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Neural Networks Involved in Adolescent Reward Processing: An Activation Likelihood Estimation Meta-Analysis of Functional Neuroimaging Studies

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Abstract

Behavioral responses to, and the neural processing of, rewards change dramatically during adolescence and may contribute to observed increases in risk-taking during this developmental period. Functional MRI (fMRI) studies suggest differences between adolescents and adults in neural activation during reward processing, but findings are contradictory, and effects have been found in non-predicted directions. The current study uses an activation likelihood estimation (ALE) approach for quantitative meta-analysis of functional neuroimaging studies to: 1) confirm the network of brain regions involved in adolescents' reward processing, 2) identify regions involved in specific stages (anticipation, outcome) and valence (positive, negative) of reward processing, and 3) identify differences in activation likelihood between adolescent and adult reward-related brain activation. Results reveal a subcortical network of brain regions involved in adolescent reward processing similar to that found in adults with major hubs including the ventral and dorsal striatum, insula, and posterior cingulate cortex (PCC). Contrast analyses find that adolescents exhibit greater likelihood of activation in the insula while processing anticipation relative to outcome and greater likelihood of activation in the putamen and amygdala during outcome relative to anticipation. While processing positive compared to negative valence, adolescents show increased likelihood for activation in the posterior cingulate cortex (PCC) and ventral striatum. Contrasting adolescent reward processing with the existing ALE of adult reward processing (Liu et al., 2011) reveals increased likelihood for activation in limbic, frontolimbic, and striatal regions in adolescents compared with adults. Unlike adolescents, adults also activate

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executive control regions of the frontal and parietal lobes. These findings support hypothesized elevations in motivated activity during adolescence.

Introduction

Adolescents are more likely than either adults or children to take risks. Preventable situations, such as vehicle accidents, substance use, suicide, and homicide, are the leading causes of death in people ages 10-24 in the United States (Eaton et al., 2012; SAMHSA, 2012) and this risk of mortality likely extends to other cultures. Animal models suggest a biological mechanism since risky behavior during the adolescent period is not specific to humans; for example, adolescent as compared to adult rats show increased risk-taking, novelty seeking, and voluntary alcohol consumption (Doremus et al., 2005; Spear, 2011; Wilmouth & Spear, 2009). Given the public health costs of adolescent risk taking, research has focused on examinations of the neural mechanisms that support it, particularly developmental changes in brain networks that mediate motivational processing (Ernst et al., 2006; Luciana et al., 2012; Steinberg, 2010).

The link between motivational processing and adolescent risk-taking is based on the idea that in order to meet expectations associated with adult roles and to facilitate a sense of personal agency, adolescents are biologically driven to seek contexts that are novel and that bring the potential for positive reinforcement (Wahlstrom et al., 2010a; Luciana and Collins, 2012; Luciana et al., 2012). When confronted by such situations, adolescents may be motivationally biased toward reward pursuit because of heightened sensitivity to incentive-based stimuli, perhaps to the point of neglecting threat-based cues (Van Leijenhorst et al., 2010b). Accordingly, adolescents would be expected to show greater anticipation to potentially rewarding stimuli and heightened responses when rewards are received, as compared to adults or to children. Importantly, these patterns may extend beyond behavior to neural activations within networks typically associated with reward processing during incentive-based tasks. Task-based neuroimaging provides a means of testing these hypotheses.

The development of reward processing is a rapidly growing area of research, and brain activation differences in subcortical regions associated with reward and reward-based learning, such as the ventral striatum (VS), have been observed in adolescents, as compared with children or adults (e.g. Ernst et al., 2005; Galvan, 2010). However, findings are inconsistent. Studies have found both hyper- and hypo-activation in the VS and interconnected regions during different stages of motivational processing (e.g., Bjork et al., 2010; Geier et al., 2010), and use of similar task designs does not always yield equivalent results. These contradictory findings may result from different developmental stages or ages of participants, cohort effects, or the influence of distinct task demands (Galvan, 2010; Richards et al., 2013). Accordingly, it has not yet been confirmed that, across studies, adolescents reliably activate the same regions during reward based processing as do adults (McClure et al., 2004; Liu et al., 2011; Bartra et al., 2013).

Although there is diversity in the fMRI tasks that have dominated the literature, many paradigms differentiate between stages or valences of reward processing, or both. Animal

studies indicate that reward processing can be dissociated into appetitive or motivational versus consummatory components (Robbins and Everitt, 1996; Ikemoto and Panksepp, 1999). A related theory finds evidence for dissociable neural underpinnings of 'wanting,' or incentive motivation, and 'liking,' the pleasure of reward consumption (Robinson and Berridge, 1993; Berridge, 2009). Such distinctions between different stages of reward processing are supported by studies using reward tasks during fMRI, where different patterns of brain activation have been linked to reward anticipation and reward receipt (Knutson et al., 2001). Similarly, positive reward valence and negative reward valence, which refer to the subjective states associated with gain or loss, yield distinct functional activation patterns and as a result are sometimes measured separately (Liu et al., 2007). Better characterization of neural activations that are reliably associated with distinct stages and valences of reward processing may contribute to an understanding of the temporal course of adolescent decision-making in risky contexts (Ernst et al., 2005; Spear, 2011b; Bjork et al., 2012; Blakemore and Robbins, 2012; Sturman and Moghaddam, 2012).

The heterogeneity of findings on adolescent reward processing justifies a meta-analysis to confirm that there are core brain regions activated across studies. The current project aims to shed light on this contradictory research area and to serve as a road map for future inquiries on the topic of adolescent reward processing. This study employs a coordinate-based meta-analytic method, activation likelihood estimation (ALE), to determine regions commonly activated across a large number of studies (Eickhoff et al., 2009; Turkeltaub et al., 2012). This type of analysis is valuable, because individual studies may be limited by small samples and low reliability (Eickhoff et al., 2012). Pooling data across studies that assess similar constructs allows spatial coordinates to be identified that show consistent activation patterns across hundreds of participants, allowing the most robust findings to be discerned.

Accordingly, this study's goals are to: 1) confirm brain regions involved in adolescent reward processing broadly defined, 2) identify regions with significant likelihoods of activation during different stages (anticipation, outcome) and valence (positive, negative) in adolescents as they process reward contexts, and 3) identify differences between adults and adolescents in their activation patterns. It may be that the groups activate similar regions but that there is a stronger likelihood of some regions' activation in one group or the other. Despite the diversity of methods used among individual studies, we hypothesize that, regardless of task demands, a meta-analysis will reveal that a similar set of structures show a strong likelihood of activation in both adolescents and adults (Liu et al., 2011) during reward processing. We hypothesize that these structures will represent nodes of the ascending mesocorticolimbic dopamine system (Berridge and Robinson, 1998; Goto and Grace, 2005; Wahlstrom et al., 2010b). We hypothesize that both anticipation and outcome phases of reward processing will yield likelihoods of activation in dorsal and ventral striatal regions but that the processing of outcomes will be more strongly associated with activation likelihood in orbitofrontal regions and other areas involved in reward-based learning. We predict that negative valence cues and outcomes will show blunted likelihood of activation in frontolimbic and striatal regions relative to positive valence, suggestive of failures to weigh consequences of loss events relative to gain events. We further hypothesize that adolescents (as compared to adults) will generally exhibit a heightened sensitivity to reward contexts (Luciana et al., 2012), manifested as greater likelihood of activation in subcortical

regions that are integral to reward processing (Wahlstrom et al., 2010a, 2010b). Finally, we expect adolescents, relative to adults, to show less activation likelihood in higher cortical regions associated with executive control.

Materials and Methods

Study selection

Two independent researchers identified studies investigating reward processing during adolescence. An exhaustive literature search was conducted from two databases, PUBMED and BrainMap (using Sleuth). Search terms chosen were the same as those used by Liu and colleagues (2011) in their ALE of adult reward processing. PUBMED was searched with the following terms: 1) “fMRI” AND “reward” AND “Decision” and 2) “reward decision making task” AND “fMRI” AND “human. These searches yielded a total of 516 non-overlapping studies. These searches were replicated with the added conjunctive and keyword search term: AND “adolescents,” which did not yield any additional non-overlapping results. The BrainMap database was searched with the terms “fMRI” AND “reward” which yielded an additional 167 papers, 120 of which were non-overlapping. Twelve additional articles were identified from one of the researcher's reference base, utilizing search terms “adolescent” and “reward.” These three searches conducted in October, 2014 yielded a total of 648 studies.

Studies were deemed eligible for inclusion if they met the following criteria: 1) studies were empirical and data-based, and could not be review articles, 2) results were reported in standard stereotactic space (either in Talairach or Montreal Neurological Institute, MNI, space), 3) studies employed fMRI 4), results reported peak activation coordinates from group activation maps from whole-brain analyses (and could not employ a region of interest, ROI, approach), 5) participants were adolescents, defined as ages 8 to18 years 6) special populations (i.e., psychiatric populations) were excluded, though control subjects from these studies were included. The wide age range was selected to capture the full range of adolescence as currently defined in Western culture and to capture the full range of pubertal development (Dorn et al., 2006; Forbes & Dahl, 2010), although pubertal status was rarely reported within individual studies.

All 648 studies identified from search databases were reviewed for adherence to these criteria. This review process involved at least one of the authors reading the title and abstract initially, to determine whether the study population included adolescents. A large number of studies (n=586) were excluded at this stage because they did not include adolescents. Sixty-two studies included adolescents and warranted more in depth review. These studies were evaluated by reading the title, abstract, and methods. Among these 62 studies, the most common reasons for exclusion were: using an ROI approach (6 studies), not reporting whole group activation for adolescents separately from adults or special populations (10 studies), and not reporting peak coordinates from whole brain analyses (5 studies).

Additionally, after consulting with investigators who had first-authored more than one paper included in the final list, it was determined that papers from two laboratories [(Bjork et al., 2004, 2008) and (Telzer et al., 2013a, 2013b)] included overlapping samples. Although

sample overlap is rarely accounted for within ALE analyses (Caspers et al., 2010; Liu et al., 2011; Cortese et al., 2012), it could introduce bias due to non-independence of observations. As a result, the dataset with the smaller sample within each of these two sets of studies (Bjork et al., 2004; Telzer et al., 2013b) was excluded from the current analyses.

Twenty-six studies (with thirty discrete samples or experiments) remained for the final analyses. The discrepancy results from the fact that four of the twenty-six studies included two separate adolescent samples, which are listed in the analyses as distinct experiments (Forbes et al., 2010; Van Leijenhorst et al., 2010a, 2010b; Op de Macks et al., 2011). This number of included studies is consistent with other recent ALE analyses in the field of fMRI research (e.g., Albrecht et al., 2010; Mohr et al., 2010; Bzdok et al., 2011; Belyk and Brown, 2014). The total number of participants for the overall ALE is 830. The mean weighted age of study subjects for the overall adolescent ALE is 14.10. The mean age of study participants within each included study ranged from 11.1 to 17.1 years. Based on personal correspondence with study authors, it was estimated that only 3 participants between the ages of 8 and 9 were represented in the final sample. These were retained, because they were grouped, within the selected studies, with individuals who were older. Exclusion would have compromised the sample size for the final analyses.

Studies that did not report coordinates in MNI space were grouped together based on the coordinate transformations available in GingerALE (http://brainmap.org, Research Imaging Center of the University of Texas Health Science Center, San Antonio, Texas). Coordinates were converted into MNI space using the icbm2tal space transform (Lancaster et al., 2007).

Study categorization

Coordinates that met the general inclusion criteria were recorded for the overall adolescent reward processing ALE. Studies were then further categorized based on different aspects of reward processing. Following from the organization scheme laid out in Liu et al. (2011), coordinates were categorized based on valence (positive, negative) and stage (anticipation and outcome) of reward processing. Reflecting the diversity of condition types characterized as positive and negative valence in the literature, coordinates were categorized as pertaining to positive valence when subjects won something (including money, points, juice, encouragement) (Bjork et al., 2010; Galván and McGlennen, 2013); avoided loss (Schlund et al., 2010); or received the greater of two gains (Ernst et al., 2005). Coordinates were categorized as pertaining to negative valence when subjects lost something (including money, points, juice, encouragement) (Paloyelis et al., 2012); missed a gain opportunity (Van Leijenhorst et al., 2010b); won the smaller of two amounts (Crowley et al., 2010); or received discouraging feedback or images (no studies included in the current analysis met this last criterion). Experiments that indexed positive valence (n = 27) were considerably more common than those that assessed negative valence (n = 11).

Included studies varied in terms of what each used for its contrast baseline. Some studies reported results from contrasts against no-incentive / no consequence cues (e.g., Bjork et al., 2008), some studies compared one condition against another condition (e.g., Win $4.00> Win $0.50, see Ernst et al., 2005), and some studies compared against an implicit baseline (e.g., Jarcho et al., 2012). Additionally, even though individual fMRI studies examine

different magnitudes of gain and loss separately (e.g., large, medium and small gain compared to baseline: (Jarcho et al., 2012)), in the current analyses we collapsed across different magnitudes to increase the power of the valence analyses. The extant meta-analysis of adult reward processing (Liu et al., 2011) similarly collapsed across gains and losses of varying magnitudes.

Anticipation was reflected by tasks in which participants deliberated reward-related options or outcomes prior to their delivery. Outcome was characterized as a stage in which participants received feedback about gains or losses associated with their decisions or behavior. All but two studies that were included used paradigms in which participants would have been uncertain about the nature of the outcome (positive or negative; high versus low reward). Liu et al. (2011) in a meta-analysis of adult studies also included a stage of *evaluation*, which was characterized as a stage in which participants incorporated feedback, which then influenced subsequent trials, based on principles of learning. In the current analysis, only two studies (Scott-Van Zeeland et al., 2010; Christakou et al., 2013) could be categorized in this manner, so this stage was not pursued for meta-analysis. These coordinates were nonetheless included in the main adolescent reward processing analysis. Two of the authors (MHS and KJ) reviewed each paper and reached consensus about study inclusion and categorization for stage, and valence.

Thirty experiments met the inclusion criteria for the overall adolescent reward-processing analysis (see Table 1), resulting in 846 reward-related foci in a sample of 830 subjects (Study Aim 1). Coordinates were then categorized from these thirty experiments as pertaining to different stages (anticipation, outcome) and valences (positive, negative) of reward processing.

Studies often separately report coordinates for stage and valence; as a result the same study could contribute different coordinates to both stage lists and to both valence lists. Eighteen experiments (286 foci; 613 subjects) were included in the anticipation analysis and twenty-four experiments were included in the outcome analysis (498 foci; 533 subjects; Study Aim 2). Twenty-seven experiments were included in the positive valence analysis (661 foci; 756 subjects) and eleven experiments were included in the negative valence analysis (117 foci; 266 subjects; Study Aim 2). It was not possible to examine the interactive effects between stage and valence with adequate power because of the small number of studies that indexed negative valence (n=11); of these, only 5 studies reported coordinates for anticipation of a negative valence event.

For the purpose of contrasting adolescent and adult reward processing, an additional ALE of adult reward processing was conducted using coordinates provided by Liu and colleagues from their research on the topic (2011); this consisted of 655 experiments (5214 foci; 11,904 subjects; Study Aim 3).

Because many definitions of adolescence exclude individuals that are below 12 years old, all ALEs were replicated in post hoc analyses excluding the ten studies that included subjects younger than 12 in their sample (see Table 1) to verify that results were not inordinately

impacted by inclusion of these younger participants. For the overall adolescent ALE, this resulted in 499 foci from 585 subjects.

ALE meta-analyses

ALE meta-analyses were computed in GingerALE v2.3, a BrainMap program (Eickhoff et al., 2009, 2012; Turkeltaub et al., 2012). Peak activation coordinates across a number of studies examining similar behavioral processes are pooled together. ALE differs from other meta-analytic techniques, because the goal of ALE is to identify the spatial coordinates of brain regions and networks involved in a function or behavior of interest, as opposed to estimating the true effect size of a given phenomenon. Coordinates from pooled studies are used to produce activation likelihood estimates for every voxel in the brain. In this method, every voxel's ALE score represents its likelihood of being activated given its proximity to one of the peak activation coordinates from included studies, using three-dimensional Gaussian probability densities centered at the coordinates. The widths of these Gaussian distributions around peak activation coordinates are calculated based on the sample size of each experiment (Eickhoff et al., 2009). The modeled activation map from each study is then combined into an unthresholded ALE map representing the convergence of activation likelihoods for every voxel across all of the studies. This unthresholded group ALE is compared to a null distribution map derived from a permutation procedure of randomly generated activation likelihoods. This produces a statistical map of p-values from the ALE scores, indicating the probability that any voxel in the brain is included within the region surrounding one of the contributing peak activation coordinates.

Meta-analyses of sub-lists

Using these methods, a series of ALE meta-analyses were conducted. The first analysis included all of the reward-related foci for adolescents, regardless of stage or valence. Next, meta-analyses were conducted separately for two stages (anticipation, outcome) and two valences (positive, negative). Each stage and valence was examined on its own, and then contrast analyses (see below) were implemented to compare stages and valences. Significance in the overall, stage, and valence ALE analyses was determined using a cluster-level inference corrected threshold of $p<0.05$, 5000 thresholding permutations, and an uncorrected p-value of < 0.001 as the cluster forming threshold (Eickhoff et al., 2012). Finally, using the coordinates for the overall adult reward processing ALE provided by Liu and colleagues (2011) and the thresholding parameters outlined in their manuscript, we reproduced the findings reported in their study as a validation check of our procedures. This ALE was used for contrasting the likelihood of reward related brain activity in adolescents compared with adults.

Contrast Analyses between sub-lists

Contrast, or subtraction, analyses were conducted to determine brain areas that showed differences in activation likelihood in different stages and valences (Laird et al., 2005). An additional contrast analysis was conducted between the overall reward-related ALE for adolescents compared to the overall reward-related ALE for adults (Liu et al., 2011), to identify regions that were more likely to be activated in either of these populations. During contrast analyses, ALE scores are calculated for every voxel as the difference in ALE values

between the meta-analysis of the two contrasting coordinate lists independently. To determine statistical significance, these values are then compared to a null distribution based on the difference in ALE values for two randomly distributed sets of voxels. In the current study, a smoothing kernel of 10 mm FWHM was employed for contrast analyses. For these analyses, an uncorrected p-value of <.01 and a minimum cluster size of 60 voxels (480 mm^3) were used to determine statistical significance against a null distribution (derived from 5000 permutations).

Results

Three overarching questions were pursued in our analyses. Namely, we sought to confirm the network of brain regions involved in adolescent reward processing broadly defined. Next we wanted to determine the regions involved in valence and stage of processing, and to determine whether any regions were more likely to be activated during anticipation versus outcome (stage of processing) or during positive versus negative conditions (valence) of reward processing. Last, we sought to determine whether there were differences between adolescents and adults in their likelihood of activating specific brain regions during reward processing.

All ALE tables in the current study report brain regions based on the coordinates (in MNI space) provided for the maximum ALE values or maximum ALE difference scores (reported as z-scores, for the contrast analyses). Brain regions reported in tables are derived from the Harvard-Oxford subcortical and cortical structural atlases. Because large clusters encompassed multiple brain regions (many of which are not reflected by the peak coordinates listed in the tables), likelihood of activation in regions within each cluster that were found to be significant is reported in the text (and in figures).

Confirmation of Regions Involved in Adolescent Reward Processing

To address the nature of the network implicated in reward-relevant processing, an analysis that included all adolescent reward-related foci that met inclusion criteria, regardless of stage of reward processing (anticipation, outcome, or evaluation) or valence (positive or negative) was conducted. A significant likelihood of reward-related activity was found bilaterally in the dorsal and ventral striatum, insula, PCC, paracingulate gyrus, amygdala, lateral occipital gyrus, and occipital pole, all areas that have been implicated in similar meta-analyses of adult reward processing (Liu et al., 2011b; Bartra et al., 2013). Results can be found in Table 2 and in Figure 1 (top panel). This analysis confirms that adolescents generally activate a similar set of subcortical structures as adults when processing reward-relevant contexts. Evidence of higher cortical activation likelihood was notably absent.

ALE Results for Adolescent Stage of Processing: Anticipation versus Outcome

Separate meta-analyses were conducted to examine the neural representation of reward anticipation and outcome. Concordant with our hypotheses, significant likelihood of activation was found bilaterally in the ventral and dorsal striatum, OFC, frontal opercular regions, and anterior insula during both the anticipation stage (Figure 1, second panel; Table 3) and outcome stage (Figure 1, third panel; Table 3) of reward processing.

Contrast analyses (Figure 2; Table 4) reveal a stronger likelihood of neural representation in the left insula and frontal operculum during anticipation as compared to outcome. Contrast analyses also reveal a stronger likelihood of neural representation in the left putamen and amygdala during outcome compared to anticipation.

ALE Results for Adolescent Valence of Processing: Positive versus Negative Contexts

Separate meta-analyses were also conducted to examine the neural representation of positive and negative valence.

As expected, positive valence (Figure 1, fourth panel; Table 3) was associated with likelihood of activation bilaterally in the ventral and dorsal striatum, OFC, insula, paracingulate gyrus, and PCC. Negative valence (Figure 1, fifth panel; Table 3) was associated with a significant likelihood of activation in the left dorsal striatum, precuneous, and brain stem and right thalamus, supplementary motor cortex, insula, and precentral gyrus.

Contrast analysis (Figure 2, bottom panel; Table 4) shows increased likelihood for activation in the right PCC, subcallosal cortex, nucleus accumbens, and lateral occipital cortex during positive compared to negative valence processing. No significant neural substrates were found in the contrast of negative greater than positive valence processing.

ALE Results for Adolescent and Adult Contrast Analyses

Contrast analyses were conducted to examine differences between overall adolescent reward processing and overall adult reward processing (Figure 3; Table 5), using the coordinates from the existing study of adults on this topic (Liu et al., 2011).

No significant neural substrates were found where overall adult reward processing showed greater activation likelihoods than overall adolescent reward processing. However, in support of our predictions, contrast analyses revealed an increased likelihood for activation in adolescents compared with adults in the bilateral ventral and dorsal striatum, insula, OFC, anterior cingulate cortex (ACC), PCC, frontal opercular regions, paracingulate gyrus, subcallosal cortex; right amygdala, right occipital pole; and left lateral occipital cortex. To confirm that the discrepant sample sizes between adolescent and adult foci were not influencing the contrast analyses, the adult list was randomly divided into multiple sub-lists with comparable numbers of foci to the adolescent sample (Laird et al., 2005). Again, no findings for the adults>adolescent contrast emerged. Findings for adolescent>adults across the sub-lists consistently showed similar regions as reported above, in Table 5, and as shown in Figure 3.

Finally, to exclude the possibility that findings were inordinately influenced by the inclusion of relatively young participants, all ALE analyses were repeated excluding participants below the age of 12. Findings did not vary from what is described above.

Discussion

This study employs an ALE approach -- a quantitative, meta-analytic method – that makes it possible to base conclusions regarding neural correlates of adolescent reward processing on

a synthesis of the broad literature. Three central questions were explored: 1) what are the core brain regions involved in adolescent reward processing, 2) what regions are likely to be activated during specific stages and valences, and 3) what distinctions characterize brain networks supporting adolescent versus adult behavior.

Brain Regions Involved in Adolescent Reward Processing

We included data from 830 participants across 26 studies (with a total of 30 unique samples/experiments). Pooling coordinates across studies revealed a core network of regions involved in adolescent reward processing, broadly defined. Major nodes included the ventral and dorsal striatum, insula, and PCC. These regions overlap the subcortical regions identified in similar ALEs of adult reward processing (Liu et al., 2011; Bartra et al., 2013) and include major dopaminergic projection regions (e.g., accumbens region of the ventral striatum), and regions (anterior insula) that are associated with salience, affective control, and the processing risk and uncertainty (Menon & Uddin, 2010; Mohr et al. , 2010; Preuschoff et al., 2008). The posterior cingulate region is part of the brain's hub architecture as well as a core node in the default mode network (Leech and Sharp, 2014); it participates in a number of functions, including attention, episodic memory, and awareness. Although implicated in adult reward processing (Liu et al., 2011), its likelihood of activation appears to be more pronounced in adolescents. These regions cohere in a manner that is consistent with prior studies of animal (Schultz, 2000) and human (Liu et al., 2011; Bartra et al., 2013) behavior, generally confirming that adolescents activate a similar set of subcortical regions as adults in perceiving, processing, and responding to reward-based contexts.

Notably, Liu et al. (2011) also reported strong activation likelihoods for numerous regions of the dorsal and ventral prefrontal cortex as well as superior and inferior parietal areas. The lack of significance of these regions in the current ALE suggests that in adolescents, reward processing is driven more strongly by limbic, paralimbic, and striatal regions without reliable contributions from higher cortical regions. The dorsolateral prefrontal cortex in concert with parietal regions is integral to the brain's executive control network, as discerned from studies of the brain's intrinsic functional connectivity (Beckmann et al., 2005; Seeley et al., 2007; Heine et al., 2012). In adults, the executive control network recruits sustained attention, working memory monitoring and manipulation processes, and flexibility so that behavioral options can be assessed relative to the current environmental context, past experience, and outcome contingencies (Seeley et al., 2007) prior to response initiation. In adolescents, this network continues to mature (Fair et al., 2007; Sherman et al., 2014), such that increasing within-network functional connectivity is evident with increasing age. In the absence of such coherence, executive control regions may be only inconsistently activated in adolescents. Response selection in the midst of reward-based motivational situations may be less deliberate than in adults and may be weighted based on input from other regions.

Processing Stages of Reward

In the current analysis, anticipation was associated with activation likelihood in dorsal and ventral striatal regions, motor regions, insula, and the frontal operculum. These areas overlap with those generally known to be involved in incentive motivational processing (Depue and Collins, 1999) and what has been termed the “wanting” component of positive

motivation (Berridge and Kringelbach, 2013). Some of these regions overlap with those involved in processing reward outcomes given that the latter process is also associated with activation likelihood in the striatum and insula.

Direct comparison of anticipation versus receipt of gain or loss cues revealed a more preferential likelihood of activation during anticipation in the anterior insula and left frontal operculum, near the posterior extent of the inferior frontal gyrus. Liu (2011) reported a similar finding for the anterior insula in adults in addition to regions such as the supplementary motor area and anterior cingulate cortex. The ALE by Mohr and colleagues (2010) found the anterior insula, a region associated with aversive emotion processing (Reiman et al., 1997; Paulus et al., 2003), to be specifically activated during risk processing, which was the focus of their analysis. The insula is a critical component of the brain's salience network (Craig, 2009; Menon and Uddin, 2010) and participates in interoceptive awareness, the representation of physiological states associated with risk (Xue et al., 2010), and integration of such states with behavior during risky contexts that are characterized by uncertainty (Singer et al., 2009). These findings suggest that adolescents may be highly sensitive to stimulus salience and to visceral experiences as they anticipate reward-based outcomes. The surging hormones of puberty may further heighten somatosensory awareness.

In the current analysis, regions more likely to be activated during outcome versus anticipation included the putamen and amygdala. The amygdala has been long-recognized as a core node within the mesolimbocortical dopamine system (Berridge, 2004) and serves to modulate ventral striatal activity (Ernst and Fudge, 2009). In reward contexts, the nucleus accumbens region of the ventral striatum acts as a motivation-to-behavior interface, facilitating approach behavior by integrating information provided by excitatory inputs from the amygdala as well as other regions (Spear, 2011). The prominence of the amygdala in the processing of reward-based outcomes permits the emotive signals generated by such outcomes to impact future behavior. Similarly, the putamen may contribute to the learning of outcome contingencies and modulates motor responses based on reward outcomes (Hori et al., 2009; Muranishi et al., 2011).

Liu et al. (2011) found a significant likelihood of nucleus accumbens and OFC activation in adults' processing of reward outcomes versus anticipation. In contrast, the prominence of the insula, amygdala, and putamen in adolescents' stage-related processing suggests that adolescent behavior is strongly influenced by the salience of anticipated rewards and by amygdala-based valuation of outcomes.

Processing Valence of Reward

Task-related activation to positive valence stimuli and outcomes revealed a network similar to the broad one outlined above for the overall ALE, consistent with Liu et al. (2011). Positive valence is associated with a strong likelihood of activation in the ventral and dorsal striatum, insula, OFC, and PCC. Though there are fewer studies included in the current ALE that assessed responses to negative stimuli (and, accordingly, findings should be interpreted with caution), findings converge on regions including the putamen, precuneous, thalamus, precentral gyrus, and anterior insula. Relative to negative valence, positive valence yields more consistent processing in the PCC, accumbens, and lateral occipital cortex, suggesting a

link between the limbic-motor interface that allows approach to incentive-based stimuli (Depue and Collins, 1999) and the facilitation of self-referential cognitive activity that is mediated by the PCC (Johnson et al., 2002; Kelley et al., 2002). Although speculative, the findings for positive versus negative processing and anticipation relative to outcome-based processing suggest that in adolescence, incentive-seeking behavior is dominated by regions that contribute to self-referential visceral (e.g., insula) and cognitive (PCC) experience.

Among the studies that have studied loss events in adolescents, a number have found reduced responses in the amygdala, OFC, and ACC (Ernst et al., 2005; Bjork et al., 2010; Van Leijenhorst et al., 2010a). It has been hypothesized that blunted responses during threat/loss events could partially explain adolescent risk-taking, as this might indicate that the negative consequences of risks are not given appropriate weight relative to positive gain events (Luciana, 2013). We did not find differential likelihood of amygdala activation during the processing of valenced stimuli. Indeed, neither the current analysis nor the one by Liu et al. (2011) found any regions that showed stronger activation likelihoods in the processing of negative relative to positive contexts. The relative dearth of studies on loss conditions, as evidenced by this meta-analysis, suggests that more work in this area is needed, in order to assess whether inattention to such cues impacts decision-making in risk contexts.

Comparing Adolescent and Adult Reward Processing

A major finding of the current analysis is that adolescents and adults varied in activations during reward processing as supported by descriptive comparisons between our overall ALE and findings reported by Liu et al. (2011) as well as our contrast analysis. In our contrast analysis (using the coordinates for adult processing provided by Liu et al. (2011)), adolescents exhibited increased likelihood for activation in a large region that encompassed portions of the ventral and dorsal striatum, subcallosal cortex, insula, orbitofrontal region, and amygdala as well as the ACC, PCC, and paracingulate region. Although there were no regions where adults showed a greater activation likelihood relative to adolescents, the patterning of our findings is notable given the predominance of limbic and striatal regions and the relative absence of higher cortical regions with the exception of the lateral occipital cortex, which plays a crucial role in stimulus recognition (Grill-Spector et al., 2001).

Recent models of adolescent brain development predict peak levels of activation in the striatal-limbic system, particularly in the pursuit or receipt of positive incentives, and lower-than-adult levels of frontal control as indexed by activation differences in the lateral prefrontal and parietal cortices in adolescents relative to both children and adults (Casey et al., 2008; Steinberg, 2010; Luciana et al., 2012). Peaks in dopamine activity during adolescence and subsequent declines into adulthood may underlie adolescents' sensitivity to positive reward contexts (Wahlstrom et al., 2010a) given that midbrain dopamine projections to the limbic, striatal and frontal regions facilitate incentive motivation (Depue and Collins, 1999; Björklund and Dunnett, 2007; Haber, 2003). We have suggested that adolescents may experience a biologically-based readiness to respond when sources of reward are present or anticipated. This readiness may be evolutionarily adaptive in guiding

behavior toward future goals, but may also place adolescents at risk of poor decision-making in motivationally salient contexts (Luciana et al., 2012).

This model is supported by evidence of relatively increased activation likelihoods in adolescents relative to adults centered within the nucleus accumbens region of the ventral striatum (part of the first cluster represented in Table 5) given its prominence in the facilitation of incentive-guided behavior. Other regions that showed strong likelihoods of activations in adolescents relative to adults include the insula, amygdala, putamen, and anterior cingulate cortex. These regions are interconnected with the ventral striatum and form core components of the brain's incentive salience system (Menon and Uddin, 2010).

Highly processed cortical sensory inputs reach the ventral striatum through unidirectional projections from the insula as well as from the orbitofrontal cortex (Haber, 2003). The insula serves as a sensory convergence region, and there are strong connections between the insula and OFC. Thus, information processed by the insula, i.e., somatovegetative and autonomic signals (Paulus and Stein, 2006; Craig, 2009), is transferred to and used by the VS to code stimulus value and structure behavioral responses. The stronger likelihood of insular activation by adolescents relative to adults parallels findings from a recent study of striatal intrinsic functional connectivity in which it was demonstrated that the ventral striatum and insula are more tightly interconnected in adolescents than in adults (Porter et al., 2015). These findings suggest that in adolescents, incentive-related behavior may be more strongly bound to stimulus salience or to the physical arousal generated by the stimulus context. In the same study (Porter et al., 2015), the ventral striatum was more strongly interconnected to the dorsal anterior cingulate cortex in adolescents versus adults. The anterior cingulate, frequently co-activated with the anterior insula (Menon and Uddin, 2010) may play a role in integrating emotion and motivational signals pertaining to contextual salience with executive control systems (Pessoa, 2009) so that adaptive behavioral responses can be formulated and executed. Importantly, the ACC is rich in dopamine receptors and recognized as a core node within the incentive motivational system (Depue and Collins, 1999; Haber, 2003; Berridge, 2004), suggesting the possibility of a neurochemical basis for the aggregation of regions that showed stronger activation likelihoods in adolescents relative to adults. Importantly, these regions collectively code hedonic drive (nucleus accumbens, OFC, amygdala), outcome-based behavioral flexibility and learning (putamen; paracingulate), and incentive salience (insula, amygdala, ACC).

Findings from discrete studies have suggested relative peaks in limbic and striatal activation in adolescents during reward processing and reward-based learning (c.f., Galvan et al., 2006; Cohen et al., 2010) but these findings are not definitive. The current meta-analysis brings a powerful tool to the examination of this issue by consolidating findings across a broad range of paradigms and samples. Findings suggest that in adolescents, reward-based behavior is strongly driven by incentive salience and concordant activation within what has been termed the salience network.

Future Directions

In recent years, there has been a growing emphasis on the importance of not only understanding the ways that brain regions activate in response to stimuli, but also how brain

regions functionally connect to one another over time (Menon, 2013). Using methods for measuring functional connectivity, studies have added to our understanding of adolescent reward processing as it relates to risk-related behavior. One study of adolescents found that increased NAcc connectivity to the ACC and mPFC during the monetary incentive delay task correlated with a measure of drug use (Bjork et al., 2011). Another study found that the connection between the VS and the ventromedial PFC changed from adolescence into adulthood; this change correlated with a decrease in preference for immediate, smaller rewards in favor of larger, delayed rewards. That study also found that insula-vmPFC connectivity interacted with age predicting the steepness of delayed discounting (Christakou et al., 2011). We believe that one promising future direction of inquiry will be to incorporate the findings from the current meta-analysis of activation studies in guiding future studies examining the dynamic connections between brain regions during reward processing.

Limitations

This analysis is not without limitations, many of which stem from the current status of research in this area. A number of studies could not be included in this ALE given our inclusion criteria. Consistent with other ALEs, studies were excluded when they failed to report activation coordinates in whole brain analyses for adolescents separately from adults or other populations (e.g., Finger et al., 2011; Galvan et al., 2007; Hauser et al., 2014). Similarly, studies that reported only regions of interest (ROIs) based on *a priori* hypotheses were excluded (e.g., Galvan et al., 2006; Eshel et al., 2007; Shad et al., 2011). This is because ROI analyses limit detection of non-hypothesized findings, which in the context of ALE analysis would overly weigh regions with specific functional hypotheses. We acknowledge that there are many reasons one might use an ROI approach (Poldrack, 2007) despite the inability of such studies to contribute to analyses such as ours. Future studies employing an *a priori* ROI approach might report *post-hoc* findings from whole brain analyses as well, in order to facilitate inclusion in similar meta-analytic reports. Additionally, we excluded studies that only reported continuous correlations with age, as it was not possible to identify activation specific to adolescents (Christakou et al., 2011). Even after excluding a number of relevant studies, our sample (30 discrete samples from 26 studies) remains comparable in size, or larger, than other recent ALEs of task related brain activation.

Many studies included relatively small sample sizes potentially limiting the ability to observe true effects (Button et al., 2013). While the field of fMRI research is moving toward larger samples, small sample sizes can impact meta-analytic findings due to the skewed nature of the sample of studies included (Pereira and Ioannidis, 2011). An additional challenge for ALE is that it is common for multiple studies to report results using the same or overlapping samples. There is currently no accepted means of correcting for overlapping samples using ALE. In the current study, findings were based on studies without known overlap in participants.

Another possible limitation was the wide age range across studies. Some included studies narrowly limited adolescence to a range of 14-15 years of age (Van Leijenhorst et al., 2010); others included participants as young as 9-12 years (Ernst et al., 2005). The most typical

demographic information provided in the included studies was average age of participants and the standard deviation. As a result, in the current meta-analysis it was not possible to further characterize the sample beyond those characteristics or to determine whether certain discrete ages were more strongly represented. Our purpose was not to definitively establish the age range of adolescence, but rather to broadly characterize neural correlates of reward processing across this developmental period. Nonetheless, the proportion of participants below age 12 was relatively small in comparison to the full sample (and only 3 participants were below age 9). Running the analyses with and without studies that included individuals under age 12 revealed negligible differences in regions activated or regions found in the adolescent versus adults contrast. Inclusion of younger subjects is supported by hormonal evidence that puberty begins at an early age (Dorn et al., 2006; Forbes and Dahl, 2010). Unfortunately, pubertal influences could not be measured in this study. Additionally, sex differences that might impact brain development (Giedd et al., 1996) could not be examined given lack of reporting across studies.

Future meta-analyses on this topic would benefit from including studies of reward related brain activation in children, in addition to adolescents and adults. Such a study would help clarify the trajectory of reward related brain activation across development and could shed light on whether there is a peak in VS activation during the adolescent period relative to both childhood and adulthood. To date, though, an insufficient number of studies examining reward processing in children separately exist to conduct such an analysis.

Finally, there was wide variability in tasks. A recent review of reward tasks in adolescents identified sub-types of fMRI reward paradigms (i.e. passive reward tasks, instrumental-reward tasks, decision making tasks) and found neural differences related to specific features from each sub-type (Richards et al., 2013). The benefit of the ALE method is that it elucidates commonalities across diverse paradigms. This feature could also be perceived as a limitation given that activation likelihoods might vary depending on factors such as the nature of reward feedback, the baseline condition used for the reported contrast, or for different magnitudes of valence (e.g, large, medium, and small gains or losses). The studies included in this analysis predominantly included paradigms in which participants could receive differential feedback during the outcome phase of various tasks. Furthermore, in the current analysis studies were collapsed into stage and valence sub-lists despite often utilizing different baseline conditions and rewards of different magnitudes. As the field advances, future ALE analyses of reward processing may have the power to meta-analytically examine such distinctions. In addition, there was insufficient power to assess interactions between stage of processing and valence (e.g., to detect interaction effect sizes of d =.20, the current study would be underpowered at .359). Examination of such interactions would be useful in testing whether adolescents display particularly heightened responsivity to positive incentives during the anticipation phase as has been proposed (Luciana et al., 2012).

Moreover, additional research on factors such as pubertal status, developmental stage (i.e. early, middle, and, late adolescence), and sex, will further elucidate how activity in these regions changes with development. Dissociating different features of the various reward paradigms, in addition to more studies of negative valence, will further clarify how these

age-related neural changes impact behavior -- particularly risk-taking tendencies that can be ascribed to over-activity in reward processing networks. Notably, previous studies on adolescent reward processing have relied on studies of adult reward processing (Liu et al., 2011) for guiding hypothesis testing and ROI analyses (e.g., Lorenz et al., 2014). Given the differences found here between adolescent and adult reward processing, this and similar meta-analyses of adolescent reward processing can guide hypothesis testing for future studies focusing on adolescents.

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Appendix

Appendix A. List of articles included in the current ALE meta-analysis

Bjork JM, Knutson B, Hommer DW. Incentive-elicited striatal activation in adolescent children of alcoholics. Addiction. 2008; 103:1308–1319. [PubMed: 18851716]

Bjork JM, Smith AR, Chen G, Hommer DW. Adolescents, adults and rewards: comparing motivational neurocircuitry recruitment using fMRI. PLoS One. 2010; 5:e11440. [PubMed: 20625430]

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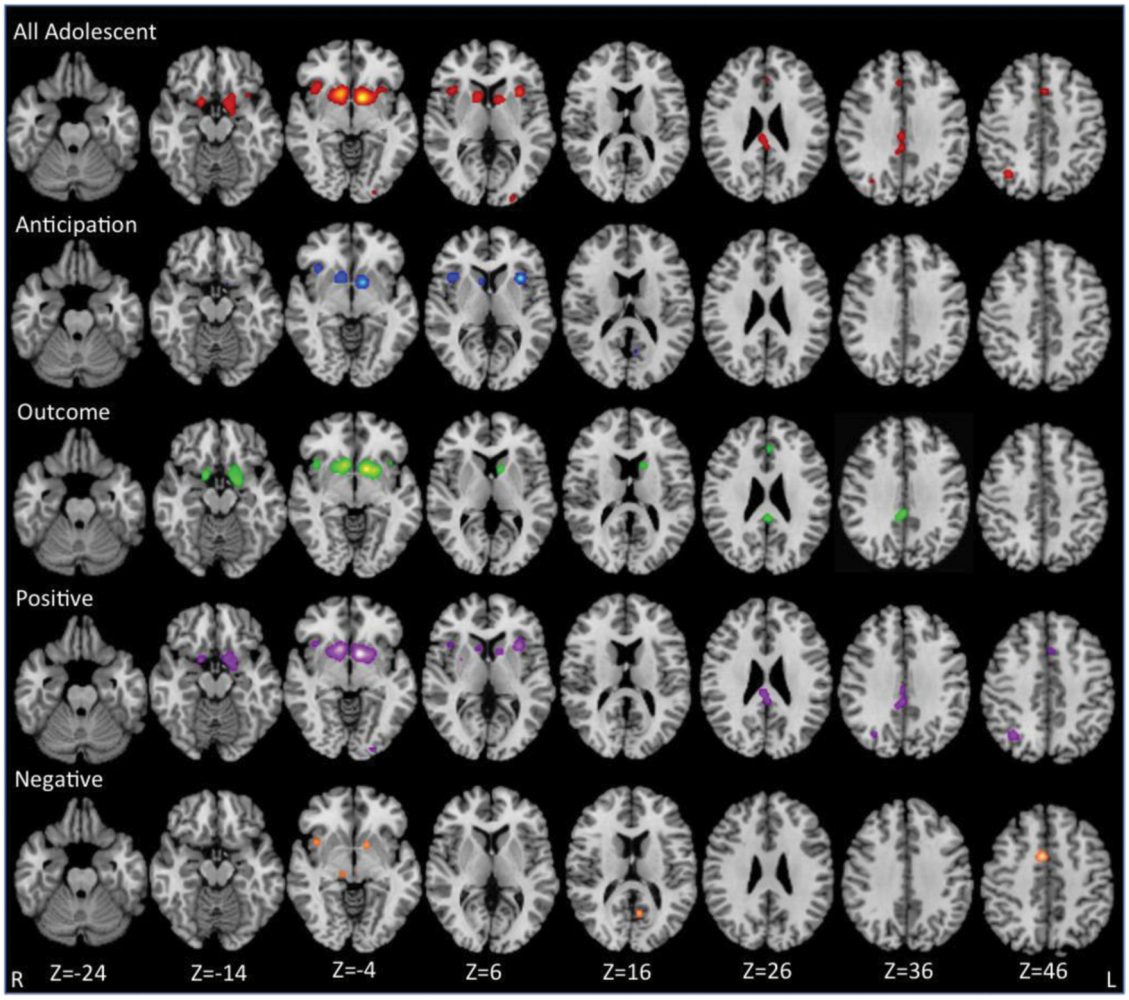

Figure 1.
Brain regions showing likelihood of brain activation in the overall adolescent ALE (top panel), stage analyses (second and third panels) and valence analyses (fourth and fifth panels).

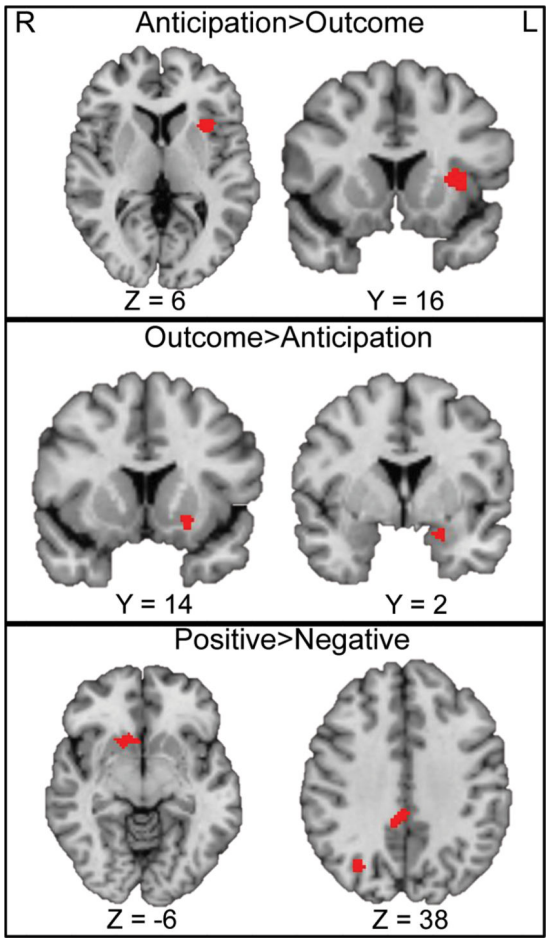

Figure 2.

Brain areas with differential activation likelihoods between valence and stage analyses. For anticipation>outcome one significant cluster was found including regions of the left insula and frontal operculum cortex. Cluster locations for outcome>anticipation included the left amygdala and putamen. Cluster locations for positive>negative included the right posterior cingulate gyrus, NAcc, subcallosal cortex, and lateral occipital cortex.

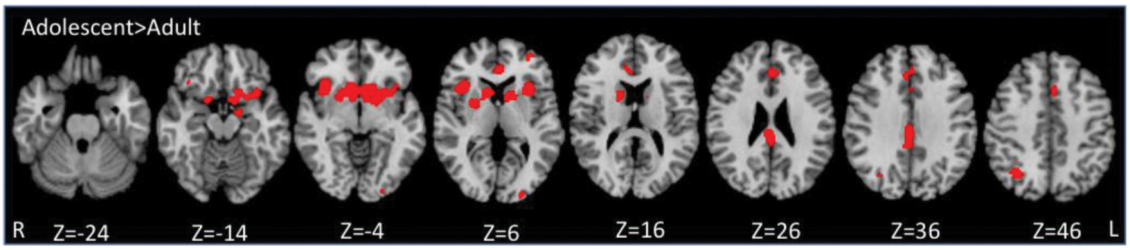

Figure 3.

Brain areas showing increased likelihood for activation in adolescents relative to adults. Cluster locations include subcortical regions such as the ventral and dorsal striatum and the amygdala as well as the anterior and posterior cingulate cortex, the orbital frontal cortex, and the lateral occipital cortex.

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Table 1

Adolescent Reward Processing Studies

Study	fMRI Task	No. of Participants	Age range (mean)	No. of Reward foci	Aspect of Reward				
					All Reward	Anticipation	Outcome	Positive	Negative
Bjork et al. (2008)	MID	13	12-16 (13.8)	22	x	x	x	x	x
Bjork et al. (2010)	MID	24	12-17 (14.8)	33	x	x	x	x	x
Cohen et al. (2010)	Probabilistic Learning	16	14-19 (15.8)	5	x	x	x	x	
Christakou et al. (2011)	Temporal Discounting	18	11.9-18 (15.3)	6	x				
Crowley et al. (2010)	Colorado Balloon Game	20	14-18 (16.5)	59	x	x	x	x	x
Cservenka et al. (2012)	Wheel of Fortune	13	13-15 (14.24)	10	x	x		x	
Delgado-Rico et al. (2013)	Risky-Gains	16	12-17 (13.88)	7	x	x	x	x	
Ernst et al. (2005)	Wheel of Fortune	16	9-17 (13.3)	21	x		x	x	x
Forbes et al. (2010)	Guessing with Monetary Rewards	26	11-13 (11.42)	30	x	x	x	x	
Forbes et al. (2010)	Guessing with Monetary Rewards	51	11-13 (12.20)	26	x	x	x	x	
Galvan et al. (2013)	Probabilistic Liguid Delivery	15	13-17 (15.33)	12	x		x	x	
Jarcho et al. (2012)	Reward Processing	26	8.75-17.17 (14.05)	81	x	x	x	x	x
May et al. (2004)	Guessing Game	12	9-16 (13.25)	32	x				
Op de Macks et al. (2011)	Jackpot Gambling	17	10-16 (13.5)	13	x		x	x	
Op de Macks et al. (2011)	Jackpot Gambling	33	10-16 (12.9)	27	x		x	x	
Paloyelis et a. (2012)	Motivated Incidental Learning	30	(15.42)	30	x	x	x	x	x
Paulsen et al. (2012)	Risky Decision-Making	17	14.2-15.9 (14.8)	24	x		x	x	x
Ripke et al. (2012)	Intertemporal Choice	195	13.7-15.5 (14.6)	41	x	x		x	
Scheres et al. (2007)	MID	11	12-17 (13.9)	19	x	x		x	
Schlund et al. (2010)	Approach-Avoidance	15	9-13 (11.1)	34	x		x	x	
Scott-Van Zeeland (2010)	Rewarded Implicit Learning	16	8-15 (12.3)	67	x		x	x	
Telzer et al. (2013a)	Family Assistance	48	14-16.5 (15.23)	19	x	x		x	x
van Duijvenvoorde et al. (2014)	Jackpot Gambling	31	10-16 (13.1); 12-19 (15.3)	9	x		x	x	

Study	fMRI Task	No. of Participants	Age range (mean)	No. of Reward foci	Aspect of Reward				
					All Reward	Anticipation	Outcome	Positive	Negative
Van Leijenhorst et al. (2006)	Cake Gambling	12	9-12 (11.3)	18	x		x	x	x
Van Leijenhorst et al. (2010)	Cake Gambling	15	12-14 (13.4)	23	x		x	x	
Van Leijenhorst et al. (2010)	Cake Gambling	15	16-17 (17.1)	34	x	x	x	x	
Van Leijenhorst et al. (2010b)	Slot Maching	16	10-12 (11.6)	20	x	x	x	x	x
Van Leijenhorst et al. (2010b)	Slot Maching	16	14-15 (15.0)	35	x	x	x	x	
Verdejo-Garcia et al. (2014)	Ultimatum Game	44	12-18(15.32)	28	x	x	x		x
Yaxley et al. (2011)	Decision-Reward Uncertainty	31	12.3-17.7 (15.5)	63	x	x	x	x	

Studies are listed that were included in the ALE, as described in the text. The age ranges of participants are in years. van Duijenvoorde et al. (2014) employed a longitudinal model in their study; therefore the age range and mean age refer to the ages at time 1 and time 2. “All reward” refers to significant foci collapsed across all domains of a task. Anticipation was defined by any task component when participants deliberated options or waited for outcomes prior to their delivery. Outcome was defined by any task component when participants received feedback about gains or losses. Positive valence refers to when participants won something (such as money, points, encouragement, etc.), received the greater of two gains, or avoided loss. Negative valence refers to when participants lost something, did not win something, won the smaller of two amounts, or received discouraging feedback or images.

Table 2

Brain regions commonly activated across adolescent reward processing studies

Brain Region	Hemisphere	Extrema Value	x	y	z	Volume (mm^3)	Cluster Number
Caudate	L	0.082	−12	8	−4	9360	1
Frontal Operculum Cortex	L	0.044	−34	18	6		
Insular Cortex	L	0.030	−38	18	−8		
Insular Cortex	L	0.028	−30	16	−8		
Amygdala	L	0.021	−18	−4	−20		
Accumbens	R	0.068	12	14	−6	5544	2
Insular Cortex	R	0.042	38	20	0	2328	3
Posterior Cingulate Gyrus	L	0.037	0	−28	30	2136	4
Lateral Occipital Cortex	R	0.035	32	−60	46	792	5
Lateral Occipital Cortex	R	0.028	30	−68	38		
Paracingulate Gyrus	L	0.034	−4	18	42	552	6
Occipital Pole	L	0.029	−26	−92	2	504	7
Paracingulate Gyrus	L	0.025	−2	34	30	424	8
Paracingulate Gyrus	R	0.025	4	30	36		

Brain regions are derived from the probabilistic Harvard-Oxford cortical and subcortical atlases and are reported based on the location of the peak values of significant clusters. The coordinates of the maximum ALE value are expressed in MNI space.

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Table 3

Brain regions activated by stage (anticipation, outcome) and valence (positive, negative) of reward processing

Brain Region	Hemisphere	ExtremaValue	x	y	z	Volume (mm^3)	Cluster Number
Anticipation							
Accumbens	L	0.038	−12	8	−6	2152	1
Caudate	R	0.029	10	12	−2	1528	2
Insular Cortex	R	0.028	38	20	2	1448	3
Frontal Operculum Cortex	L	0.041	−34	18	6	1168	4
Supplementary Motor Cortex	L	0.022	−2	2	54	512	5
Outcome							
Caudate	L	0.046	−12	10	−4	7240	1
Putamen	L	0.039	−22	10	−4		
Caudate	L	0.030	−14	14	12		
Accumbens	R	0.042	10	14	−6	3424	2
Posterior Cingulate Gyrus	L	0.026	0	−34	32	1616	3
Insular Cortex	L	0.024	−40	18	−8	544	4
Insular Cortex	R	0.021	40	14	−6	496	5
Paracingulate Gyrus	L	0.021	−2	36	28	408	6
Positive							
Caudate	L	0.065	−12	10	−4	6912	1
Caudate	L	0.023	−14	14	10		
Accumbens	R	0.058	10	14	−6	4376	2
Putamen	R	0.021	28	4	4		
Posterior Cingulate Gyrus	L	0.033	0	−32	30	2304	3
Frontal Operculum Cortex	L	0.044	−34	18	6	1248	4
Insular Cortex	R	0.026	38	20	2	936	5
Lateral Occipital Cortex	R	0.033	32	−60	46	896	6
Lateral Occipital Cortex	R	0.028	30	−68	38		
Paracingulate Gyrus	L	0.027	−4	18	44	400	7
Occipital Pole	L	0.027	−26	−92	0	368	8

Brain Region	Hemisphere	ExtremaValue	x	y	z	Volume (mm^3)	Cluster Number
Negative							
Putamen	L	0.020	−14	8	−8	680	1
Thalamus	R	0.016	14	−22	0	608	2
Supplementary Motor Cortex	R	0.017	4	6	46	464	3
Insular Cortex	R	0.016	40	12	−6	424	4
Precuneous Cortex	L	0.016	−8	−60	18	368	5
Brain Stem	L	0.015	−2	−18	−8	352	6
Precentral Gyrus	R	0.016	44	−12	54	312	7

Brain regions are derived from the probabilistic Harvard-Oxford cortical and subcortical atlases and are reported based on the location of the peak values of significant clusters. The coordinates of the maximum ALE value are expressed in MNI space.

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Table 4

Brain regions differentially activated by stage and valence

Brain Region	Hemisphere	Extrema Value	x	y	z	Volume (mm^3)	Cluster Number
Anticipation>Outcome							
Insular Cortex	L	3.036	−34.3	15.3	7.9	784	1
Frontal Operculum Cortex	L	2.848	−34	20	12		
Outcome>Anticipation							
Putamen	L	2.878	−23	12	−11	520	1
Amygdala	L	2.669	−21	4	−19		
Positive>Negative							
Posterior Cingulate Gyrus	R	3.156	1.5	−29.4	29.5	2072	1
Posterior Cingulate Gyrus	R	3.036	6	−24	29		
Posterior Cingulate Gyrus	R	2.989	2	−23.3	34		
Posterior Cingulate Gyrus	R	2.948	6	−38	35		
Posterior Cingulate Gyrus	R	2.911	1	−33	40		
Posterior Cingulate Gyrus	R	2.878	2	−24.7	32.7		
Posterior Cingulate Gyrus	R	2.848	8	−38	40		
Accumbens	R	3.036	12	19	−6	824	2
Subcallosal Cortex	R	2.848	4	20	−2		
Lateral Occipital Cortex	R	3.540	35	−59.7	44	688	3
Lateral Occipital Cortex	R	3.156	30	−64	40		
Lateral Occipital Cortex	R	2.794	28	−70	38		
Negative>Positive							
None							

Brain regions are derived from the probabilistic Harvard-Oxford cortical and subcortical atlases and are reported based on the location of the peak values of significant clusters. The coordinates of the maximum ALE value are expressed in MNI space.

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Table 5

Brain regions differentially activated by adolescent and adult populations

Brain Region	Hemisphere	Extrema Value	x	y	z	Volume (mm^3)	Cluster Number
Adolescent>Adult							
Subcallosal Cortex	R	3.719	−0.3	14.1	−1.3	24792	1
Accumbens	L	3.540	−2.8	11.5	−2.5		
Insular Cortex	R	3.353	30	16	0		
Putamen	R	3.156	22	12	−2		
Amygdala	L	2.878	−18	−2	−12		
Frontal Orbital Cortex	R	2.636	40	24	−16		
Posterior Cingulate Gyrus	R	3.719	2.1	−29.1	31.1	3192	2
Anterior Cingulate Gyrus	L	3.719	−4.9	39.1	6.2	1504	3
Anterior Cingulate Gyrus	R	3.540	6	32	16		
Paracingulate Gyrus	R	2.989	10	42	22		
Paracingulate Gyrus	L	3.719	−1.3	35.3	30	1376	4
Paracingulate Gyrus	R	2.989	4	30	36		
Lateral Occipital Cortex	R	3.719	30.2	−64.6	41.7	1232	5
Lateral Occipital Cortex	R	3.540	30.5	−61.5	48.5		
Anterior Cingulate Gyrus	L	3.719	−2	16	39	728	6
Paracingulate Gyrus	L	3.540	−5.1	18.4	42.8		
Supplementary Motor Cortex	L	3.353	−2	2	56	544	7
Occipital Pole	L	3.719	−26.1	−93.4	2	504	8
Frontal Pole	L	3.719	−35	57	6	488	9
Frontal Pole	L	3.540	−32	52	7		
Adult>Adolescent							
None							

Brain regions are derived from the probabilistic Harvard-Oxford cortical and subcortical atlases and are reported based on the location of the peak values of significant clusters. The coordinates of the maximum ALE value are expressed in MNI space. The data for the adult ALE used in the contrast analyses is from the extant ALE of adult reward processing (Liu et al., 2011).