. Neurotoxicol. Teratol. 29, 37–46.

Adolphs, R., 2001. The neurobiology of social cognition. Curr. Opin. Neurobiol. 11, 231–239.

Andersen, S.L., 2002. Changes in the second messenger cyclic AMP during development may underlie motoric symptoms in attention deficit/hyperactivity disorder (ADHD). Behav. Brain Res. 130, 197–201.

Andersen, S.L., Dumont, N.L., Teicher, M.H., 1997. Developmental differences in dopamine synthesis inhibition by (+/−)-7-OH-DPAT. Naunyn-Schmiedeberg's Arch. Pharmacol. 352 (2), 173–181.

Andersen, S.L., Thompson, A.T., Rutstein, M., Hostetter, J.C., Teicher, M.H., 2000. Dopamine receptor pruning in prefrontal cortex during the periadolescent period in rats. Synapse 37 (2), 167–169.

Anderson, R.I., Spear, L.P., 2011. Autoshaping in adolescence enhances sign-tracking behavior in adulthood: impact on ethanol consumption. Pharm. Biochem. Behav. 98, 250–260.

Andrews, M.M., Shashwath, A.M., Thomas, A.D., Potenza, M.N., Krystal, J.H., Worhunsky, P., et al., 2010. Individuals family history positive for alcholism show functional magnetic resonance imaging differences in reward sensitivity that are related to impulsivity factors. Biol. Psychiatry 69 (7), 675–683.

Anker, J.J., Carroll, M.E., 2010. Reinstatement of cocaine seeking induced by drugs, cues, and stress in adolescent and adult rats. Psychopharmacology (Berl.) 208, 211–222.

Arnsten, A.F.T., 1998. The biology of being frazzled. Science 280, 1711–1712.

Arnsten, A.F.T., 2009. Stress signaling pathways that impair prefrontal cortex structure and function. Nat. Rev. Neurosci. 1, 410–422.

Barrett, B.A., Rizzo, T., Spear, N.E., Spear, L.P., 1984. Stimulus selection in passive avoidance learning and retention: Weanling, periadolescent, and young adult rats. Behav. Neural Biol. 42, 23–32.

Baxter, M.G., Murray, E.A., 2002. The amygdala and reward. Nat. Rev. Neurosci. 3 (7), 563–573.

Behar, D., Berg, C.J., Rapoport, J.L., Nelson, W., Linnoila, M., Cohen, M., et al., 1983. Behavioral and physiological effects of ethanol in high-risk and control children: a pilot study. Alcohol. Clin. Exp. Res. 7 (4), 404–410.

Benes, F.M., Taylor, J.B., Cunningham, M.C., 2000. Convergence and plasticity of monoaminergic systems in the medial prefrontal cortex during the postnatal period; Implications for the development of psychopathology. Cerebral Cortex 10 (10), 1014–1027.

Berridge, K.C., 2004. Motivation concepts in behavioral neuroscience. Alcohol. Clin. Exp. Res. 81, 179–209.

Berridge, K.C., Kringelbach, M.L., 2008. Affective neuroscience of pleasure: reward in humans and animals. Psychopharmacology (Berl.) 199, 457–480.

Bjork, J.M., Chen, G., Smith, A.R., Hommer, D.W., 2010b. Incentive-elicited mesolimbic activation and externalizing symptomatology in adolescents. J. Child Psychol. Psychiatry 51 (7), 827–837.

Bjork, J.M., Knutson, B., Fong, G.W., Caggiano, D.M., Bennett, S.M., Hommer, D.W., 2004. Incentive-elicited brain activation in adolescents: similarities and differences from young adults. J. Neurosci. 24 (8), 1793–1802.

Bjork, J.M., Smith, A.R., Chen, G., Hommer, D.W., 2010a. Adolescents, adults and rewards: comparing motivational neurocircuitry recruitment using fMRI. PLoS One 5 (7), 1–14.

Blanchard, R.J., Yudko, E.B., Blanchard, D.E., Taukulis, H.K., 1993. High-frequency (35–70 kHz) ultrasonic vocalizations in rats confronted with anesthetized conspecifics: effects of gepirone, ethanol, and diazepam. Pharmacol. Biochem. Behav. 44, 313–319.

Brasser, S.M., Spear, N.E., 2004. Contextual conditioning in infants, but not older animals, is facilitated by CS conditioning. Neurobiol. Learn. Mem. 81, 46–59.

Brenhouse, H.C., Andersen, S.L., 2008. Delayed extinction and stronger reinstatement of cocaine conditioned place preference in adolescent rats, compared to adults. Behav. Neurosci. 122 (2), 460–465.

Brenhouse, H.C., Sonntag, K.C., Andersen, S.L., 2008. Transient D_1 Dopamine receptor expression on prefrontal cortex projection neurons: relationship to enhanced motivational salience of drug cues in adolescence. J. Neurosci. 28 (10), 2375–2382.

Brown, B.B., 2004. Adolescents' relationships with peers. In: Lerner, R.M., Steinberg, L.D. (Eds.), Handbook of Adolescent Psychology. , 2nd edition. Wiley, Hoboken, NJ, pp. 363–394.

Buchel, C., Morris, J., Dolan, R.J., Friston, K.J., 1998. Brain systems mediating aversive conditioning: an event-related fMRI study. Neuron 20 (5), 947–957.

Burgdorf, J., Knutson, B., Panksepp, J., 2000. Anticipation of rewarding electrical brain stimulation evokes ultrasonic vocalizations in rats. Behav. Neurosci. 114, 320–327.

Campbell, J.O., Bliven, T.D., Silveri, M.M., Snyder, K.J., Spear, L.P., 2000. Effects of prenatal cocaine on behavioral adaptation to chronic stress in adult rats. Neurotoxicol. Teratol. 22 (6), 845–850.
Cardinal, R.N., Parkinson, J.A., Hall, J., Everitt, B.J., 2002. Emotion and motivation: the role of the amygdala, ventral striatum, and prefrontal cortex. Neurosci. Biobehav. Rev. 26 (3), 321–352.
Carlezon Jr., W.A., Thomas, M.J., 2009. Biological substrates of reward and aversion: a nucleus accumbens activity hypothesis. Neuropharmacology 56, 122–132.
Casey, B.J., Jones, R.M., 2010. Neurobiology of the adolescent brain and behavior: implications for substance use disorders. J. Am. Acad. Child Adolesc. Psychiatry 49 (12), 1189–1201.
Cauffman, E., Shulman, E.P., Claus, E., Banich, M.T., Steinberg, L., Graham, S., 2010. Age differences in affective decision making as indexed by performance on the Iowa gambling task. Dev. Psychol. 46 (1), 193–207.
Chambers, R.A., Taylor, J.R., Potenza, M.N., 2003. Developmental neurocircuitry of motivation in adolescence: a critical period of addiction vulnerability. Am. J. Psychiatry 160 (6), 1041–1052.
Cohen, J.R., Asarnow, R.F., Sabb, F.W., Bilder, R.M., Bookheimer, S.Y., Knowlton, B.J., et al., 2010. A unique adolescent response to reward prediction errors. Nat. Neurosci. 13 (6), 669–671.
Cressman, V.L., Balaban, J., Steinfeld, S., Shemyakin, A., Graham, P., Parisot, N., et al., 2010. Prefrontal cortical inputs to the basal amygdala undergo pruning during late adolescence in the rat. J. Comp. Neurol. 518 (14), 2693–2709.
Crone, E.A., van der Molen, M.W., 2007. Development of decision making in school-aged children and adolescents: evidence from heart rate and skin conductance analysis. Child Dev. 78 (4), 1288–1301.
Crone, E.A., Zanolie, K., Van Leijenhorst, L., Westenberg, P.M., Rombouts, S.A.R.B., 2008. Neural mechanisms supporting flexible performance adjustment during development. Cogn. Affect Behav. Neurosci. 8 (2), 165–177.
Cunningham, M.G., Bhattacharyya, S., Benes, F.M., 2008. Increasing interaction of amygdala afferents with GABAergic interneurons between birth and adulthood. Cereb. Cortex 18, 1529–1535.
Cyders, M.A., Smith, G.T., 2008. Emotion-based dispositions to rash action: positive and negative urgency. Psychol. Bull. 134 (6), 807–828.
Cyders, M.A., Zapolski, T.C.B., Combs, J.L., Settles, R.F., Fillmore, M.T., Smith, G.T., 2010. Experimental effect of positive urgency on negative outcomes from risk taking and on increased alcohol consumption. Psychol. Addict. Behav. 24 (3), 367–375.
Dahl, R.E., 2001. Affect regulation, brain development, and behavioral/emotional health in adolescence. CNS Spectr. 6 (1), 60–72.
Dahl, R.E., 2004. Adolescent brain development: a period of vulnerabilities and opportunities. In: Dahl, R.E., Spear, L.P. (Eds.), Adolescent Brain Development: Vulnerabilities and Opportunities. New York Academy of Sciences, New York, pp. 1–22.
Deeley, Q., Daly, E.M., Azuma, R., Surguladze, S., Giampietro, V., Brammer, M.J., et al., 2008. Changes in male brain responses to emotional faces from adolescence to middle age. Neuroimage 40 (1), 389–397.
Delgado, M.R., Nystrom, L.E., Fissell, C., Noll, D.C., Fiez, J.A., 2000. Tracking the hemodynamic responses to reward and punishment in the striatum. J. Neurophysiol. 84 (6), 3072–3077.
Desor, J.A., Beauchamp, G.K., 1987. Longitudinal changes in sweet preferences in humans. Physiol. Behav. 39, 639–641.
Doremus, T.L., Brunell, S.C., Rajendran, P., Spear, L.P., 2005. Factors influencing elevated ethanol consumption in adolescent relative to adult rats. Alcohol. Clin. Exp. Res. 29 (10), 1796–1808.
Doremus-Fitzwater, T.L., Varlinskaya, E.I., Spear, L.P., 2007. Impact of Repeated Stress on Responsivity to Ethanol-induced Changes in Social Behavior in Adolescent and Adult Rats. Society for Neuroscience, San Diego, CA.
Doremus-Fitzwater, T.L., Varlinskaya, E.I., Spear, L.P., 2010. Motivational systems in adolescence: possible implications for age differences in substance abuse and other risk-taking behaviors. Brain Cogn. 72, 114–123.
Doremus-Fitzwater, T.L., Spear, L.P., 2011. Amphetamine-induced incentive sensitization of sign-tracking behavior in adolescent and adult female rats. Behav. Neurosci. 125 (4), 661–667.
Douglas, L.A., Varlinskaya, E.I., Spear, L.P., 2003. Novel object place conditioning in adolescent and adult male and female rats: Effects of social isolation. Physiol. Behav. 80, 317–325.
Douglas, L.A., Varlinskaya, E.I., Spear, L.P., 2004. Rewarding properties of social interactions in adolescent and adult male and female rats: impact of social versus isolate housing of subjects and partners. Dev. Psychobiol. 45, 153–162.
Dumont, N.L., Andersen, S.L., Thompson, A.P., Teicher, M.H., 2004. Transient dopamine synthesis modulation in prefrontal cortex: in vitro studies. Dev. Brain Res. 150 (2), 163–166.
Dunn, A.J., 1988. Stress-related activation of cerebral dopaminergic systems. Ann. N.Y. Acad. Sci. 537, 188–205.
Ernst, M., Fudge, J.L., 2009. A developmental neurobiological model of motivated behavior: anatomy, connectivity and ontogeny of the triadic nodes. Neurosci. Biobehav. Rev. 33, 367–382.
Ernst, M., Nelson, E.E., Jazbec, S., McClure, E.B., Monk, C.S., Leibenluft, E., et al., 2005b. Amygdala and nucleus accumbens in responses to receipt and omission of gains in adults and adolescents. Neuroimage 25 (4), 1279–1291.
Ernst, M., Pine, D.S., Hardin, M.G., 2005a. Triadic model of the neurobiology of motivated behavior in adolescence. Psychol. Med. 36 (3), 299–312.
Ernst, M., Romeo, R.D., Andersen, S.L., 2009. Neurobiology of the development of motivated behaviors in adolescence: a window into a neural systems model. Pharmacol. Biochem. Behav. 93, 199–211.
Esmorís-Arranz, F.J., Mèndez, C., Spear, N.E., 2008. Contextual fear conditioning differs for infant, adolescent, and adult rats. Behav. Proc. 78, 340–350.
Everitt, B.J., Parkinson, J.A., Olmstead, M.C., Arroyo, M., Robledo, P., Robbins, T.W., 1999. Associative processes in addiction and reward: the role of amygdala-ventral striatral subsystems. Ann. N.Y. Acad. Sci. 877, 412–438.
Fareri, D.S., Martin, L.N., Delgado, M.R., 2008. Reward-related processing in the human brain: developmental considerations. Dev. Psychopathol. 20, 191–1211.
Figner, B., Mackinlay, R.J., Wilkening, F., Weber, E.U., 2009. Affective and deliberative processes in risky choice: age differences in risk taking in the Columbia Card Task. J. Exp. Psychol. Learn. Mem. Cogn. 35 (3), 709–730.
Forbes, E.E., Dahl, R.E., 2010. Pubertal development and behavior: hormonal activation of social and motivational tendencies. Brain Cogn. 72, 66–72.
Forbes, E.E., Ryan, N.D., Phillips, M.L., Manuck, S.B., Worthman, C.M., Moyles, D.L., et al., 2010. Healthy adolescents' neural response to reward: associations with puberty, positive affect, and depressive symptoms. J. Am. Acad. Child Adolesc. Psychiatry 49 (2), 162–172, e165.
Friemel, C.M., Spanagel, R., Schneider, M., 2010. Reward sensitivity for a palatable food reward peaks during pubertal developmental in rats. Behav. Neurosci. 4.
Galvan, A., 2010. Adolescent development of the reward system. Front. Hum. Neurosci. 4.
Galvan, A., Hare, T., Voss, H., Glover, G., Casey, B.J., 2007. Risk-taking and the adolescent brain: who is at risk? Dev. Sci. 10 (2), F8–F14.
Galvan, A., Hare, T.A., Parra, C.E., Penn, J., Voss, H., Glover, G., et al., 2006. Earlier development of the accumbens relative to oribitofrontal cortex might underlie risk-taking behavior in adolescents. J. Neurosci. 26 (25), 6885–6892.
Gardner, E.L., 1999. The neurobiology and genetics of addiction: implications of the reward deficiency syndrome for therapeutic strategies in chemical dependency. In: Elster, J. (Ed.), Addiction: Entries and Exits. Russell Sage Foundation, New York, pp. 57–119.
Gardner, M., Steinberg, L., 2005. Peer influence on risk taking, risk preference, and risky decision making in adolescence and adulthood: an experimental study. Dev. Psychol. 41 (4), 625–635.
Geier, C.F., Luna, B., 2009. The maturation of incentive processing and cognitive control. Pharmacol. Biochem. Behav. 93, 212–221.
Geier, C.F., Terwilliger, R., Teslovich, T., Velanova, K., Luna, B., 2010. Immaturities in reward processing and its influence on inhibitory control in adolescence. Cereb. Cortex 20, 1613–1629.
Giedd, J.N., 2004. Structural magnetic resonance imaging of the adolescent brain. Ann. N.Y. Acad. Sci. 1021, 77–85.
Giedd, J.N., Vaituzis, A.C., Hamburger, S.D., Lange, N., Rajapakse, J.C., Kaysen, D., Vauss, Y.C., Rapoport, J.L., 1996. Quantitative MRI of the temporal lobe, amygdala, and hippocampus in normal human development: ages 4–18 years. J. Comp. Neurol. 355, 223–230.
Goto, Y., Otani, S., Grace, A.A., 2007. The Yin and Yang of dopamine release. Neuropharmacology 53 (5), 583–587.
Goto, Y., Grace, A.A., 2008. Limbic and cortical information processing in the nucleus accumbens. Trends Neurosci. 31 (11), 552–558.
Grace, A.A., 2007. Stress-induced pathophysiology within the schizophrenia patient brain: a model for the delayed on set of psychosis and its circumvention by anxiolytic agents. In: Romer, D., Walker, E.F. (Eds.), Adolescenet Pathology and the Developing Brain: Integrating Brain and Prevention Science. Oxford University Press, New York, pp. 245–263.
Grace, A.A., Floresco, S.B., Goto, Y., Lodge, D.J., 2007. Regulation of firing of dopaminergic neurons and control of goal-directed behaviors. Trends Neurosci. 30 (5), 220–227.

Green, A.S., Grahame, N.J., 2008. Ethanol drinking in rodents: is free-choice drinking related to the reinforcing effects of ethanol? Alcohol 42 (1), 1–11.
Gunnar, M.R., Wewerka, S., Frenn, K., Long, J.D., Griggs, C., 2009. Developmental changes in HPA activity over the transition to adolescence: normative changes and associations with pubertal stage. Dev. Psychopathol. 21, 69–85.
Gunther Moor, B., van Leijenhorst, L., Rombouts, S.A., Crone, E.A., Van der Molen, M.W., 2010. Do you like me? Neural correlates of social evaluation and developmental trajectories. Soc. Neurosci. 5 (5–6), 461–482.
Guyer, A.E., Monk, C.S., McClure-Tone, E.B., Nelson, E.E., Roberson-Nay, R., Adler, A.D., et al., 2008. A developmental examination of amygdala response to facial expressions. J. Cogn. Neurosci. 20 (9), 1565–1582.
Hardin, M.G., Schroth, E., Pine, D.S., Ernst, M., 2007. Incentive-related modulation of cognitive control in health, anxious, and depressed adolescents. J. Child Psychol. Psychiatry 48 (5), 446–454.
Hare, T.A., Tottenham, N., Galvan, A., Voss, H.U., Glover, G.H., Casey, B.J., 2008. Biological substrates of emotional reactivity and regulation in adolescence during an emotional go-no-go task. Biol. Psychiatry 63 (10), 927–934.
Hartup, W.W., Stevens, N., 1997. Friendship and adaptation in the life course. Psych. Bull. 121, 335–370.
Holm, S.M., Forbes, E.E., Ryan, N.D., Phillips, M.L., Tarr, J.A., Dahl, R.E., 2009. Reward-related brain function and sleep in pre/early pubertal and mid/late pubertal adolescents. J. Adolesc. Health 45, 326–334.
Infurna, R.N., Spear, L.P., 1979. Developmental changes in amphetamine-induced taste aversions. Pharmacol. Biochem. Behav. 11 (1), 31–35.
Jazbec, S., Hardin, M.G., Schroth, E., McClure, E., Pine, D.S., Ernst, M., 2006. Age-related influence of contingencies on a saccade task. Exp. Brain Res. 2006 (174), 4.
Johnston, L.D., O'Malley, P.M., Bachman, J.G., Schulenberg, J.E., 2009. Monitoring the Future National Results on Adolescent Drug Use: Overview of Key Findings 2008, pp. 1–79 (NIH Publication no. 09-7401).
Keil, A., Freund, A.M., 2009. Changes in the sensitivity to appetitive and aversive arousal across adulthood. Psychol. Aging 24 (3), 668–680.
Killgore, W.D.S., Oki, M., Yurgelun-Todd, D.A., 2001. Sex-specific developmental changes in amygdala responses to affective faces. Neuroreport 12 (2), 427–433.
Killgore, W.D.S., Yurgelun-Todd, D.A., 2007. Neural correlates of emotional intelligence in adolescent children. Cogn. Affect. Behav. Neurosci. 7 (2), 140–151.
Kim, J.H., Li, S., Richardson, R., 2011. Immunohistochemical analyses of long-term extinction of conditioned fear in adolescent rats. Cereb. Cortex 21, 530–538.
Knapska, E., Maren, S., 2009. Reciprocal patterns of c-Fos expression in the medial prefrontal cortex and amydgala after extinction and renewal of conditioned fear. Learn. Mem. 16 (8), 486–493.
Larson, R., Lampman-Petraitis, C., 1989. Daily emotional states as reported by children and adolescents. Child Dev. 60, 1250–1260.
Larson, R.W., Moneta, G., Richards, M.H., Wilson, S., 2002. Continuity, stability, and change in daily emotional experience across adolescence. Child Dev. 73 (4), 1151–1165.
Li, C., Frantz, K., 2009. Attenuated incubation of cocaine seeking in male rats trained to self-administer cocaine during periadolescence. Psychopharmacology (Berl.) 204 (4), 725–733.
Liston, C., McEwen, B.S., Casey, B.J., 2009. Psychosocial stress reversibly disrupts prefrontal processing and attentional control. Proc. Nat. Acad. Sci. 106 (3), 912–917.
Markham, J.A., Morris, J.R., Juraska, J.M., 2007. Neuron number decreases in the rat ventral, but not dorsal, medial prefrontal cortex between adolescence and adulthood. Neuroscience 144, 961–968.
Matsumoto, M., Hikosaka, O., 2009. Two types of dopamine neuron distinctly convey positive and negative motivational signals. Nature 459 (11), 837–841.
McCallum, J., Kim, J.H., Richardson, R., 2010. Impaired extinction retention in adolescent rats: effects of D-cycloserine. Neuropsychopharmacology 35, 2134–2142.
McCutcheon, J.E., Marinelli, M., 2009. Technical spotlight: age matters. Eur. J. Neurosci. 29, 997–1014.
McClure, E.B., Monk, C.S., Nelson, E.E., Zarahn, E., Leibenluft, E., Bilder, R.M., et al., 2004. A developmental examination of gender differences in brain engagement during evaluation of threat. Biol. Psychiatry 55 (11), 1047–1055.
Millstein, S.G., Halpern-Felscher, B.L., 2002. Perceptions of risk and vulnerability. J. Adolesc. Health 31S, 10–27.
Monk, C.S., McClure, E.B., Nelson, E.E., Zarahn, E., Bilder, R.M., Leibenluft, E., et al., 2003. Adolescent immaturity in attention-related brain engagement to emotional facial expressions. Neuroimage 20, 420–428.
Nelson, E.E., Leibenluft, E., McClure, E., Pine, D.S., 2005. The social re-orientation of adolescence: a neuroscience perspective on the process and its relation to psychopathology. Psychol. Med. 35, 163–174.
Nitschke, J.B., Sarinopoulos, I., Mackiewicz, K.L., Schaefer, H.S., Davidson, R.J., 2006. Functional neuroanatomy of aversion and its anticipation. Neuroimage 29 (1), 106–116.
Pattwell, S.S., Bath, K.G., Casey, B.J., Ninan, I., Lee, F.S., 2011. Selective early-acquired fear memories undergo temporary suppression during adolescence. Proc. Natl. Acad. Sci. U. S. A. 108 (3), 1182–1187.
Pautassi, R.M., Myers, M., Spear, L.P., Molina, J.C., Spear, N.E., 2008. Adolescent, but not adult, rats exhibit ethanol-mediated appetitive second-order conditioning. Alcohol. Clin. Exp. Res. 32 (11), 1–12.
Peters, J., Bromberg, U., Schneider, S., Brassen, S., Menz, M., Banaschewski, T., et al., 2011. Lower ventral striatal activation during reward anticipation in adolescent smoker. Am. J. Psychiatry 168 (5), 540–549.
Pine, D.S., Fyer, A., Grun, J., Phelps, E.A., Szeszko, P.R., Koda, V., et al., 2001. Methods for developmental studies of fear conditioning circuitry. Biol. Psychiatry 50 (3), 225–228.
Post, G.B., Kemper, H.C.G., 1993. Nutritional intake and biological maturation during adolescence. The Amsterdam growth and health longitudinal study. Eur. J. Clin. Nutr. 47, 400–408.
Quas, J.A., Hong, M., Alkon, A., Boyce, W.T., 2000. Dissociations between psychobiologic reactivity and emotional expression in children. Dev. Psychobiol. 37 (3), 153–175.
Riediger, M., Schmiedek, F., Wagner, G.G., Lindenberger, U., 2009. Seeking pleasure and seeking pain. Psychol. Sci. 20 (12), 1529–1535.
Robinson, D.L., Zitzman, D.L., Smith, K.J., Spear, L.P., 2011. Fast dopamine release events in the nucleus accumbens of early adolescent rats. Neuroscience 176, 296–307.
Robinson, T.E., Berridge, K.C., 2003. Addiction. Annu. Rev. Psychol. 54, 25–53.
Rodriguez de Fonseca, F., Ramos, J.A., Bonnin, A., Fernandez-Ruiz, J.J., 1993. Presence of cannabinoid binding sites in the brain from early postnatal ages. Neuroreport 4, 135–138.
Romeo, R.D., McEwen, B.S., 2006. Stress and the adolescent brain. Ann. N.Y. Acad. Sci. 1094, 202–214.
Romer, D., Duckworth, A.L., Sznitman, S., Park, S., 2010. Can adolescents learn self-control? Delay of gratification in the development of control over risk taking. Prev. Sci. 11 (3), 319–330.
Rosen, H.J., Levenson, R.W., 2009. The emotional brain: combining insights from patients and basic science. Neurocase 153, 173–181.
Rubinow, M.J., Juraska, J.M., 2009. Neuron and glia numbers in the basolateral nucleus of the amygdala from preweaning through old age in male and female rats: a stereological study. J. Comp. Neurol. 512 (6), 717–725.
SAMHSA, 2006. Results from the 2005 National Survey on Drug Use and Health: National Findings, National Survey on Drug use and Health Series H-30. DHHS Publication, Rockville, MD (SMA 06-4194).
Sandner, G., Oberling, P., Silveira, M.C., Di Scala, G., Rocha, B., Bagri, A., Depoortere, R., 1993. What brain structures are active during emotions? Effects of brain stimulation elicited aversion on c-fos immunoreactivity and behavior, 58 (1–2), 9–18.
Scheres, A., Milham, M.P., Knutson, B., Castellanos, F.X., 2007. Ventral striatal hyporesponsiveness during reward anticipation in attention-deficit/hyperactivity disorder. Biol. Psychiatry 61, 720–724.
Schramm-Sapyta, N.L., DiFeliceantonio, A.G., Foscue, E., Glowacz, S., Haseeb, N., Wang, N., et al., 2010. Aversive effects of ethanol in adolescent versus adult rats: potential causes and implication for future drinking. Alcohol. Clin. Exp. Res. 34 (12), 2061–2069.
Schramm-Sapyta, N.L., Morris, R.W., Kuhn, C.M., 2006. Adolescent rats are protected from the conditioned aversive properties of cocaine and lithium chloride. Pharmacol. Biochem. Behav. 84 (2), 344–352.
Schlund, M.W., Siegle, G.J., Ladouceur, C.D., Silk, J.S., Cataldo, M.F., Forbes, E.E., Dahl, R.E., Ryan, N.D., 2010. Neuroimage 52, 710–719.
Schuckit, M.A., 1994. Low level of response to alcohol as a predictor of future alcoholism. Am. J. Psychiatry 151 (2), 184–189.
Seeman, P., Bzowej, N.H., Guan, H.-C., Bergeron, C., Becker, L.E., Reynolds, G.P., et al., 1987. Human brain dopamine receptors in children and aging adults. Synapse 1, 399–404.
Shram, M.J., Funk, D., Li, X., Le, A.D., 2006. Periadolescent and adult rats respond differently in tests measuring the rewarding and aversive effects of nicotine. Psychopharmacology (Berl.) 186, 201–208.
Simon, J.J., Walther, S., Fiebach, C.J., Friederich, H.C., Stippich, C., Weisbrod, M., et al., 2009. Neural reward processing is modulated by approach- and avoidance-related personality traits. Neuroimage 49 (2), 1868–1874.
Smith, A.B., Halari, R., Giampetro, V., Brammer, M., Rubia, K., 2011. Developmental effects of reward on sustained attention networks. Neuroimage 56 (3), 1693–1704.

Somerville, L.H., Casey, B.J., 2010. Developmental neurobiology of cognitive control and motivational systems. Curr. Opin. Neurobiol. 20, 236–241.
Somerville, L.H., Jones, R.M., Casey, B.J., 2010. A time of change: behavioral and neural correlates of adolescent sensitivity to appetitive and aversive environmental cues. Brain Cogn. 72, 124–133.
Spear, L.P., 2000. The adolescent brain and age-related behavioral manifestations. Neurosci. Biobehav. Rev. 24, 417–463.
Spear, L.P., 2007. The developing brain and adolescent-typical behavior patterns: an evolutionary approach. In: Walker, E., Romer, D. (Eds.), Adolescent Psychopathology and the Developing Brain: Integrating Brain and Prevention Science. Oxford University Press, New York, pp. 9–30.
Spear, L.P., Varlinskaya, E.I., 2005. Adolescence: alcohol sensitivity, tolerance, and intake. In: Galanter, M. (Ed.), Recent Developments in Alcoholism, Volume 17: Alcohol Problems in Adolescents and Young Adults. Kluwer Academic/Plenum Publishers, New York, pp. 143–159.
Steinberg, L., 2004. Risk taking in adolescence. What changes, and why? Ann. N.Y. Acad. Sci. 1021, 51–58.
Steinberg, L., 2007. Risk taking in adolescence: new perspectives from brain and behavioral science. Curr. Dir Psych. Sci. 16 (2), 55–59.
Steinberg, L., 2008. A social neuroscience perspective on adolescent risk-taking. Dev. Rev. 28, 78–106.
Steinberg, L., Belsky, J., 1996. An evolutionary perspective on psychopathology in adolescence. In: Cicchetti, D., Toth, S. (Eds.), Richester Symposium on Developmental Psychopathology, vol. 7. University of Rochester Press, Rochester, NY, pp. 93–124.
Steinberg, L., Graham, S., O'Brien, L., Woolard, J., Cauffman, E., Banich, M., 2009. Age differences in future orientation and delay discounting. Child Dev. 80 (1), 28–44.
Ströhle, A., Stoy, M., Wrase, J., Schwarzer, S., Schlagenhauf, F., Huss, M., et al., 2008. Reward anticipation and outcomes in adult males with attention-deficit/hyperactivity disorder. Neuroimage 39, 966–972.
Stroud, L., Foster, E., Panpandonatos, G.D., Handwerger, K., Granger, D.A., Kivlighan, K.T., et al., 2009. Stress response and the adolescent transition: performance versus peer rejection stressors. Dev. Psychopathol. 21, 47–68.
Sturman, D.A., Mandell, D.R., Moghaddam, B., 2010. Adolescents exhibit behavioral differences from adults during instrumental learning and extinction. Behav. Neurosci. 124 (1), 16–25.
Tarazi, F.I., Baldessarini, R.J., 2000. Comparative postnatal development of dopamine D_1, D_2, and D_4 receptors in rat forebrain. Int. J. Dev. Neurosci. 18 (1), 29–37.
Teicher, M.hH., Krenzel, E., Thompson, A.P., Andersen, S.L., 2003. Dopamine receptor pruning during the peripubertal period is not attenuated by NMDA receptor antagonism in the rat. Neurosci. Lett. 339 (1), 169–171.
Thiel, K.J., Okun, A.C., Neisewander, J.L., 2008. Social reward-conditioned place preference: a model revealing an interaction between cocaine and social context rewards in rats. Drug Alcohol. Depend. 96, 202–212.
Thiel, K.J., Sanabria, F., Neisewander, J.L., 2009. Synergistic interaction between nicotine and social rewards in adolescent male rats. Psychopharmacology (Berl.) 204, 391–402.
Thomas, K.M., Drevets, W.C., Dahl, R.E., Ryan, N.D., Birmaher, B., Eccard, C.H., et al., 2001. Amygdala response to fearful faces in anxious and depressed children. Arch. Gen. Psychiatry 58, 1057–1063.
Torres, O.V., Tejeda, H.A., Natividad, L.A., O'Dell, L.E., 2008. Enhanced vulnerability to the rewarding effects of nicotine during the adolescent period of development. Pharmacol. Biochem. Behav. 90, 658–663.
Truitt, W., Sajdyk, T.J., Dietrich, A.D., Oberlin, B., McDougle, C., Shekhar, A., 2007. From anxiety to autism: spectrum of abnormal social behaviors modeled by progressive disruption of inhibitory neuronal function in the basolateral amygdala in Wistar rats. Psychopharm 191, 107–118.
Tseng, K.Y., O'Donnell, P., 2006. Dopamine modulation of prefrontal cortical interneurons changes during adolescence. Cereb. Cortex 17 (5), 1235–1240.
Ung, R.L., Zitzman, D.L., Spear, L.P., Robinson, D.L., 2010. Differences in elicited dopamine transients in response to stimuli presented during Pavlovian approach conditioning in adult versus adolescent rats. In: Society for Neuroscience Meeting, San Diego.
Vaidya, J.G., Grippo, A.J., Johnson, A.K., Watson, D., 2004. A comparative developmental study of impulsivity in rats and humans. Ann. N. Y. Acad. Sci. 1021, 395–398.
van Duijvenvoorde, A.C.K., Zanolie, K., Rombouts, S.A.R.B., Raijmakers, M.E.J., Crone, E.A., 2008. Evaluating the negative or valuing the positive? Neural mechanisms supporting feedback-based learning across development. J. Neurosci. 28 (38), 9495–9503.
van Leijenhorst, L., Crone, E.A., Bunge, S.A., 2006. Neural correlates of developmental differences in risk estimation and feedback processing. Neuropsychologia 44, 2158–2170.
Van Leijenhorst, L., Zanolie, K., Van Meel, C.S., Westenberg, P.M., Rombouts, S.A.R.B., Crone, E.A., 2010a. What motivates the adolescent? Brain regions mediating reward sensitivity across adolescence. Cereb. Cortex 20 (1), 61–69.
Van Leijenhorst, L., Moor, B.G., Op de Macks, Z.A., Rombouts, S.A.R.B., Westenbert, P.M., Crone, E.A., 2010b. Adolescent risky decision-making: neurocognitive development of reward and control regions. Neuroimage 51, 345–355.
Varlinskaya, E.I., Spear, L.P., 2002. Acute effects of ethanol on social behavior of adolescent and adult rats: role of familiarity of the test situation. Alcohol. Clin. Exp. Res. 26 (10), 1502–1511.
Varlinskaya, E.I., Spear, L.P., 2008. Social interactions in adolescent and adult Sprague–Dawley rats: impact of social deprivation and test context familiarity. Behav. Brain Res. 188, 398–405.
Venkatraman, V., Huettel, S.A., Chuah, L.Y.M., Payne, J.W., Chee, M.W.L., 2011. Sleep deprivation biases the neural mechanisms underlying economic preferences. J. Neurosci. 31 (10), 3712–3718.
Vázquez, D.M., 1998. Stress and the developing limbic-hypothalamic-pituitary-adrenal axis. Psychoneuroendocrin 23, 663–700.
Verdejo-García, A., Perez-Garcia, M., Bechara, A., 2006. Emotion, decision-making and substance dependence: a somatic-marker model of addiction. Curr. Neuropharmacol. 4, 17–31.
Vetter-O'Hagen, C., Varlinskaya, E.I., Spear, L., 2009. Sex differences in ethanol intake and sensitivity to aversive effects during adolescence and adulthood. Alcohol Alcohol. 44 (6), 547–554.
Volkow, N., Fowler, J., Wang, G.-J., 2003. The addicted human brain: insights from imaging studies. J. Clin. Invest. 111 (10), 1444–1451.
Volkow, N.D., Wang, G.-J., Telang, F., Fowler, J.S., Logan, J., Jayne, M., et al., 2007. Profound decreases in dopamine release in striatum in detoxified alcoholics: possible orbitofrontal involvement. J. Neurosci. 27 (46), 12700–12706.
Wahlstrom, D., Collins, P., White, T., Luciana, M., 2010. Developmental changes in dopamine neurotransmission in adolescence: behavioral implications and issue in assessment. Brain Cogn. 72, 146–159.
Walker, E.F., McMillan, A., Mittal, V., 2007. Neurohormones, neurodevelopment, and the prodrome of psychosis in adolescence. In: Romer, D., Walker, E.F. (Eds.), Adolescent Psychopathology and the Developing Brain: Integrating Brain and Prevention Science. Oxford University Press, New York, pp. 264–283.
Walker, E.F., Sabuwalla, Z., Huot, R., 2004. Pubertal neuromaturation, stress sensitivity, and psychopathology. Dev. Psychopathol. 16 (4), 807–824.
Weickert, C.S., Webster, M.J., Gondipalli, P., Rothmond, D., Fatula, R.J., Herman, M.M., et al., 2007. Postnatal alterations in dopaminergic markers in the human prefrontal cortex. Neuroscience 144, 1109–1119.
White, A.M., Swartzwelder, H.S., 2005. Age-related effects of alcohol on memory and memory-related brain function in adolescents and adults. In: Galanter, M. (Ed.), Recent Developments in Alcoholism, Volume 17: Alcohol Problems in Adolescents and Young Adults. Kluwer Academic/Plenum Publishers, New York, pp. 161–176.
Willey, A.R., Varlinskaya, E.I., Spear, L.P., 2009. Social interactions and 50 kHz ultrasonic vocalizations in adolescent and adult rats. Behav. Brain Res. 202, 122–129.
Wilmouth, C.E., Spear, L.P., 2009. Hedonic sensitivity in adolescent and adult rats: taste reactivity and voluntary sucrose consumption. Pharmacol. Biochem. Behav. 92, 566–573.
Wrosch, C., Miller, G.E., 2009. Depressive symptoms can be useful: self-regulatory and emotional benefits of dysphoric mood in adolescence. J. Pers. Soc. Psychol. 96 (6), 1181–1190.
Zald, D., 2003. The human amygdala and the emotional evaluation of sensory stimuli. Brain Res. Rev. 41 (1), 88–123.
Zigmond, M., Castro, S., Keefe, K., Abercrombie, E., Sved, A., 1998. Role of excitatory amino acids in the regulation of dopamine synthesis and release in the neostriatum. Amino Acids 14, 57–62.