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The Role of Potential Losses in Adolescent Decision-Making Under Risk

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The Role of Potential Losses in Adolescent Decision-Making Under Risk

A dissertation submitted in partial satisfaction of the

requirements for the degree Doctor of Philosophy

in Psychology

by

Emily Elizabeth Barkley-Levenson

2013

ABSTRACT OF THE DISSERTATION

The Role of Potential Losses in Adolescent Decision-Making Under Risk

by

Emily Elizabeth Barkley-Levenson

Doctor of Philosophy in Psychology

University of California, Los Angeles, 2013

Professor Adriana Galván, Chair

Adolescence is a developmental period characterized by increased risk-taking behavior. Current neurodevelopmental models of adolescent risky decision-making explain this behavior based on an imbalance in development of reward and regulatory regions in the brain. This has led many researchers to focus on the ontogeny of reward processing, finding adolescents to be behaviorally and neurally hypersensitive to rewards relative to adults. However, current research has not investigated adolescent sensitivity to potential losses, a fundamental component of many risky choices. In this dissertation, I use a multi-method program of research, including experimental tasks, surveys, functional magnetic resonance imaging (fMRI), and psychophysiology, to explore how the potential for both gains and losses contribute to adolescent risky decision-making. My research demonstrates that adolescents, like adults, are more sensitive to losses than to gains when deciding whether or not to accept a risk. However, adolescents recruit more cognitive resources than adults when choosing to avoid risk, suggesting that adult patterns of risk-

avoidance become less effortful across development. Furthermore, adolescents are actually more neurobehaviorally sensitive to changes in value than adults are, suggesting that hypersensitivity to value may underlie observed sensitivity to reward in adolescents. Finally, I present evidence suggesting that higher baseline levels of a proxy for dopamine contribute to greater sensitivity to value during risky decision-making with the potential for loss. Taken together, these findings suggest the possibility of a role for dopamine in modulating the neural response to value (and not simply to reward) observed functionally in the ventral striatum, which in turn influences risk-taking behavior.

The dissertation of Emily Elizabeth Barkley-Levenson is approved.

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

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I. Introduction

Adolescence is a developmental period marked by change and exploration. While the cognitive, social and emotional maturation that adolescents undergo are essential for success in adulthood, the distinct neurobehavioral conditions of adolescence also increase vulnerability to unhealthy behaviors, such as substance abuse and risky sexual behavior, which occur with greater frequency during the peak in risk-taking observed in adolescence. Recent advances in developmental neuroscience have identified key differences in the adolescent brain relative to children and adults that are believed to underlie risky decision-making. However, much of this research has centered on adolescent sensitivity to potential and experienced rewards, despite the fact that most decisions commonly characterized as risky include not only the consideration of potential for gain but also for loss. In this dissertation, I use a multi-method program of research, including experimental tasks, surveys, functional magnetic resonance imaging (fMRI), and psychophysiology, to explore how the potential for both gains and losses contribute to adolescent risky decision-making.

Neuroimaging of Adolescent Risky Decision-Making

One prominent neurodevelopmental theory of adolescent risky decision-making suggests that it is due to the imbalance in development of reward and regulatory regions (e.g. Casey et al., 2008; Steinberg, 2008). Evidence from neuroimaging during risky choice supports this model. When adolescent and adult participants made risky choices in a probabilistic gambling task, adolescents were found to have lower activation in dorsal ACC and OFC/VMPFC, regions associated with cognitive control (Eshel et al., 2007). Additionally, lower activation in these regions was correlated with greater risk-taking behavior on the task. Furthermore, research suggests a distinct interaction between these regions in adolescents, with increased response in

prefrontal areas during rewarded trials of a visual response inhibition task, as well as heightened ventral striatum activity (Geier et al., 2010). These findings suggest that the adolescent reward system may actually bias cognitive control mechanisms towards actions leading to immediate reward. In another study, high-risk choices were associated with activation in VMPFC, which showed an inverted U-shaped pattern from childhood to adulthood, with the peak in adolescence (van Leijenhorst, Gunther Moor et al., 2010). In contrast, low-risk choices were associated with activation in lateral PFC. These findings support the neurobiological model of adolescence put forth by Casey and colleagues (2008) that takes into consideration both the delayed developmental trajectory of the prefrontal cortical regions and the more rapid maturation of the limbic subcortical regions. This model identifies a distinct period during adolescence when behavior is influenced more by the functionally responsive limbic regions associated with risk-taking than by the still immature cognitive control regions, an imbalance that predicts an inverted U-shaped function peaking in adolescence for behavioral and neural measures related to risk-taking. This dual-system model is supported by behavioral evidence of a curvilinear pattern of reward-seeking but a linear decrease in impulsivity across adolescence (Steinberg, 2008). Other behavioral and neurobehavioral models of adolescent decision-making have highlighted different components of the decision-making process, such as the role of the amygdala in promoting harm-avoidance behaviors under the triadic model (Ernst et al., 2005) and the transition toward heuristic or gist-based processing in fuzzy trace theory (Reyna & Ellis, 1994). The current research does not purport to validate one model over another; rather, these neurobehavioral models of adolescent decision-making under risk offer useful frameworks for generating testable hypotheses about adolescent risk-taking.

Adolescent Neural Responsiveness to Gains and Losses

Developmental neuroimaging has begun investigating the heightened functional sensitivity of the limbic regions in adolescence, primarily by focusing on sensitivity to rewards. Adolescents consistently show greater activation in the ventral striatum in response to experienced rewards relative to adults (Cohen et al., 2010, Ernst et al., 2005, Galván et al., 2006, van Leijenhorst, Zenolie et al., 2010, but see Bjork et al., 2010 for reduced striatal activation relative to adults). Adolescents also show a greater striatal response to anticipated rewards than do adults (Geier et al., 2010). Less is known, however, about the adolescent response to losses. A few studies have observed less striatum activation in adolescents than adults in response to monetary loss (Galván et al., 2006, Guyer et al., 2006) and omission of monetary gains (Ernst, Nelson et al., 2005), consistent with the idea that adolescents are hypersensitive to rewards and hyposensitive to losses. However, other research has shown increased activation in the striatum in adolescents relative to adults in response to both appetitive and aversive taste stimuli (Galvan & McGlennen, 2013), with a more pronounced difference in response to aversive stimuli. This is consistent with a meta-analysis of neural responses to value in adults, identifying activation in the striatum in response to both positive and negative values (Bartra et al., 2013). Further exploration of the representation of potential and experienced losses in the adolescent brain is necessary to disentangle these findings.

Investigating the role of both gains and losses is critical for a complete understanding of adolescent risk-taking behavior. Optimal decision-making under risk is generally believed to require assessment of both the potential rewards and punishments and the computation of a subjective value for each choice (Rangel et al., 2008). By focusing on rewards alone, researchers are unable to fully explore how the adolescent brain represents value during risky decision-making and how that representation informs choice. The research presented here provides a first

step towards a more complete understanding of the neurobehavioral mechanisms underlying adolescent decision-making under risk.

Overview of Studies

Study 1. This study examines the impact of potential losses as well as gains on adolescent decisions during risky choice in a laboratory task. For this study, adolescent and adult participants underwent fMRI during a gambling task with the potential for both gains and losses, and completed questionnaires measuring real-world risk-taking behaviors. Behaviorally, it was observed that potential loss had a significantly greater effect than potential gain on the choice to accept or reject a risk, a pattern that did not differ between adolescents and adults. These results are discussed in the context of Prospect Theory, a model of decision-making under risk that explains the observed asymmetry between loss and gain sensitivity. At the neural level, we show that adolescents recruit significantly more frontostriatal circuitry than adults when choosing to reject risky gambles, suggesting that despite their behavioral similarities, adolescents may employ significantly more cognitive control resources than adults in order to avoid risk. Finally, neural results were correlated with self-reported likelihood of risk-taking, and we found that during risk-seeking behavior, adolescent activation in medial prefrontal cortex (mPFC) was negatively correlated with self-reported likelihood of risk taking, while no relationship was observed in adults. Because the mPFC is consistently implicated as part of the neural "valuation system", this finding suggests that individual differences in the assessment of value of risky choices may contribute to differences in the propensity to take real-world risks.

Study 2. This study analyzed the same behavioral and neuroimaging data as study 1, this time investigating the neural response to changing expected values of risky gambles (regardless of the participant's decision to seek or avoid risk on a given trial). Behaviorally, changes in

expected value had a stronger influence over the choice to accept or reject a gamble for adolescents than for adults, for gambles with negative as well as positive expected values. Neurobiologically, all participants showed parametric activation in predicted "valuation system" regions, including mPFC and dorsolateral prefrontal cortex (DLFPC), in response to increasing expected value. However, increasing activation in the ventral striatum in response to increasing expected value was unique to adolescents. These behavioral and neural data suggest that adolescents are biased to a greater extent than adults by the value of available options. These results are discussed in the context of the existing literature on adolescent reward sensitivity; it is theorized that adolescent hypersensitivity to rewards may actually be reflective of heightened sensitivity to changes in value, which is simply being captured in the gain domain by the stimuli employed in other studies.

Study 3. Because risk, reward and value are all commonly associated with activation in the ventral striatum, which is highly innervated by dopaminergic neurons from the midbrain, we sought to explore whether differences in dopamine levels reflect differences in value sensitivity or reward-seeking behavior during risky decision-making. Since it is not possible to measure dopamine levels noninvasively in youth, we used a proxy for dopamine, eye blink rate, to address this question. Baseline eye blink rate was collected for all participants as a measure suggestive of possible individual differences in dopamine levels, while we attempted to directly manipulate dopamine levels by administering to participants either an appetitive or aversive taste stimulus (in the form of milk chocolate or bitter dark chocolate). Participants then completed a risky decision-making task; in the task, participants chose among three different decision strategies: probability-maximizing (an option that increases the probability of gaining money in the task), gain-maximizing (an option that increases the value of the possible reward without

altering probabilities) and loss-minimizing (an option that reduces the value of the possible loss without altering probabilities). Participants did not show changes in blink rate on the basis of taste stimulus condition. However, eye blink rate did significantly predict use of the P_{max} strategy, which has been characterized as a decision strategy that ignores reward magnitude (Venkatraman et al., 2009). Higher eye blink rates were associated with fewer uses of the P_{max} strategy; therefore, participants whose eye blink rates are believed to be reflective of lower dopamine levels appear to be the least sensitive to value in a risky context.

II. Behavioral and Neural Correlates of Loss Aversion and Risk Avoidance in Adolescents and Adults

Introduction

Adolescence is often described as a period of increased risk-taking behavior (e.g. reckless driving, substance use, risky sexual practices) (Arnett, 1992, 1999; Dahl, 2004; Steinberg, 2008). Many psychological theories of adolescence pose that a sense of invulnerability is normative in this developmental phase (e.g. Lapsley & Hill, 2010), and suggest that this causes adolescents to underweight possible negative consequences when they make risky decisions. However, economic models of risk-taking, such as prospect theory (Kahneman & Tversky, 1979), have suggested that losses "loom larger" than gains for most individuals – the aversiveness of a potential loss is greater than the desirability of an equal potential gain, a behavioral phenomenon known as loss aversion. The relationships between theories of risk originating in behavioral economics and those originating in developmental psychology have not been extensively studied, and integrating these literatures is necessary to expand our understanding of the effects of loss on adolescent decision-making. Exploring the role of both potential gains and potential losses in predicting risk-taking is critical to understanding how adolescents and adults make the choice to engage in or avoid a real-life risk, and why these choices may differ across development.

Few behavioral studies of risk-taking behavior have focused specifically on adolescent responses to potential loss. Both children and adults have been shown to be more risk-seeking when choosing between a guaranteed small loss and the chance of a larger loss than when choosing between a guaranteed small gain and the chance of a larger gain (e.g. Levin & Hart, 2003; Levin et al., 2007); however, in other studies this pattern has been observed only in adults (Weller et al., 2011) and in younger children (age 5-8) and older children (age 9-13) but not in

adolescents (age 14-20) or adults (age 21-64) (Harbaugh et al., 2002). On a similar task where participants selected between two gambles, adolescents have been shown to prefer a lower probability of a large loss to a higher probability of a small loss, but reverse this preference in the domain of gains (Rao et al., 2011). This response pattern is consistent with the same economic theories that predict loss aversion, but loss aversion itself has not been measured in adolescents. One study (Harbaugh et al., 2001) found that both children and adults display similar levels of the endowment effect (a behavioral phenomenon where participants demand more money to sell a good in their possession than to buy the same good, which is typically believed to be driven by loss aversion); However, there remains the possibility that loss aversion in a risky context would differ from the riskless context in which the endowment effect is measured, and that loss aversion would show nonlinear developmental trends. Therefore, the measurement of loss aversion and sensitivity to potential loss in adolescents remains an important and open area of study.

Evidence from developmental neuroscience has mostly focused on rewards, and consistently demonstrates increased neural sensitivity to gains during adolescence (but see Bjork et al. 2010, 2004). An early study of children and adolescents responding to monetary gains and losses found increased activation in ventral striatum (VS) and lateral and medial orbitofrontal cortex (OFC) for gains relative to losses (May et al., 2004), a finding consistent with similar studies conducted in adults (e.g. Delgado et al., 2000; Rolls, 2000). In a direct comparison of children, adolescents and adults responding to positive reward outcomes of varying magnitudes, adolescents showed significantly greater activation in VS relative to children and adults (Galván et al., 2006); this activation was associated with self-reported risk taking (Galván et al., 2007). Increased VS activation in response to reward for adolescents relative to children and adults has

been replicated in other studies (Geier et al., 2010; Van Leijenhorst et al., 2010a, 2010b), supporting an inverted U-shaped function of striatal sensitivity to reward that peaks in mid adolescence. Dual systems models of adolescent brain development (Casey et al., 2008; Steinberg et al., 2008) suggest that adolescents show heightened reward sensitivity relative to other age groups due to the late developmental trajectory of the PFC and its interaction with maturational changes in the striatum across adolescence and into early adulthood.

These reward studies have led to important advancements in understanding the role that potential gains play in risk-taking in adolescence. Surprisingly, however, the findings are less clear about the role of potential losses in influencing adolescent risk-taking. Most fMRI studies of monetary loss have focused on how the adolescent brain responds to a loss outcome (Helfinstein et al., 2011; Van Leijenhorst et al., 2010b) or to a cue predicting a loss (Guyer et al., 2006), but it is unclear how a potential loss may sway risky choice in adolescents. Exploring the role of both potential gains and potential losses in predicting risk taking is critical to understanding how adolescents and adults make the choice to engage in or avoid a real-life risk, why these choices may differ across development, and how they may be influenced.

Tom and colleagues (2007) examined the neural representation of potential gains and potential losses during risky decision-making using a mixed gambles task (gambles with a 50/50 chance of a gain or loss of varying amounts) commonly implemented in the behavioral economics literature (e.g. Rabin & Thaler, 2001; Tversky & Kahneman, 1992). They did not find separate brain systems for gains and losses, but found areas in the brain, including the VS, ventromedial prefrontal cortex (VMPFC), ventral anterior cingulate cortex (ACC), and medial OFC, that were sensitive to the potential for both gains and losses, in which activation increased parametrically with increasing potential gains and decreased parametrically with increasing

potential losses. Furthermore, the negative slope of the decrease in activation in VS and VMPFC for increasing losses was greater than the corresponding positive slope of the increase in activation in the same regions for increasing gains; this finding was consistent with the pattern of loss aversion, the tendency of individuals to prefer avoiding losses over seeking gains, which has been demonstrated in behavioral research (Kahneman & Tversky, 1979, 1984).

In the current study, our goal was to investigate the poorly understood impact of potential losses and loss aversion on adolescent decision making and neural response using functional magnetic resonance imaging (fMRI) and the mixed gambles task described previously (Tom et al 2007). We aimed to examine the impact of potential losses as well as gains on adolescent behavior during risky choice, and to observe how behavioral and neural responses to potential gains and potential losses differ between adolescents and adults. We also investigated whether neural responses to potential losses would be predictive of actual risk-taking in these participants. We hypothesized that adolescents would display less loss aversion than adults, and that their choices on the mixed gambles task would be more strongly influenced by potential gains. We also predicted that adolescents would show more activation than adults in VS and VMPFC when accepting gambles, and that this risk-based neural activation would be associated with higher self-reported risk taking. We predicted that adolescents would reject fewer trials overall than adults, and that when rejecting gambles they would show more activation in prefrontal cortex than adults, consistent with requiring greater behavioral inhibition to avoid risk-taking.

Methods

Participants. Sixteen healthy right-handed adult participants (ages 25-30, mean age 28.1 years, *SD* = 1.8 years, nine female) and nineteen healthy right-handed adolescent participants (ages 13-

17, mean age 15.5 years, *SD* = 1.3 years, 10 female) were recruited through poster and internet advertisements approved through the UCLA Institutional Review Board (IRB) and through the Galván Lab participant database. All participants provided informed consent, and participants under the age of 18 provided assent while their parent or guardian completed the informed consent procedure. Participants were excluded from participation if they had a previous diagnosis of psychiatric or neurologic illness or developmental delay, were taking psychoactive medication at the time of the study, or had metal in their bodies.

Materials

Risk-Taking Measures. Participants completed three self-report questionnaires during an initial behavioral testing session. Both adolescent and adult participants completed the Adolescent Risk Taking scale (Alexander et al., 1990), a six-item scale in which they reported the number of times in their life they had engaged in risky activities, such as shoplifting and riding in a car with a dangerous driver, by selecting from one of three options: "never," "once or twice," or "several times". Participants also completed the Domain-Specific Risk Taking Scale (DOSPERT; Weber et al., 2002; Figner et al., in preparation), a well-validated 40-item measure of one's perceived risk of, benefit of, and likelihood of engaging in risky events. Versions of the DOSPERT for adults, adolescents (ages 14-17) and children (ages 9-13) were administered based on participant age (Figner et al., in preparation). For example, the child version of the DOSPERT investigates ethical risk-taking by asking participants to consider the scenario, "stealing someone else's best friend," while adolescents are asked to consider "dating someone else's boyfriend or girlfriend" and adults are asked to consider "having an affair with a married man or woman." The DOSPERT uses a 7-point Likert scale for each of the assessment dimensions ("not at all risky" to "extremely risky," "no benefits at all" to "great benefits," and

"extremely unlikely" to "extremely likely") and includes scenarios in the domains of financial, ethical, recreational, social, and health risk.

Monetary Experience Questionnaire. For this study, we created a questionnaire to investigate the valence and arousal of participants' feelings toward receiving $20 and the possibility of gaining or losing that sum. The purpose of this questionnaire was to encourage participants to feel connected to the money with which they were endowed during the behavioral testing session, in order to prevent the "house money effect" (increased risk-taking behavior that is observed when the money at stake is not the participant's own; Thaler & Johnson, 1990). In addition, the results of this questionnaire were used to verify that participants of different ages have a similar understanding of and appreciation for money. Participants responded to each question using a 5-point Likert scale, with each point represented by a face icon depicting the corresponding emotion (from a very unhappy face to a very happy face) or degree of arousal (from a very calm face to a very excited face). In addition to reporting these feelings, participants wrote a brief statement about what they would do with the money if they won it, and answered questions about how much money they receive from employment, allowance, and other sources.

Mixed Gambles fMRI task. During the fMRI scan, participants completed a novel version of the mixed gambles task originally designed by Tom et al. (2007). The version implemented in the current study was modified to be developmentally appropriate, through the addition of a scale showing the response options at the bottom of each trial presentation and the use of white text on a black screen to avoid attentional biases (see Figure 1).

In the task, participants were presented with a series of gambles with a 50% probability of gaining the amount shown on one side of a "spinner" and a 50% probability of losing the amount shown on the other side. During the response interval of 3000 milliseconds (ms),

participants responded whether they accepted that gamble for real money, by pressing one of four buttons corresponding to a four-point Likert scale (strongly accept, weakly accept, weakly reject, strongly reject). Rather than a binary response, four responses were used to make it more difficult for participants to default to a simple choice rule; this response design was previously used in the task from Tom et al. (2007). However, for data analysis purposes the responses were binarized such that both strong and weak accept responses were coded as 1 and both weak and strong reject responses were coded as 0. The gain and loss amounts were independently manipulated, with gain amounts ranging from +$5 to +$20 in $1 increments and loss amounts ranging from -$5 to -$20 in $1 increments, for a total of 144 trials. Randomly interspersed within these trials were 24 gain-only trials and 24 loss-only trials, with values drawn from the same range, for a total of 192 trials across four runs. These gain-only and loss-only trials provided confirmation that participants were engaged with the task, as they should reject all loss-only trials and accept all gain-only trials. The side of the "spinner" in which the gain and loss appeared and the order of the stimuli were counterbalanced across participants. A variable "jittered" inter-stimulus interval then followed, averaging 2700 ms, before the next gamble was presented in the same fashion.

The participants were informed that they would never see the outcomes of the gambles during the experiment, and that at the end of the experiment one gamble would be selected at random to be played for real money. If the participant had rejected the selected gamble during the experiment it would have no effect on their payment, and if they had accepted the gamble during the experiment its outcome would be resolved through a random coin-flip program, with the participant winning or losing the amount in the gamble depending on the outcome of the coin flip. Participants were told that they had the opportunity to lose or gain up to $20 (based on the

theoretical possibility that the gamble with the highest gain or highest loss could be selected) and that their payment depended on their responses to the gambles in the task. This served to encourage participant engagement in the task and convince them of the veracity of the experimental protocol. Participants were instructed to bring $20 (which they were paid during the behavioral testing session) to the scan, which was matched by $20 of the experimenter's money.

Procedure

Behavioral testing session. A behavioral testing session was held approximately one week prior to the fMRI scan. All participants began by completing the appropriate informed consent/assent form for their age group. Adult participants and the parents/guardians of the adolescent participants completed an fMRI screening form and study intake form to ensure participant eligibility. All participants then completed a one-hour behavioral testing session consisting of the Adolescent Risk Taking scale, the DOSPERT, and a brief index of IQ (i.e. the Wechsler Abbreviated Scale of Intelligence, vocabulary and matrix reasoning subscales, adolescent $M = 104$, $SD = 14.3$, adult $M = 110$, $SD = 15.2$). Following completion of the tasks, participants were paid $20. Participants were informed in advance of the risk of gaining or losing money during the fMRI portion of the experiment, as described above. Thus, the $20 constituted a portion of the participants' payment for the entire experiment, while endowing them with the payment in advance was intended to prevent the "house money effect" from influencing their task performance. Participants completed the monetary feelings questionnaire after receiving their payment. Adolescent participants were acclimated to the scanning environment with a mock MRI scanner and to hear the sounds of various functional and structural sequences.

fMRI session. Approximately one week after the behavioral testing session, participants returned for the fMRI portion of the study, which lasted ~60 minutes. Prior to entering the scanner, participants were instructed in the rules of the task and completed a block of 10 practice trials, ensuring that all participants understood the task fully. Participants had the opportunity to clarify any questions and to complete the practice block again if further practice was needed. In the scanner, participants completed four 4-minute runs of the mixed gambles task (48 trials per run, for a total of 192 trials). Participants viewed a movie while structural MRI scans were collected. Following completion of the scan, participants were paid for their completion of the task; payment was designed so that no participant actually lost money, ensuring that all participants received at least $25 for their completion of the fMRI session (in accordance with the UCLA institutional review board payment scale). However, to elicit naturalistic risk-taking behavior, participants were unaware of this during completion of the loss aversion task.

Imaging procedure. Scanning was performed on a 3-Tesla Siemens Trio MRI machine in the Ahmanson-Lovelace Brain Mapping Center at UCLA. For the functional runs, 140 T2*-weighted echoplanar images (EPIs) were collected (33 slices; slice thickness, 4 mm; TR, 2000 ms; TE, 30 ms; flip angle, 90°; matrix, 64 x 64; field of view, 200). Two structural MRI images were collected as well: a T2-weighted matched-bandwidth high-resolution scan (following the same slice prescription as the EPIs) and a T1-weighted magnetization-prepared rapid- acquisition gradient echo image (MPRAGE; 160 sagittal slices; slice thickness, 1 mm; TR, 2000 ms; TE, 2100 ms; matrix, 192 x 192; field of view, 256).

Imaging Data Preprocessing and Analysis. Data preprocessing and analysis were conducted using FSL version 4.1 (www.fmrib.ox.ac.uk/fsl). Images were motion-corrected using MCFLIRT and denoised using MELODIC independent components analysis. Data were

smoothed using a 5 mm full-width-half-maximum Gaussian kernel and filtered with a nonlinear high-pass filter (66 sec cutoff). A three-step registration process was used to align individual participant data into standard Montreal Neurological Institute (MNI) space. EPI images were first registered to the matched-bandwidth image, then to the MPRAGE image, and finally to MNI space. Data from participants whose head movements exceed 3 mm in translational or rotational movement was not included in the analyses. One adolescent participant was excluded on the basis of motion, and behavioral and neural analyses were completed using the remaining eighteen adolescent participants (10 female, age M = 15.4 years, SD = 1.4 years) and all sixteen adult participants. For the participants included, there were no significant differences between adolescents and adults in translational motion (adolescent M = .17 mm, SD = .15 mm, adult M = .13 mm, SD = .10 mm, $t(32) = .980$, $p = .335$) or rotational motion (adolescent M = .003 mm, SD = .003 mm, adult M = .002 mm, SD = .001 mm, $t(32) = 1.468$, $p = .152$).

Data analysis was conducted using FEAT, first at an individual subject-level and then using a mixed-effects model at the group analysis level. Z-statistic images were thresholded at a cluster-level of $z > 2.3$ and a corrected significance threshold of $p \leq 0.05$.

Statistical analyses were performed on each participant's data using a general linear model. For each participant, we separately modeled the onsets of the trials they accepted and the trials they rejected, using a 1-second duration. Six motion parameters were also included as covariates in the model for each run for each of the participants. At the group level, the main effects of trials that participants accepted and trials that they rejected were each modeled relative to an implicit baseline (all remaining activation that is not explicitly included in the model), and contrasts between accepted and rejected trials were computed for all participants and independently for

adolescents and adults. In addition, whole-brain contrasts between adolescents and adults were computed for all accepted trials and for all rejected trials separately using two-tailed T tests.

To ensure that there were no baseline differences between groups, we performed an analysis of resting activation when the participant was viewing a blank screen (i.e. not performing the task). Participants viewed a blank screen at the end of each run after the last trial was completed. Because of the jittered design, the amount of time from the last trial until the end of the run ranged from 10 to 24 seconds on each run (M=16 s). No significant differences in baseline activation were observed between adolescent and adult participants. This analysis convinces us that the observed neural differences between groups is not driven by baseline differences and instead are due to differences in response to the task.

Loss Aversion. We computed a behavioral measure of loss aversion using logistic regression. This regression technique allows for the prediction of a binary response variable (i.e. the choice to accept or reject each gamble, coded as 1 or 0) from the independent variables of gain amount and loss amount. The logistic regression yielded regression coefficients (β) that represent the size of the contribution of the gain amount and loss amount to the participant's decision. The coefficient of loss aversion, lambda (λ) was then calculated from the regression coefficients using the following formula:

$$\lambda = -\beta_{Loss}/\beta_{Gain}$$

Larger values of λ reflect greater sensitivity to losses relative to gains, and values of $\lambda > 1$ reflect loss aversion. Correlational analyses were conducted to determine whether loss aversion varied as a function of age. In addition, we created a hierarchical linear model, with gain amount and loss amount as level 1 predictors, age group as a level 2 predictor, and binary choice as the

outcome variable, to test whether the extent to which gain and loss amounts influenced choice differed between age groups.

Results

Behavioral results

Monetary Experience Questionnaire. Upon receiving the $20 endowment, adolescent and adult participants reported similar levels of happiness (adolescent $M = 4.33$, $SD = .77$, adult $M = 4.12$, $SD = .89$, $t(32) = .735$, $p = .467$) and arousal (adolescent $M = 2.89$, $SD = 1.08$, adult $M = 2.88$, $SD = 1.20$, $t(32) = .035$, $p = .972$). The amount of monthly spending money participants reported was not significantly correlated with happiness (adolescent $r = -.003$, $p = .990$; adult $r = .028$, $p = .919$) or arousal (adolescent $r = -.024$, $p = .927$, adult $r = -.088$, $p = .746$) upon endowment. Adolescent and adult participants also did not differ from one another in their happiness (adolescent $M = 4.22$, $SD = .65$, adult $M = 4.25$, $SD = .68$, $t(32) = -.122$, $p = .904$) or arousal (adolescent $M = 3.56$, $SD = .92$, adult $M = 3.38$, $SD = 1.10$, $t(32) = .524$, $p = .604$) after receiving their payment for the task. Neither adolescents nor adults showed a significant difference between their happiness upon receiving the initial endowment and upon receiving their final payment (adolescent $t(17) = -.622$, $p = .542$, adult $t(15) = .620$, $p = .544$). Both groups reported greater excitement following receipt of their final payment than their initial endowment (adolescent $t(17) = 2.61$, $p = .018$, adult $t(15) = 3.16$, $p = .006$); this may be due to the fact that the final payment was guaranteed, while the endowment was at risk during the task, as well as to the fact that all participants received more than $20 as their final payment (adolescent $M =$ $26.89, $SD =$ $1.08, adult $M =$ $27.81, $SD =$ $1.42). Neither age nor amount of money received had an effect on how happy participants were after receiving payment for the task, $b_{age} = .003$, $t(31) = .016$, $p = .987$, $b_{amount} = .189$, $t(31) = .995$, $p = .328$.

Risk Taking Questionnaires. Adolescent and adult participants did not differ from one another in their total real-world risk-taking behavior on the Adolescent Risk Taking scale (adolescent $M = 4.82$, $SD = 2.86$, adult $M = 5.81$, $SD = 2.74$, $t(31) = -1.01$, $p = .318$. On the DOSPERT scale, adolescent and adult participants showed no differences in their reported likelihood of risk-taking (adolescent $M = 3.40$, $SD = .69$, adult $M = 3.56$, $SD = 1.18$, $t(32) = -.487$, $p = .630$), perceived riskiness (adolescent $M = 4.32$, $SD = .77$, adult $M = 4.29$, $SD = .83$, $t(32) = .097$, $p = .92$), and perceived benefits (adolescent $M = 2.84$, $SD = .77$, adult $M = 3.19$, $SD = .96$, $t(32) = -1.17$, $p = .251$).

For adolescent participants, scores on the Adolescent Risk Taking scale were positively correlated with perceived riskiness ($r = ,484$, $p = .049$), while for adult participants they were positively correlated with likelihood of risk-taking ($r = .595$, $p = .015$). When both age groups were combined, Adolescent Risk Taking scale scores correlated positively with both likelihood of risk-taking ($r = .469$, $p = .006$) and perceived benefits ($r = .389$, $p = .025$).

Across both age groups, male and female participants did not differ from one another in Adolescent Risk Taking scale scores (male $M = 5.93$, $SD = 3.35$, female $M = 4.78$, $SD = 2.21$, $t(31) = -1.19$, $p = .244$), or DOSPERT ratings of likelihood (male $M = 3.64$, $SD = .82$, female $M = 3.34$, $SD = 1.04$, $t(32) = -.909$, $p = .370$), riskiness (male $M = 4.35$, $SD = .82$, female $M = 4.27$, $SD = .78$, $t(32) = -.284$, $p = .779$), or benefits (male $M = 3.08$, $SD = .91$, female $M = 2.95$, $SD = .85$, $t(32) = -.436$, $p = .667$).

Mixed Gambles Task. Adolescent and adult participants performed similarly on the mixed gambles task. Independent samples t-tests revealed that adolescents and adults showed no differences in reaction time to accept a gamble (adolescent $M = 1460$ ms, $SD = 330$ ms, adult $M = 1410$ ms, $SD = 310$ ms, $t(32) = .469$, $p = .642$) or to reject a gamble (adolescent $M = 1460$ ms,

SD = 310 ms, adult *M* = 1330 ms, *SD* = 270 ms, *t*(32) = 1.362, *p* = .183). Adolescents and adults also did not differ in the percentage of overall trials they accepted (adolescent *M* = 35.9%, *SD* = 18.3%, adult *M* = 35.1%, *SD* = 14.0%, *t*(32) = .149, *p* = .882) or in the mean expected value of the trials they accepted (adolescent *M* = $1.96, *SD* = $0.97, adult *M* = $1.88, *SD* = $1.14, *t*(32) = .208, *p* = .836) and the trials they rejected (adolescent *M* = -$1.12, *SD* = $0.69, adult *M* = -$1.06, *SD* = $0.83, *t*(32) = -.24, *p* = .81). In addition, adolescents and adults did not differ in the percentage of gain-only trials they accepted (adolescent *M* = 69.3%, *SD* = 18.6%, adult *M* = 57.0%, *SD* = 28.0%, *t*(32) = 1.52, *p* = .138) or the percentage of loss-only trials they rejected (adolescent *M* = 87.2%, *SD* = 15.5%, adult *M* = 81.2%, *SD* = 16.3%, *t*(32) = 1.11, *p* = .275). Taken together, these findings demonstrate that adolescents and adults had a similar understanding of the expectations of the task and completed it in a similar way.

Performance on the mixed gambles task did not show any sex differences. Female and male participants did not differ in their reaction times to accept (female *M* = 1423 ms, *SD* = 308 ms, male *M* = 1447 ms, *SD* = 337 ms, *t*(32) = -.224, *p* = .824) or to reject a gamble (female *M* = 1370 ms, *SD* = 262 ms, male *M* = 1432 ms, *SD* = 340 ms, *t*(32) = -.598, *p* = .554). They also did not differ in the percentage of overall trials they accepted (female *M* = 38.3%, *SD* = 14.7%, male *M* = 32.4%, *SD* = 17.6%, *t*(32) = .249, *p* = .291) or in the mean expected value of the trials they accepted (female *M* = $1.85, *SD* = $0.90, male *M* = $2.00, *SD* = $1.20, *t*(32) = -.402, *p* = .690) and the trials they rejected (female *M* = -$1.13, *SD* = $0.61, male *M* = -$1.05, *SD* = $0.89, *t*(32) = -.314, *p* = .755). Female and male participants did not differ in the percentage of gain-only trials they accepted (female *M* = 64.3%, *SD* = 23.2%, male *M* = 62.7%, *SD* = 25.5%, *t*(32) = .183, *p* = .856) or the percentage of loss-only trials they rejected (female *M* = 83.5%, *SD* = 16.5%, male *M* = 85.3%, *SD* = 15.8%, *t*(32) = -.330, *p* = .743).

Loss Aversion. A behavioral coefficient of loss aversion (λ) was computed for each participant using the logistic regression procedure described above. After the exclusion of one statistical outlier from the adolescent population (who accepted too few gambles to generate an accurate λ term using logistic regression), no significant differences in loss aversion were observed between adolescents (M = .99, SD = 1.98) and adults (M = 1.11, SD = 1.47), $t(31) = -.205$, $p = .84$. Both adolescents and adults demonstrated a range of behavioral patterns from loss seeking (willing to accept gambles where the loss amount was greater than the gain amount) to loss averse (only willing to accept gambles where the loss amount was less than the gain amount), with coefficients of loss aversion for adolescents between -4.9 and 5.7, and those for adults between -3.0 and 3.3. No significant differences in loss aversion were observed between male participants (M = 1.05, SD = .70) and female participants (M = 1.04, SD = 2.28), $t(31) = -.016$, $p = .987$.

Across all participants, hierarchical linear modeling revealed a significant effect of the slope of gains on outcome ($\beta = .20$, $t(33) = 5.69$, $p < .001$) and the slope of losses on outcome ($\beta = -.24$, $t(33) = -7.35$, $p < .001$), where increasing potential gains increased the likelihood of an accept response while increasing potential losses decreased it (Figure 2). Furthermore, post-hoc analyses revealed that the coefficient for losses is significantly different from the coefficient for gains, $X^2(1) = 3.86$, $p = .047$, such that increasing loss amounts have a significantly greater effect on choice than increasing gain amounts do. However, age group had no effect on the slope for gains ($\beta = -.01$, $t(32) = -.11$, $p = .91$) or for losses ($\beta = -.04$, $t(32) = -.63$, $p = .53$).

Relationship between Self-Report Questionnaires and Mixed Gambles Behavior. Across all participants, the percentage of mixed gamble trials that were accepted showed no

significant correlation with scores on the Adolescent Risk Taking scale (r = .124, p = .491) or with the DOSPERT likelihood (r = .176, p = .326), perceived riskiness (r = -.031, p = .863), or perceived benefits (r = .084, p = .636) scales. Similarly, across all participants the coefficient of loss aversion did not correlate with Adolescent Risk Taking (r = .106, p = .563), likelihood (r = .090, p = .620), perceived riskiness (r = .009, p = .959), or perceived benefits (r = .182, p = .310) scores. When the data for adolescent and adult participants are analyzed separately, these correlations remain not significant.

FMRI Results

Accept Trials. On trials in which participants accepted the presented gambles, significant activation was observed relative to an implicit baseline. Whole-brain omnibus analyses of the contrast of Accepted Trials > Baseline revealed activation in anterior cingulate cortex (ACC), frontal pole, VS, insula, precentral gyrus, and occipital cortex (see coordinates in Table 1). Direct comparisons to investigate sex differences revealed significantly greater activation for male participants than female participants in ACC, precuneous corex and cerebellum (see coordinates in table 1). Direct group comparisons between adolescents and adults for the contrasts Accepted Trials > Baseline revealed no significant differences in activation between adolescents and adults on accept trials.

Reject Trials. On trials in which participants rejected the presented gambles, significant activation was observed relative to an implicit baseline. Whole-brain omnibus analyses for the Rejected Trials > Baseline contrast revealed activation in regions similar to those observed for accepted trials (ACC, frontal pole, VS, insula, precentral gyrus, occipital cortex; see coordinates in Table 1). Direct comparisons to investigate sex differences revealed significantly greater

activation for male participants than female participants in frontal pole and cerebellum (see coordinates in Table 1). Direct group comparison between adolescents and adults for the contrast Rejected Trials > Baseline revealed significantly greater activation for adolescents than for adults in the left caudate (peak activation at *x, y, z* MNI coordinates in mm: -16, 18, 18), bilateral frontal pole (0, 64, 8), and right occipital pole (-12, -94, 18) (Figure 3). Significantly greater activation was observed for adults than for adolescents in the postcentral gyrus (-54, -20, 28).

Contrasts Between Accepted and Rejected Trials. To examine the specific activation to accepted trials compared to rejected trials, a contrasts of Accepted Trials > Rejected Trials and Rejected Trials > Accepted Trials were examined. Significantly greater activation was observed for accepted trials than for rejected trials in bilateral ACC, right VS, bilateral angular gyrus, bilateral superior frontal gyrus, and right middle frontal gyrus, while significantly greater activation was observed for rejected trials than for accepted trials in left temporal pole, left postcentral gyrus, right superior frontal gyrus, and left hippocampus (Table 1). Direct comparisons to investigate sex differences revealed significantly greater activation for male participants than female participants in angular gyrus for the contrast Accepted Trials > Rejected Trials (Table 1). No significant differences between male and female participants were observed for the contrast Rejected Trials > Accepted Trials. Direct group comparisons between adolescents and adults for the contrasts Accepted Trials > Baseline, Accepted Trials > Rejected Trials, and Rejected Trials > Accepted Trials revealed no significant differences in activation between adolescents and adults.

Neural Activation and Risk-Taking. Whole-brain regression analyses were conducted separately for adolescents and adults to examine the relationship between neural activation on the task and the DOSPERT as a measure of real-life risk-taking (Figure 4). For adults, a

significant negative correlation was observed between activation from the Rejected Trials > Baseline contrast and the benefits of risk-taking DOSPERT scale in medial prefrontal cortex (peak voxel x =-2, y =48, z =34) and precentral gyrus (x = 34, y = - 34, z = 70). This relationship was not significant for adolescent participants. In adolescents, there was a significant negative correlation between activation from the Accepted Trials > Baseline contrast and the likelihood of risk-taking DOSPERT scale in medial prefrontal cortex (x = 4, y = 26, z = 42). There were no other significant correlations for adults between neural activation and the DOSPERT likelihood or risks scales when rejecting trials, nor were there significant correlations between neural activation and any of the DOSPERT scales when accepting trials. For adolescents, there were no significant correlations between neural activation and any of the DOSPERT scales when rejecting trials, nor were there significant correlations with the DOSPERT likelihood or risk scales when accepting trials.

Discussion

The behavioral findings from this study are the first to directly compare quantifiable measures of adolescent and adult loss aversion under risk. We found that adolescents and adults are similarly loss-averse when considering mixed gambles. Across age groups, loss amounts were shown to have a greater impact on choice than gain amounts. While prospect theory has established that losses loom larger than gains during adult decision-making (Kahneman & Tversky, 1979), these findings suggest that the same dictum can hold true for adolescents as well. Although initially surprising, this finding is consistent with the idea that adolescents and adults do not differ in risk perception or appraisal (Steinberg, 2004). Because risk aversion is generally considered to be caused by loss aversion (Köbberling & Wakker, 2005), behavioral

similarities in aversion to loss may contribute to adolescents displaying the same cognitive understanding of risk as adults.

Adolescents and adults performed similarly on other behavioral measures of the mixed gambles task as well; they accepted and rejected similar proportions of mixed gambles, and did not differ significantly in the expected value of the trials they accepted and rejected. Although these findings deviate from our initial hypotheses, they are consistent with other gambling tasks that have not observed behavioral differences between adolescents and adults (e.g. Bjork et al., 2004; Eshel et al., 2007). The lack of behavioral differences observed on the mixed gambles task may be explained by the theory that performance on these types of tasks reflects maturity in risk perception among adolescents; because they perceive risk similarly, adolescents and adults are willing to accept similar amounts of risk on this risk-taking task. It is also interesting to note that regardless of age, the behavior of participants on the non-mixed gambles (gain-only and loss-only) deviated from what would be considered normatively optimal by accepting a small percentage of loss-only trials and rejecting a small percentage of gain-only trials. These deviations may have been due to the difficulty of overriding a prepotent response of evaluating mixed gambles, since gain-only and loss-only trials made up only 25% of all trials in the task (i.e. participants may have responded to the trials as though they were mixed gambles, and only realized their error after responding).

While adolescents and adults responded similarly to mixed gambles on a behavioral level and used a similar neural network while accepting gambles during the task, they demonstrated different underlying neural responses to the process of rejecting gambles. Though they rejected the same proportion of trials as adults, adolescents displayed greater corticostriatal recruitment (i.e. greater activation in the caudate and frontal pole) than adults to achieve this behavioral

performance. These findings suggest a difference in neural development during the avoidance of risk; although neuroimaging studies have examined the choice between risky options and certain options in gambling tasks (e.g. Levin & Hart, 2003), this study directly explored the choice between accepting and avoiding risk in adolescents and adults. It is possible that adding affectively arousing components to a choice (e.g. peer influences, dynamic task designs that increase tension and exhilaration) overwhelm the reward-sensitive regions of the adolescent decision-making system and lead to increased risk-seeking behavior, similar to the elevated risk-taking observed in other arousing tasks (Gardner & Steinberg, 2005; Figner et al., 2009).

In addition, the relationship between measured real-world risk-taking and reported perceptions of risk-taking differed between adolescents and adults. For adults, the likelihood of risk-taking measure of the DOSPERT predicted reported real-world risk-taking on the Adolescent Risk Taking scale. For adolescents, likelihood was not associated with real-world risk-taking; instead, scores on the Adolescent Risk Taking scale were positively correlated with perceived riskiness. Because most of the risky behaviors measured on the Adolescent Risk Taking scale typically only occur during adolescence (e.g. sneaking out of the house, acting on a dare), these findings may capture separate aspects of the experience of risk-taking across development. The adult data suggest that having had a propensity for risk-taking in adolescence is related to having a propensity for risk-taking as an adult. For adolescent participants, who are still in the process of establishing their risk-taking tendencies, a different relationship is seen. Adolescents who identify the most risk in situations are also those who are most likely to have engaged in typically adolescent risk behaviors, suggesting that they may in fact actively seek out risky activities while having accurate risk perceptions, consistent with other studies of adolescent risk behavior (Reyna & Farley, 2006; Steinberg, 2004).

The relationship between behavioral measures of risk-taking and neural activation while accepting and rejecting gambles also differed for adolescents and adults. For adolescents, higher reported likelihoods of risk-taking were associated with decreased MPFC activation when accepting gambles. For adults, no neural activation correlated with likelihood of risk taking. In adults, higher reported benefits of risk-taking were associated with decreased MPFC activation when rejecting gambles, but no relationship was seen between neural activation and benefits of risk-taking in adolescents. These findings suggest that developmental changes in both brain and behavior may lead to shifts in what information is most important to individuals when assessing risk. Because the MPFC has been implicated in the representation of value during risky decision-making (e.g. Hare et al., 2008; Levy et al., 2010), this finding may suggest that adolescents who are more inclined toward real-world risk-taking rely less on value assessments when evaluating choices than less risk-prone adolescents do. Risk-taking adolescents may rely instead on "hot" cues such as affective arousal that are not captured by the mixed gambles task. Future studies are necessary to test this possibility.

The experimental paradigm employed here has several strengths. It provides the opportunity to observe both risk-seeking and risk-averse behaviors, and because each gamble is treated as an independent event and the outcomes of the gambles are not displayed, the results are not confounded by prediction error or learning. However, the procedure also has some limitations. Although adolescent and adult participants reported similar emotional responses to receiving their monetary endowment for the task, it is still possible that monetary risk is less meaningful for adolescents than adults because they are responsible for fewer expenses in their daily lives. In addition, the relatively small sample size in this study precluded examination of age-related differences within the adolescent population. Other studies have observed peaks in

risk-taking behavior and neural reward sensitivity during middle adolescence (e.g. van Leijenhorst et al., 2010a), which a larger adolescent sample would provide the opportunity to explore.

This study provides valuable insight into the differing patterns of neural activation underlying behaviorally similar levels of loss aversion in adolescents and adults. The increased neural activation required by adolescents to perform in an adult manner on a non-emotionally-arousing task may help to resolve some of the mixed findings within the adolescent risk-taking literature: adolescents may have the ability to refrain from elevated levels of risk-taking, but require additional cognitive and neural resources to do so. Contrary to the popular perception of adolescents as disregarding the potential negative consequences of risk-taking, these behavioral and neural findings suggest that adolescents can be averse to loss and adept at risk avoidance. For adolescents, the choice to take a risk may be weighted by the addition of social or affective factors under certain experimental tasks or real-world circumstances. Recognizing the interplay of these systems, and the conditions that may bias adolescents toward successful avoidance or maladaptive seeking of risk, is a critical step towards understanding when and how to intervene in adolescent behavior to encourage healthy outcomes.

Figure 1. Example of a trial from the mixed gambles task. Participants had 3000 ms in which to respond to the gamble by pressing one of four keys. A jittered inter-stimulus interval followed, after which participants viewed and responded to a new gamble. Participants did not experience the outcomes of the gambles during the scan.

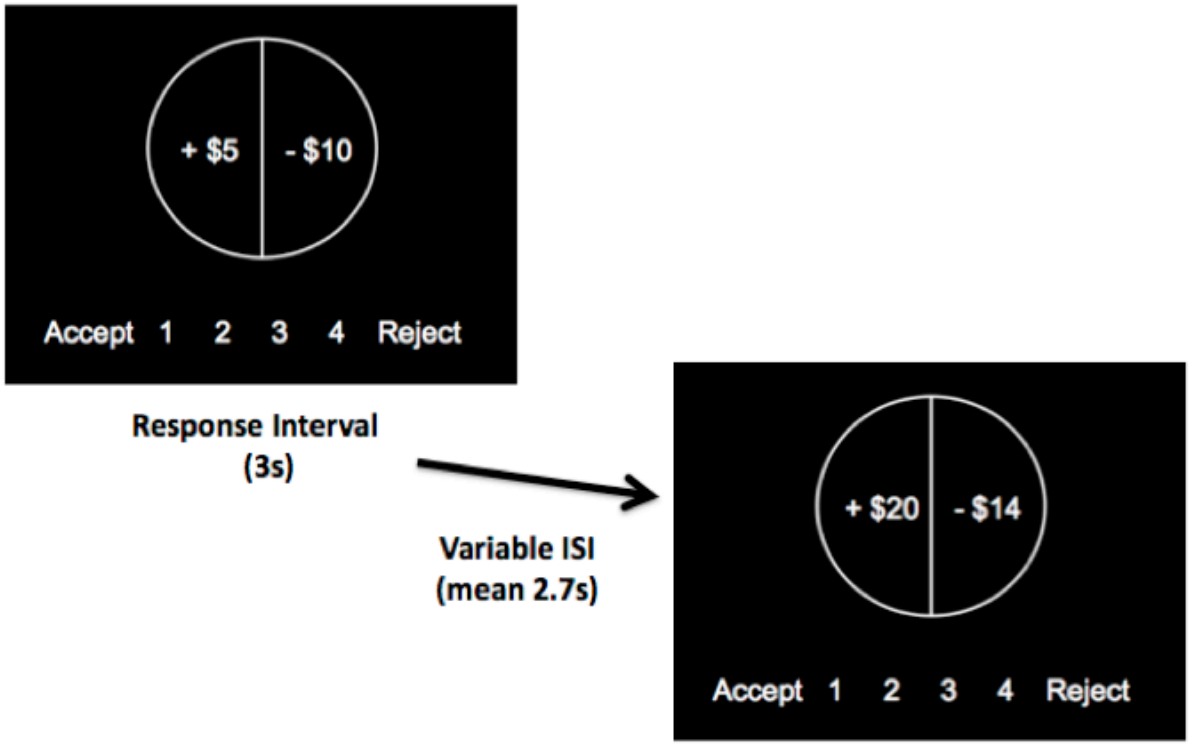


Figure 2. The effects of increasing gain amounts and loss amounts on response choice for adolescents and adults. For both age groups, increasing gain amounts increased the likelihood of accepting a gamble (A) while increasing loss amounts decreased the likelihood of accepting a gamble (B). The magnitude of the slope for losses was significantly greater than that for gains.

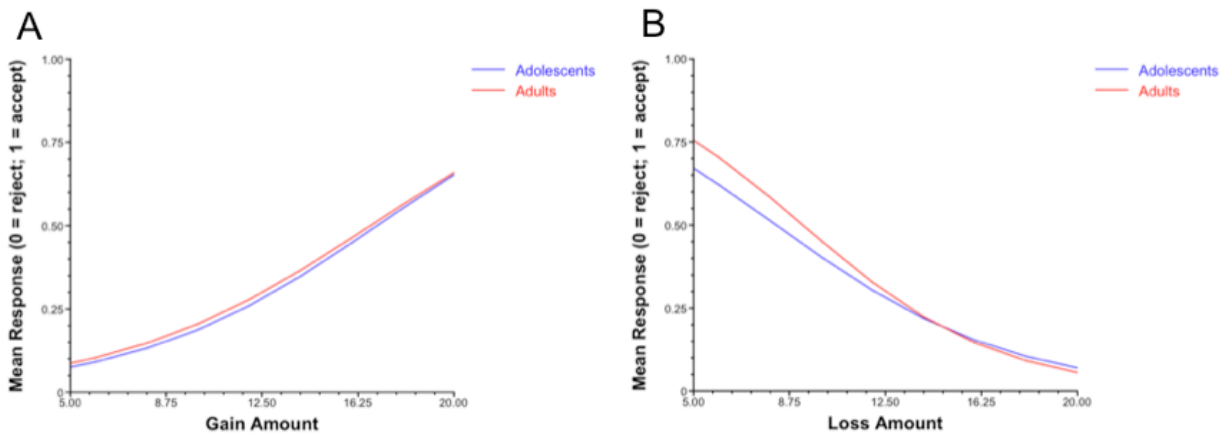


Figure 3. The contrast Rejected Trials > Baseline for Adolescents > Adults. (A) Greater activation is observed in adolescents than adults in the frontal pole, $p < .001$, cluster size = 1080 voxels. (B) Greater activation is observed in adolescents than adults in the caudate, $p < .02$, cluster size = 486 voxels. All activation is cluster corrected for multiple comparisons.

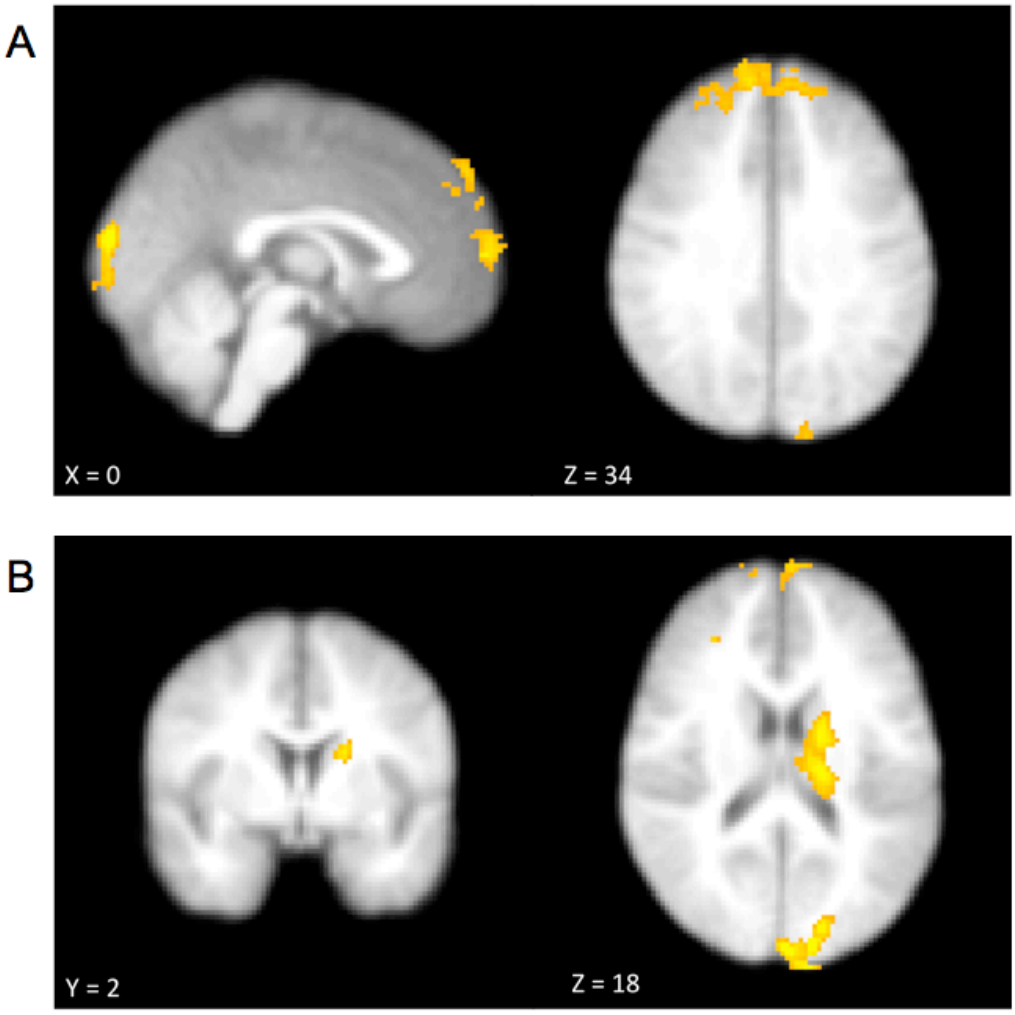


Figure 4. A. Peak voxel neural activation in MPFC (cluster size = 436 voxels, $p < .03$) and precentral gyrus (cluster size = 704 voxels, $p < .01$) in the Rejected Trials > Baseline contrast correlated negatively with self-reported benefits of risk-taking (measured on a Likert scale from 1 to 7) in adults (left) but not in adolescents (right). B. Peak voxel neural activation in MPFC (cluster size = 559 voxels, $p < .001$) in the Accepted Trials > Baseline contrast correlated negatively with self-reported likelihood of risk-taking (measured on a Likert scale from 1 to 7) in adolescents (left) but not in adults (right).

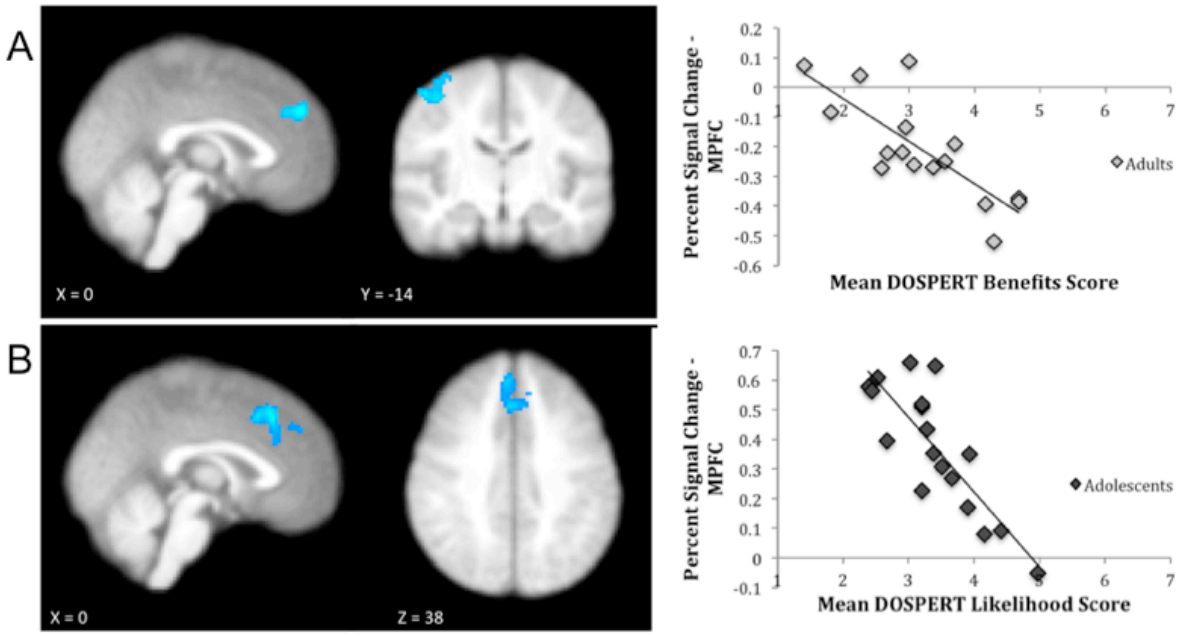


Table 1. Significant regions identified in whole-brain analyses for accepted and rejected trials and contrasts

Region		*X*	*Y*	*Z*	Max Z
Accepted Trials					
Occipital Cortex	R/L	26	-90	-12	9.50
		-18	-98	0	8.40
Frontal Pole	R/L	46	36	20	6.75
		-46	36	20	5.14
Precentral Gyrus	R/L	46	6	26	7.41
		-58	6	30	6.18
Anterior Cingulate Cortex	R/L	10	30	20	5.66
		-8	26	28	4.98
Ventral Striatum	R/L	18	14	-2	7.08
		-20	6	4	7.12
Insula	R/L	42	-2	8	3.65
		-42	-4	8	5.85
Accepted Trials – Men > Women					
Anterior Cingulate Cortex	R	12	34	16	3.74
Precuneous Cortex	R	6	-60	38	3.63
Cerebellum	L	-28	-56	-44	3.48
Rejected Trials					
Occipital Cortex	R/L	26	-90	-10	8.98
		-18	-98	0	8.57
Frontal Pole	R/L	52	40	18	6.14
		-40	40	14	4.94
Precentral Gyrus	R/L	48	8	28	7.25
		-44	4	28	6.87
Anterior Cingulate Cortex	R/L	6	24	32	6.48
		-4	22	34	6.92
Ventral Striatum	R/L	20	10	2	6.45
		-22	8	-4	6.70
Insula	R/L	42	0	4	4.06
		-42	4	0	4.51
Rejected Trials – Men > Women					
Frontal Pole	R	32	40	32	3.72
Cerebellum	L	-50	-50	-44	3.66
Accepted > Rejected					
Angular Gyrus	R/L	42	-56	44	5.09
		-42	-58	50	5.37
Middle Frontal Gyrus	R	40	26	46	4.32
Superior Frontal Gyrus	R/L	22	30	50	3.89
		-18	28	50	4.30
Anterior Cingulate Cortex	R/L	12	34	18	4.11

		-6	40	16	4.22
Ventral Striatum	R	12	16	0	4.60
Accepted > Rejected – Men > Women					
Angular Gyrus	R/L	46	-50	40	2.61
		-32	-72	46	2.25
Rejected > Accepted					
Temporal Pole	L	-44	10	-40	4.10
Postcentral gyrus	L	-12	-38	56	4.16
Superior Temporal Gyrus	R	62	-14	0	3.42
L Hippocampus	L	-26	-14	-24	3.48

III. Neural Representation of Expected Value in the Adolescent Brain

Introduction

Adolescence is characterized by heightened sensitivity to rewards (Galván, 2013). This phenotype is subserved by exaggerated neural response in ventral striatum (VS) to the anticipation (Geier et al., 2010) and receipt of expected (Ernst et al., 2005, Galván et al., 2006, van Leijenhorst et al., 2010) and unexpected reward (Cohen et al., 2010) in adolescents versus other age groups. The question remains, however, why rewards exert greater influence on behavior in adolescents, and whether this is mediated by ontogenetic differences in the subjective value that the adolescent brain attributes to available rewards.

Subjective value (SV) is defined as the value that an individual places on a stimulus (Knutson et al., 2008). To make a choice, an organism determines the SV of each alternative and then selects the one with the greatest SV (Rangel et al., 2008; Bartra et al., 2013). A recent meta-analysis of 206 studies of SV in adults identified the ventromedial prefrontal cortex (VMPFC) and VS as a "valuation system"(Bartra et al., 2013). These regions represent SV during choice for monetary stimuli (Hare et al., 2008, Kable & Glimcher, 2007, Levy et al., 2010, Peters & Büchel, 2009, Tobler et al., 2009, Tom et al., 2007), charitable donations (Hare et al., 2010), consumer goods (Knutson et al., 2007), and food (Hare et al., 2009, Lim et al., 2011, Litt et al., 2011, Plassmann et al., 2007, 2010, O'Doherty et al., 2006), although there is some disagreement about the relative contributions of each region specifically to valuation (e.g. Hare et al., 2008, Kable & Glimcher, 2009). Despite the wealth of knowledge on the neural correlates of SV in adults, no previous studies have examined the neurobiological development of SV.

One approach to understanding the neural computation of SV is through measurement of expected value (EV), the sum of all of the possible outcomes of a particular choice multiplied by

their probabilities (Trepel et al., 2005). In adults, increasing EV yields parametric activation increases in bilateral VS, midbrain, medial prefrontal cortex (MPFC) and dorsolateral prefrontal cortex (DLPFC) (Knutson et al., 2005, Yacubian et al., 2006, Tobler et al., 2007, Rolls et al., 2008, Gluth et al., 2013).

It is currently unknown if there are ontogenetic differences in how EV is represented in the brain and whether these differences confer a greater influence in value-based choices in adolescents versus adults. We investigated the adolescent and adult response to parametrically increasing EV using a simple mixed gambles task during functional magnetic resonance imaging (fMRI). We hypothesized that adolescents would exhibit greater behavioral sensitivity to increasing EV. Neurobiologically, we predicted that both groups would show similar increasing MPFC activation with increasing EV but that VS activation would modulate in proportion to increasing EV more for adolescents than for adults, given the strong evidence for adolescent sensitivity in the VS in response to rewards more generally.

Methods

Participants

Sixteen healthy right-handed adult participants (ages 25–30, mean age 28.1 years, SD = 1.8 years; 9 female) and 19 healthy right-handed adolescent participants (ages 13–17, mean age 15.5 years, SD = 1.3 years; 10 female) were recruited through poster and internet advertisements approved through the UCLA Institutional Review Board and through a database of prior research participants. All participants reported no prior diagnosis of psychiatric or neurologic illness or developmental delays, had no metal in their bodies, and were not taking psychoactive medication. One adolescent participant was excluded on the basis of exceeding

3mm of motion during the MRI scan; analyses were completed using the remaining eighteen adolescents (mean age 15.4 years, SD = 1.4 years; 10 female) and all sixteen adults.

Materials

During the fMRI scan, participants completed a variation of the gambling task originally reported by Tom et al. (2007). In this task, participants were presented with a series of gambles with a 50% probability of gaining the amount shown on one side of a "spinner" and a 50% probability of losing the amount shown on the other side (Figure 1). The gain and loss amounts were independently manipulated, with gain amounts ranging from +$5 to +$20 in $1 increments and loss amounts ranging from −$5 to −$20 in $1 increments, for a total of 144 trials. Randomly interspersed within these trials were 24 gain-only trials and 24 loss-only trials, with values drawn from the same range, for a total of 192 trials across four runs. These gain-only and loss-only trials allowed for a broader range of EVs within the task than mixed gambles alone would provide. The EVs of the mixed gambles ranged from -$7.50 to +$7.50, while the EVs of the gain-only gambles ranged from +$6 to +$19 and the EVs of the loss-only gambles ranged from -$6 to -$19. The side of the "spinner" in which the gain and loss appeared and the order of the stimuli were counterbalanced across participants. For each trial, participants decided whether or not they would be willing to play that gamble for real money. Participants were informed that one of the trials that they chose to accept would be selected at the end of the scan and played for real money, with that amount of money added to or subtracted from their overall payment for the study. This procedure was designed to encourage a choice on each trial that was consistent with the participant's actual feelings about that gamble.

MRI Scanning Procedure

Scanning was performed on a 3-Tesla Siemens Trio MRI machine in the Ahmanson-Lovelace Brain Mapping Center at UCLA. For the functional runs, 140 T2*-weighted echoplanar images (EPIs) were collected (33 slices; slice thickness, 4 mm; TR, 2000 ms; TE, 30 ms; flip angle, 90˚; matrix, 64 × 64; and field of view, 200). The first eight volumes of each functional run were automatically discarded. Two structural MRI images were collected as well: a T2-weighted matched-bandwidth high-resolution scan (following the same slice prescription as the EPIs) and a T1-weighted magnetization-prepared rapid- acquisition gradient echo image (MPRAGE; 160 sagittal slices; slice thickness, 1 mm; TR, 2000 ms; TE, 2100 ms; matrix, 192 × 192; and field of view, 256).

Data Preprocessing and Analysis

Data preprocessing and analysis were conducted using FSL version 4.1 (www.fmrib.ox.ac.uk/fsl). Images were motion-corrected using MCFLIRT and denoised using MELODIC independent components analysis. Data were smoothed using a 5 mm full-width-half-maximum Gaussian kernel and filtered with a nonlinear high-pass filter (66 s cutoff). A three-step registration process was used to align individual participant data into standard Montreal Neurological Institute (MNI) space. EPI images were first registered to the matched-bandwidth image, then to the MPRAGE image, and finally to MNI space. There were no significant differences between adolescents and adults in translational motion ($M_{adolescent}$ = .17 mm (*SD* = .15 mm), M_{adult} = .13 mm (*SD* = .10 mm), $t(32) = .980$, $p = .335$) or rotational motion ($M_{adolescent}$ = .003 mm (*SD* = .003 mm), M_{adult} = .002 mm (SD = .001 mm), $t(32) = 1.468$, $p = .152$).

Data analysis was conducted using FEAT, first at an individual subject-level and then using a mixed-effects model at the group analysis level. Z-statistic images were thresholded at a

cluster-level of $z > 2.3$ and a corrected significance threshold of $p \leq 0.05$. Statistical analyses were performed on each participant's data using a general linear model (GLM) to observe neural activation associated with increasing and decreasing EV. Each participant's data were modeled using a three-column parametric regressor that contained the onset time of each gamble, a standardized reaction time (RT) of 1 second, and the de-meaned EV of each gamble. Six motion parameters were also included as covariates in the model for each run for each of the participants. The regressor of interest was convolved with a canonical hemodynamic response function. A fixed-effects model was used at the second level to combine all four task runs for each participant. At the group level, a positive parametric main effect was modeled to identify neural regions where activation increased with increasing EV, and a negative parametric main effect was modeled to identify regions where activation decreased with increasing EV. Because adolescent and adult participants did not differ significantly in the EV of the trials that they chose to accept or reject during the mixed gambles task (Barkley-Levenson et al., 2013), we collapsed across age group for the initial analysis of neural response to EV.

Based upon the findings of the whole-brain group-level analysis and *a priori* hypotheses, we also conducted age-related contrasts in selected regions of interest (ROIs to investigate whether the observed effects were driven more strongly by adolescents or adults. ROIs were created using 6-mm spheres surrounding the peak voxels from the positive (showing increasing activation with increasing EV) whole-brain group-level analysis for MPFC (X = -6, Y = 38, Z = 14) and dorsolateral prefrontal cortex (DLPFC; X = 46, Y = 32, Z = 34). Given our *a priori* hypotheses about the role of the VS in representing value differentially across development, ROIs were created for right VS (X = 10, Y = 14, Z = -4) and left VS (X = -10, Y = 6, Z = -8) using the peak voxels from the uncorrected group-level analysis. In addition, ROIs were created

from the negative (showing decreasing activation with increasing EV) whole-brain group-level analysis using the same procedure for right amygdala (X = 18, Y = -6, Z = -20), left amygdala (X = -24, Y = -6, Z = -22), right insula (X = 42, Y = -10), and left insula (X = -40, Y = -14, Z = 0). The mean percent signal change was extracted from each ROI and the values were compared for adolescents and adults using two-tailed T tests. For visualization, statistical maps of all analyses were projected onto an average brain. All fMRI data shown were cluster-corrected at Z=2.3, $p<0.05$ and controlled for multiple comparisons in FSL.

Results

Behavioral Results

An analysis of variance (ANOVA) analysis revealed a main effect of trial type on accept rates ($F(2,32) = 54.90$, $p < .001$). Across all participants, trials with positive EV (EV+ trials) were accepted significantly more often than trials with EV of zero (EV_0 trials) ($M_{EV+} = 56.74\%$ ($SD = 21.07\%$), $M_{EV0} = 37.34\%$ ($SD = 27.63\%$), $t(33) = 4.714$, $p = .000$), which were accepted significantly more often than trials with negative EV (EV- trials) ($M_{EV-} = 15.88\%$ ($SD = 13.36\%$), $t(33) = 5.770$, $p = .000$). No significant differences were observed between adolescent and adult participants in the percentage of EV+ trials accepted ($M_{adolescent} = 58.46\%$ ($SD = 20.96\%$), $M_{adult} = 54.79\%$ ($SD = 21.69\%$), $t(32) = .502$, $p = .619$), percentage of EV_0 trials accepted ($M_{adolescent} = 36.20\%$ ($SD = 26.90\%$), $M_{adult} = 38.64\%$ ($SD = 29.35\%$), $t(32) = -.253$, $p = .802$) or the percentage of EV- trials accepted ($M_{adolescent} = 15.38\%$ ($SD = 13.86\%$), $M_{adult} = 16.44\%$ ($SD = 13.21\%$), $t(32) = -.228$, $p = .821$).

Hierarchical linear modeling revealed a significant effect of the slope of EV on response ($\beta = .25$, $t(32) = 4.69$, $p < .001$), where increasing EV increased the likelihood of an accept response. The model also showed a significant effect of age group ($\beta = -.11$, $t(32) = -1.98$, p

=.05) such that parametric changes in positive EV had a greater effect on response for adolescents than for adults (Figure 2).

No significant differences were observed between adolescent and adult participants in RT for EV+ trials ($M_{adolescent}$ = 1405 ms (*SD* = 299 ms), M_{adult} = 1346 ms (*SD* = 262 ms), $t(32) = .609$, $p = .547$), or EV- trials ($M_{adolescent}$ = 1418 ms (*SD* = 307 ms), M_{adult} = 1294 ms (*SD* = 251 ms), $t(32) = 1.280$, $p = .210$), though there was a trend towards adolescents taking significantly longer than adults to respond on EV_0 ($M_{adolescent}$ = 1437 ms (*SD* = 307 ms), M_{adult} = 1294 ms (*SD* = 251 ms), $t(32) = 2.033$, $p = .052$).

GLM Results

Whole-brain analyses revealed significant activation associated with parametrically increasing EV in the superior MPFC (X = -6, Y = 38, Z = 14), paracingulate gyrus (X = 4, Y = 32, Z = 30), DLPFC (X = 46, Y = 32, Z = 34), and bilateral clusters encompassing the lateral occipital cortex, angular gyrus and supramarginal gyrus (X = 42, Y = -58, Z = 52; X = -36, Y = -66, Z = 50); activation in these regions increased with increasing EV (Figure 3A). The negative parametric contrast, identifying regions wherein activation decreased with increasing EV, revealed significant activation in bilateral regions including amygdala (X = 18, Y = -6, Z = -20; X = -24, Y = -6, Z = -22), parahippocampal gyrus (X = 24, Y = -34, Z = 18; X = -22, Y = -38, Z = -18), hippocampus (X = 24, Y = -14, Z = -18; X = -24, Y = -14, Z = -22), and insula (X = 42, Y = -10, Z = 0; X = -40, Y = -14, Z = 0) (Figure 3B).

Comparison by Age Group

ROI analyses revealed a significant parametric activation difference in response to increasing EV between adolescents and adults in the left VS, $t(32) = 2.17$, $p = .038$ (Figure 4). In left VS, adolescents showed greater neural sensitivity to increasing EV than did adults. No

significant differences between adolescents and adults in response to increasing EV were observed in ROI analyses for MPFC, DLPFC, or right VS. In addition, no significant differences in negative parametric activation in response to increasing EV were observed in ROI analyses for right amygdala, left amygdala, right insula or left insula.

Discussion

The aim of this study was to identify neural representation of EV in the adolescent brain. Consistent with the strong consensus in the adult literature (Bartra et al., 2013), we observed activation of MPFC and DLPFC and adjacent cortical regions during EV computations. Our observation of decreased activation in insula in response to increasing EV is also supported by existing findings (Kim et al., 2010, Rolls et al., 2008). These data suggest that in cortical regions, neural representation of EV changes minimally beyond adolescence. However, we observed developmental differences in the VS, such that adolescents exhibited significantly greater activation than adults (who showed virtually no activation in this region), suggesting that maturational changes in neural representation of valuation during adolescence are most robust in the VS.

The Role of EV on Adolescent Choices

There are a few plausible explanations for the greater VS sensitivity in adolescents during computation of EV. One possibility is that adolescents are less adept than adults at computing EV and so VS activation is simply a response to the potential monetary earnings. However, the observed similarities among adolescents and adults in preference for trials with positive EV and low acceptance rate of trials with negative EV suggests that adolescents are just as capable as adults at discriminating the EV trial types. A second possibility is that the adolescent brain places greater value on potential rewards than does the adult brain. Support for this speculation

is found in the finding that parametric increases in EV were more influential in increasing the likelihood of accepting the gambles in adolescents, particularly on the highest EV trials. In fact, these data suggest that adolescents were making more optimal choices than adults in the face of positive EV; for instance, on trials with a positive EV of $6 (as shown in Figure 1), adolescents accepted the gamble at a rate of 65% (compared to 48% in adults). We speculate that on these EV+ trials, the likelihood of accepting the gamble was higher in the adolescents because they were swayed by the possibility of winning the larger dollar amount and less focused on the chance of losing the relatively smaller amount. On these trials, the heightened adolescent sensitivity to reward was in fact adaptive because it led to a more rational choice (i.e. accepting a gamble with high positive EV). Despite the allure of the positive dollar amounts, however, the adolescents discerned between the different trial types; on trials with negative EV, their likelihood of accepting the gamble was, like adults, virtually zero. Together, the behavioral data on the positive and negative EV trials suggest that while adolescents are as astute as adults when presented with a disadvantageous choice, their heightened sensitivity in reward circuitry leads to better choices than adults on advantageous trials. Perhaps this adaptable behavior is evidence for a more flexible reward system (Crone & Dahl, 2012), one that encourages more or less approach behavior based on dynamic options.

Finally, an alternative possibility is that age-related differences in sensitivity to value may have been observed because there are developmental differences in subjective value for small sums of money. While the objective EV of any particular gamble is fixed, economic theories suggest that subjective value is a concave (rather than linear) function, which is sensitive to differences in individual states of wealth (Kahneman & Tversky, 1984). By this reasoning, for a gamble of +$20/-$5 (with EV=$7.50) an adolescent with less disposable income would place a

larger subjective value on the chance to win $7.50 than an adult with a larger income would, making the adolescent's VS more responsive to small changes in EV. The stronger influence of change in EV on adolescent choice than on adult choice during the mixed gambles task supports this idea. Subsequent studies could explore this question by varying the magnitude of EVs more dramatically within a task or by attempting to equate subjective, rather than objective, values across age groups.

Ontogenetic Differences in Neural Representation of EV

Similar to previous studies, these findings provide evidence for an exaggerated neural response to rewards in adolescents versus adults in the VS (Ernst et al., 2005, Galván et al., 2006, Galván and McGlennen, 2013; Geier et al., 2010, van Leijenhorst et al., 2010). The current study extends these previous findings by offering a possible explanation for adolescent sensitivity to reward and may help disentangle some of the divergent results in the adolescent literature (Bjork et al 2004, 2010). The sensitivity to EV observed in this study may underlie adolescent sensitivity to experienced reward because adolescents may experience rewards as having greater subjective value than adults do. fMRI studies that find less activation in VS in adolescents versus adults (Bjork et al 2004, 2010), or no age-related differences, may have used computer tasks that do not elicit developmental differences in subjective value. Findings from this study may also help to explain adolescent sensitivity to prediction error (Cohen et al., 2010). Because prediction error is measured as a deviation from EV, an increased sensitivity to value would produce a greater positive prediction error signal in response to an unexpected reward. Thus, heightened adolescent sensitivity to EV may explain the nonlinear developmental trajectory in reward circuitry as previously reported.

Limitations and Conclusions

One limitation of the current study is the relatively small sample size. Another limitation is the lack of a pre-adolescent participant group (i.e., ages 8-12). Some developmental research has identified patterns that are quadratic rather than linear, with peaks in behavioral response or neural activation during middle adolescence and declining for both younger and older individuals (e.g., van Leijenhorst, 2010). Others observe behavioral and neural patterns that increase or decrease continuously with age (e.g., Galván et al., 2006). Without including pre-adolescents it is not possible to say with certainty whether the observed difference is a uniquely adolescent sensitivity to EV or part of an ongoing developmental trajectory.

In summary, this study deepens our understanding of adolescent reward responsiveness by identifying neural differences in sensitivity to EV across development. Further, these data suggest that adolescents are biased to a greater extent than adults by the value of available options and may partially explain the observed adolescent sensitivity to reward and positive prediction error. Collectively, these behavioral and neural data provide evidence for ontogenetic differences in how computation of value is used to bias reward-related behavior.

Figure 1. Example of three trials from the mixed gambles task. Participants responded within 3000 ms by pressing one of four keys. A jittered inter-stimulus interval followed before the subsequent trials. Gamble outcomes were not revealed during the scan.

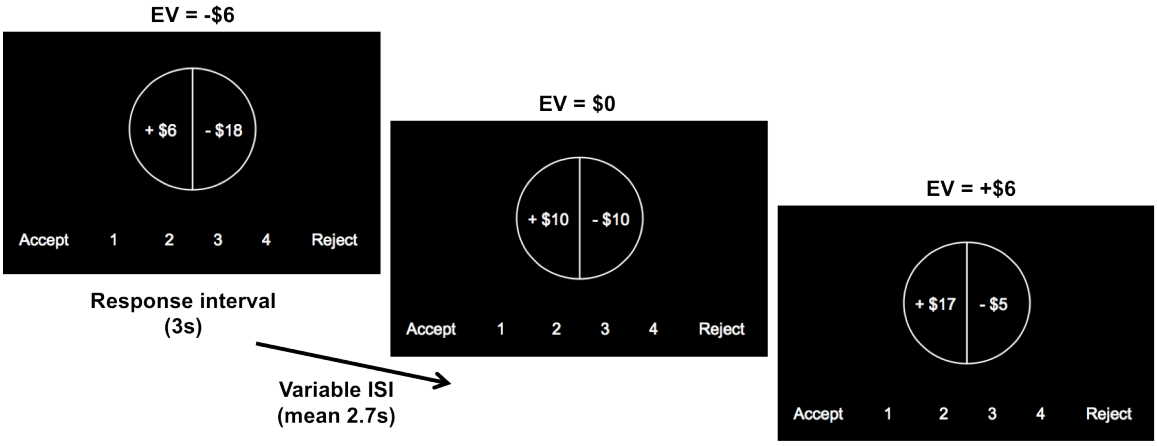


Figure 2. The effect of increasing EV on mixed gamble response for adolescents and adults. For both groups, increasing EV increased the likelihood of accepting a gamble. The influence of increasing EV on response was greater for adolescents versus adults.

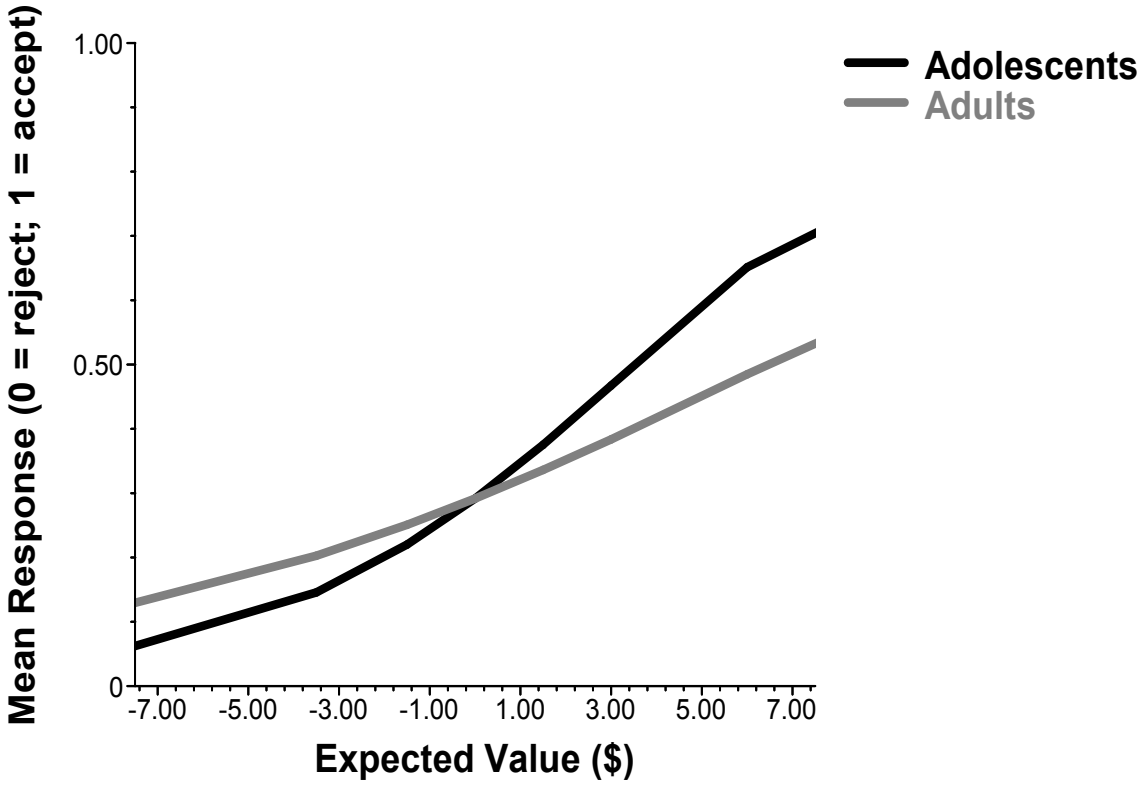


Figure 3. Parametric analyses revealed neural activation that changes in proportion with increasing EV. (A) Regions showing increasing activation with increasing EV. (B) Regions showing decreasing activation with increasing EV.

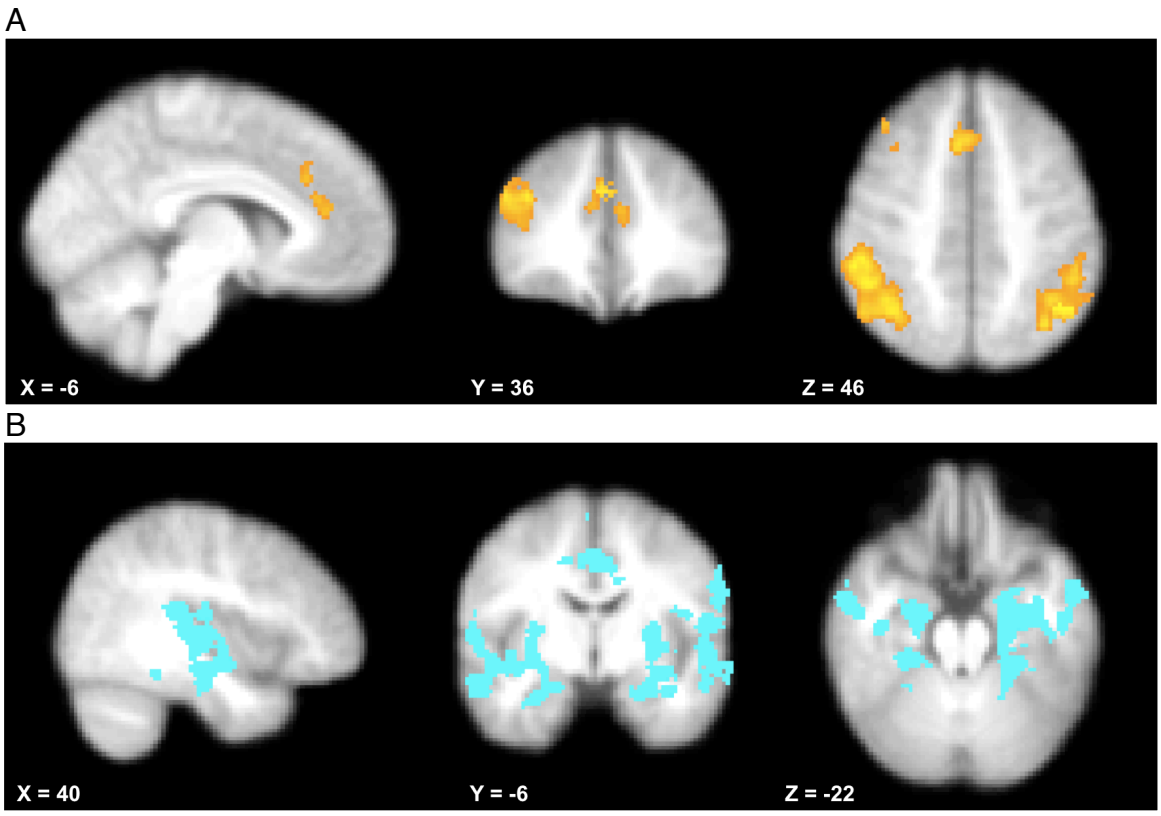
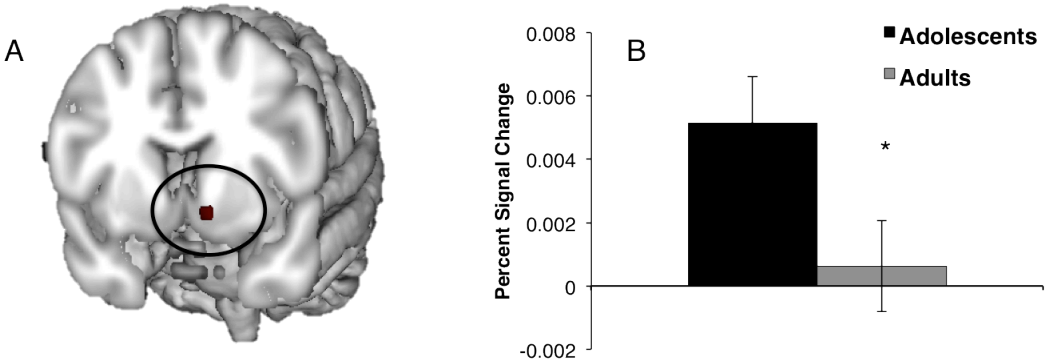


Figure 4. (A) ROI for left VS, a 6-mm sphere centered at X = -10, Y = 6, Z = -8. (B) There was a significant developmental difference in VS, $t(32) = 2.17$, $p = .038$.



IV. Eye Blink Rate Predicts Decision Strategy in Adolescents

Introduction

Adolescence is a developmental period characterized by increased sensitivity to rewards. A growing body of literature has employed functional magnetic resonance imaging (fMRI) to investigate the neural substrates of adolescent responsiveness to reward, and evidence consistently demonstrates that the adolescent ventral striatum is hyper-responsive to the anticipation and experience of reward relative to other age groups (Cohen et al., 2010, Ernst et al., 2005, Galván et al., 2006, Geier et al., 2010, May et al., 2004, van Leijenhorst et al., 2010). While these studies focus on a systems-level understanding of adolescent reward responsiveness, the underlying neurochemical mechanisms remain less clearly defined.

The striatum is innervated by dopamine neurons from the substantia nigra and ventral tegmental area (cf. Schultz, 2000), and various measures of dopamine function have been associated with reward expectation (e.g., de la Fuente-Fernández et al., 2002, Schultz, 1998). Converging evidence from the animal literature shows that the number of D_1 and D_2 dopamine receptors in the striatum peak during adolescence before undergoing pruning (Teicher et al., 1995). Direct investigation of dopamine in the adolescent brain, however, poses a challenge. In humans, the most common approach to studying neurotransmitters directly is positron emission tomography (PET), the use of which is prohibitively invasive for adolescents due to the necessity of injecting radioactive ligands into the participant. Noninvasive approaches to directly investigating the role of dopamine in reward sensitivity are therefore necessary.

One technique that captures aspects of dopaminergic functioning without the invasiveness of PET is the measurement of eye blinks (Karson et al., 1982). This technique has been shown in non-human primates to correlate positively with D1 and D2 receptor availability

(Elsworth et al., 1991). Work with human clinical populations supports this, demonstrating that eye blink rate (EBR) is suppressed in individuals with Parkinson's disease (Karson et al., 1982), a condition in which patients suffer from dopamine depletion. EBR has also been shown to be elevated in unmedicated patients with schizophrenia (Karson, 1983), another disorder where dopamine is hypothesized to play a role. Similarly, higher EBR is associated with impaired motor response inhibition (Colzato et al., 2009), consistent with the role of dopamine in impulsivity (Frank et al., 2007). In addition, EBR has been shown to increase in children and adolescents who were administered ziprasidone, an indirect dopamine agonist (Sallee et al., 2003), suggesting that EBR is an effective proxy for direct dopamine measurement in adolescents as well as in adults.

The present study aims to investigate the relationship between dopamine and adolescent reward sensitivity using a risky decision-making task and the measurement of baseline EBR in adolescent participants. We focus on decision-making under risk for two reasons. First, risky behavior is associated with increased dopamine levels (Riba et al., 2008, Zald et al., 2008). Second, risk-taking provides an easily understandable paradigm in which to introduce the potential for losses as well as gains, as the lay definition of risk tends to focus on the potential for negative outcomes (Schonberg et al., 2011). In this task, participants choose among three different decision strategies: probability-maximizing (an option that increases the probability of gaining money in the task), gain-maximizing (an option that increases the value of the possible reward without altering probabilities) and loss-minimizing (an option that reduces the value of the possible loss without altering probabilities). The inclusion of a loss dimension is infrequently employed in adolescent research, but is essential to understanding the extent to which adolescent sensitivity to reward is actually reflective of overall sensitivity to value. In the current study, we

hypothesized that if dopamine is driving adolescent reward-seeking behavior, participants with higher dopamine levels (as measured by EBR) would more frequently select strategies increasing reward (either by gain-maximizing or probability-maximizing). If, however, striatal dopamine levels are related to increased sensitivity to value in both the gain and the loss domain, we would expect to see reduced probability-maximizing choices (as this choice is considered by Venkatraman et al. (2009) to be a "simplifying" strategy that ignores reward magnitude) relative to either gain-maximizing or loss-minimizing choices, which both require manipulation of an extreme value on the task.

Methods

Participants

Seventeen adolescent participants (age range 13-18, M = 15.6 years, SD = 1.6 years, 8 female) were recruited through Internet advertisements approved through the UCLA Institutional Review Board and through a database of prior research participants. All participants were fluent in English and reported no current diagnosis of psychiatric or neurologic illness or developmental delays.

Materials

Baseline eye blink rate. Prior to any other components of the study, participants completed a 5-minute session during which their spontaneous eye blinks were video recorded using the program PhotoBooth. Participants were instructed to view a black screen with a fixation cross and to remain awake during the 5-minute period.

Survey measures. During the first session of the study, participants completed a series of surveys. Among other measures, participants completed the Adolescent Domain-Specific Risk Taking Scale (DOSPERT; Figner et al., in preparation), a 40-item measure of one's perceived

risk of, benefit of, and likelihood of engaging in risky events. The DOSPERT uses a 7-point Likert scale for each of the assessment dimensions ("not at all risky" to "extremely risky," "no benefits at all" to "great benefits," and "extremely unlikely" to "extremely likely") and includes scenarios in the domains of financial, ethical, recreational, social, and health risk, designed to be developmentally appropriate for participants ages 14-17. For ease of direct comparisons among participants, 13-year-old and 18-year-old participants also completed the Adolescent DOSPERT. Participants also completed the Arnett Inventory of Sensation-Seeking (AISS; Arnett, 1994), which has been shown to characterize sensation-seeking behavior in adolescents, and the Stanford Sleepiness Scale (SSS; Hoddes et al., 1973), a one-item measure of alertness at the time of assessment.

Taste priming. At each visit, participants sampled 0.5 ounces of either an appetitive chocolate sample (Lindt Excellence Extra Creamy Milk Chocolate) or an aversive chocolate sample (Lindt Excellence 90% Cocoa Supreme Dark Chocolate). Participants then reported their liking of the sample on a questionnaire consisting of three 9-point Likert scales, with a minimum score of 3 and a maximum score of 27. A pilot study of 18 adult and 6 adolescent participants revealed that the appetitive chocolate was liked significantly more than the aversive chocolate ($M_{\text{aversive}} = 8.83$, $SD_{\text{aversive}} = 6.03$, $M_{\text{appetitive}} = 21.83$, $SD_{\text{appetitive}} = 4.11$, $t(23) = -8.14$, $p < .001$). This priming was designed to modulate dopamine levels within each participant.

Roulette Game. Participants completed a total of two runs of the Roulette Game (RG; Figure 1), a novel version of a task originally designed by Payne (2005). In this task, participants were presented with a series of "wheel" gambles with a 1/3 probability of gaining money (ranging from +$3.50 to +$8), a 1/3 probability of losing money (ranging from -$4 to -$8.50) and a 1/3 probability of receiving $0. A total of 400 trials were created and divided among 5 runs of

80 trials each; the run number and order were counterbalanced across participants. After viewing the gamble for 1s, participants were presented with an amount of money (ranging from $1 to $2.50) and instructed to add that amount of money to one of the three spaces on the "wheel", changing the value of that gamble. Thus, on each trial the participant made a choice employing one of three strategies. A gain-maximizing (G_{max}) choice was one where the participant chose to add money to the positive-value space on the "wheel", increasing the maximum possible amount they could win. A probability-maximizing (P_{max}) choice was one where the participant added money to the reference ($0) space, increasing the probability of winning some amount of money from 1/3 to 2/3. Finally, a loss-minimizing (L_{min}) choice was one where the participant added money to the negative-value space, reducing the value of the potential loss. Because the probabilities of each space were equal, the expected value of the gamble remained unchanged regardless of participant choice; therefore, no one strategy can be considered optimal, and different strategies may be seen as reflecting different but equally valid approaches to risk-taking. Participants were informed that one trial (including the money added by the participant to the chosen space) would be selected at random at the end of the study and its outcome would be resolved for real money, with any gain or loss being added to or subtracted from their $15 base pay for the session. This design incentivized participants to respond based on their actual preferences for every trial. In actuality, each trial was resolved such that either the reference or gain amount was selected at random, ensuring that all participants received at least $15 for the testing session.

Procedure

The study took place across two sessions. At the first session, all participants under the age of 18 completed informed assent while their parents or guardians provided informed consent;

18-year-old participants provided informed consent. During the first session, participants completed the baseline eye blink recording, all survey measures, one taste priming condition (either appetitive or aversive), and one run of the RG. Eye blinks were also recorded during the RG. At the second session, participants again completed baseline eye blink recording, the SSS, the taste priming condition not administered at session 1, and a second run of the RG. At the end of each session, participants received a base payment of $15 adjusted by the value of the outcome of a randomly selected trial from the RG.

Eye blink rate analysis. Two independent raters who were blinded to taste condition counted the total number of blinks in each of the recordings made during baseline and task sessions. Any times when participants' eyes were not visible were removed from the total time, and eye blink rate (EBR), measured as blinks per visible minute (BPVM), was calculated for each recording. The intraclass correlation coefficient between the two raters was .92 ($p < .001$) for session 1 baseline, .88 ($p < .001$) for session 1 task, .98 ($p < .001$) for session 2 baseline, and .85 ($p < .001$) for session 2 task; because of satisfactory inter-rater reliability, the raters' scores were averaged for each condition.

Results

Eyeblink Rate Results

EBR was highly correlated between baseline session 1 (M = 18.16 BPVM, SD = 10.45 BPVM) and baseline session 2 (M = 17.59 BPVM, SD = 13.71 BPVM), r = .844, $p < .001$, and the two session EBRs did not differ significantly from one another, $t(16) = .312$, $p = .76$. An average baseline EBR was therefore computed for all subsequent analyses. No significant difference was observed in EBR during task following the appetitive taste priming condition (M = 12.57 BPVM, SD = 8.46 BPVM) and following the aversive taste priming condition (M =

12.36 BPVM, *SD* = 7.76 BPVM), $t(16) = -.138$, $p = .89$. Because no differences were observed between the taste conditions, all subsequent results discussed will be collapsed across taste conditions. Average baseline EBR was marginally positively correlated with sensation seeking ($r = 439$, $p = .078$). Baseline EBR was not correlated with any other survey measures.

Roulette Game Results

An analysis of variance (ANOVA) revealed a marginally significant difference in the number of trials in which participants employed each decision strategy, $F(2, 32) = 3.127$, $p = .057$. Post-hoc analyses revealed that participants chose the L_{min} strategy significantly more than the G_{max} strategy ($M_{Lmin} = 38.44$, $SD = 22.81$, $M_{Gmax} = 17.79$, $SD = 16.97$, $t(16) = -2.46$, p = .026), although L_{min} use did not differ significantly from use of the P_{max} strategy ($M_{Pmax} = 23.76$, $SD = 20.47$, $t(16) = -1.52$, $p = .149$) (Figure 2). Within-subjects contrasts confirmed a significant linear relationship between G_{max}, P_{max} and L_{min} strategy use, $F(1, 16) = 6.05$, $p = .026$. There was no effect of age on number of G_{max} choices, P_{max} choices or L_{min} choices. An ANOVA revealed no significant difference in response times among the different decision strategies, $F(2, 28) = .458$, $p = .637$, and within-subjects contrasts revealed no significant linear ($F(1, 14) = 1.44$, $p = .249$) or quadratic ($F(1, 14) = .192$, $p = .668$) relationship with the response times to make G_{max}, P_{max} and L_{min} choices.

Relationship Between EBR and Decision Strategy

A significant negative correlation was observed between baseline EBR and use of the P_{max} decision strategy, $r(15) = -.528$, $p = .029$. Because participant sleepiness would be expected to influence blink rates, we conducted a linear regression controlling for alertness, as measured by the average rating on the SSS. Controlling for alertness, baseline EBR still marginally significantly predicted P_{max} choice, $\beta = -.50$, $t(14) = -2.06$, $p = .059$; alertness had no effect on

P_{max} choice, $\beta = -.08$, $t(14) = -.317$, $p = .756$. Baseline EBR was not significantly correlated with use of the G_{max} strategy ($r(15) = -.264$, $p = .307$) or L_{min} strategy ($r(15) = .278$, $p = .280$).

Discussion

The results of this study demonstrate the efficacy of EBR as an individual difference measure in adolescents. Consistent with findings in non-human primates (Elsworth et al., 1991), the highly positive correlation between EBR measured on two different days demonstrates that baseline EBR is stable across time in human adolescents. Furthermore, the positive relationship between sensation seeking and EBR supports the idea that EBR is, in fact, related to dopaminergic activity in adolescents. A positive relationship has been shown between novelty seeking – which has been described as the core behavior of sensation seeking (Zuckerman & Kuhlman, 2000) – and dopamine in animal models (Bardo et al., 1996). In humans, novelty seeking has been linked with a dopamine gene polymorphism associated with increased dopamine levels (Golimbet et al., 2007) and with reduced D_2 receptor availability (Suhara et al., 2001, Kaasinen et al., 2004), while sensation-seeking has been shown to have an inverted-U relationship with $D_{2/3}$ receptor availability (Gjedde et al., 2010), which is interpreted as a positive relationship between sensation-seeking and dopamine concentration. From these findings it can be inferred that the positive correlation between EBR and sensation seeking is reflective of a positive relationship between EBR and dopamine concentration, possibly driven by D_2 receptor availability.

The negative correlation between number of P_{max} choices and EBR suggests that dopamine concentration may influence decision strategy on the RG, wherein individuals with the lowest dopamine concentration are the most likely to employ the P_{max} strategy. The P_{max} strategy has been characterized as one that ignores reward magnitude (Venkatraman et al., 2009). Therefore,

participants who have the lowest dopamine levels appear to be the least sensitive to value in a risky context. This is consistent with the current understanding of the neurobiology of reward and value. Dopaminergic activity in the ventral striatum has been associated with reward responsiveness in humans (Kalivas & Nakamura, 1999, de la Fuente-Fernández et al., 2002) and non-human primates (Schultz, 2000); furthermore, fMRI has shown that the adolescent ventral striatum is highly sensitive to reward (e.g., Cohen et al., 2010, Ernst et al., 2005, Galván et al., 2006, Geier et al., 2010, van Leijenhorst et al., 2010,) and to changes in value, as demonstrated in chapter 3.

The pattern of behavior observed on the RG in this study differs from prior studies employing similar tasks (Payne, 2005; Venkatraman et al., 2009), which find more frequent use of P_{max} than the G_{max} or L_{min} strategies. Several relevant differences between these earlier tasks and the RG may contribute to this difference. For example, participants in the Payne (2005) study did not receive incentive-compatible payments following completion of the task, and participants in the studies of Venkatraman et al. (2009, 2011) were guaranteed a base payment of $40 even if they experienced the greatest possible loss on the RG; in contrast, the current participants faced the possibility of receiving only $6 as payment for their time if they experienced the greatest possible loss on the RG. The smaller reward magnitudes employed here may have served to make losses highly salient relative to prior versions of the task, eliciting greater L_{min} behavior than was observed in other studies. In addition, the paradigm from Venkatraman et al. (2009, 2011) uses a forced-choice approach wherein participants must select either the P_{max} choice or one of the other two choices (either G_{max} or L_{min}, but not both in the same trial). It is possible that P_{max} may dominate in a binary choice, but when all options are

considered together different variables become more salient and different strategies are selected at greater rates.

The lack of a significant change in EBR based on taste priming conditions may be due to a number of factors. While some studies have shown dynamic changes in EBR following manipulation of dopamine levels (Elsworth et al., 1991), it is possible that any changes in dopamine release due to either appetitive or aversive taste stimuli are not large enough to be picked up by an indirect measure like EBR. Alternatively, it may be that both appetitive and aversive taste stimuli modulate dopamine in a similar direction. This is consistent with fMRI data showing increased activation in the ventral striatum for both increasing rewards and increasing penalties (Bartra et al., 2013). Future studies will be necessary to disentangle these two possible explanations.

Overall, these data strongly suggest that EBR in adolescents can be used as a measure of individual differences in dopamine levels. Furthermore, these data suggest a negative relationship between dopamine concentrations and value-sensitive responses during risky decision-making, providing support at the neurotransmitter level for a relationship that previously could only be inferred by fMRI in adolescents. These promising findings lay the foundation for further use of EBR as a measure of dopamine in adolescents, in order to better understand the mechanisms underlying individual differences in adolescent sensitivity to value under risk.

Figure 1. Example of a trial from the Roulette Game. Participants view a gamble for 1000 ms. Participants are then shown an amount of money and are asked to choose which space on the wheel they wish to add that amount to. The choice phase is self-paced. After making a choice, participants experience a 500 ms inter-trial interval before viewing the next gamble.

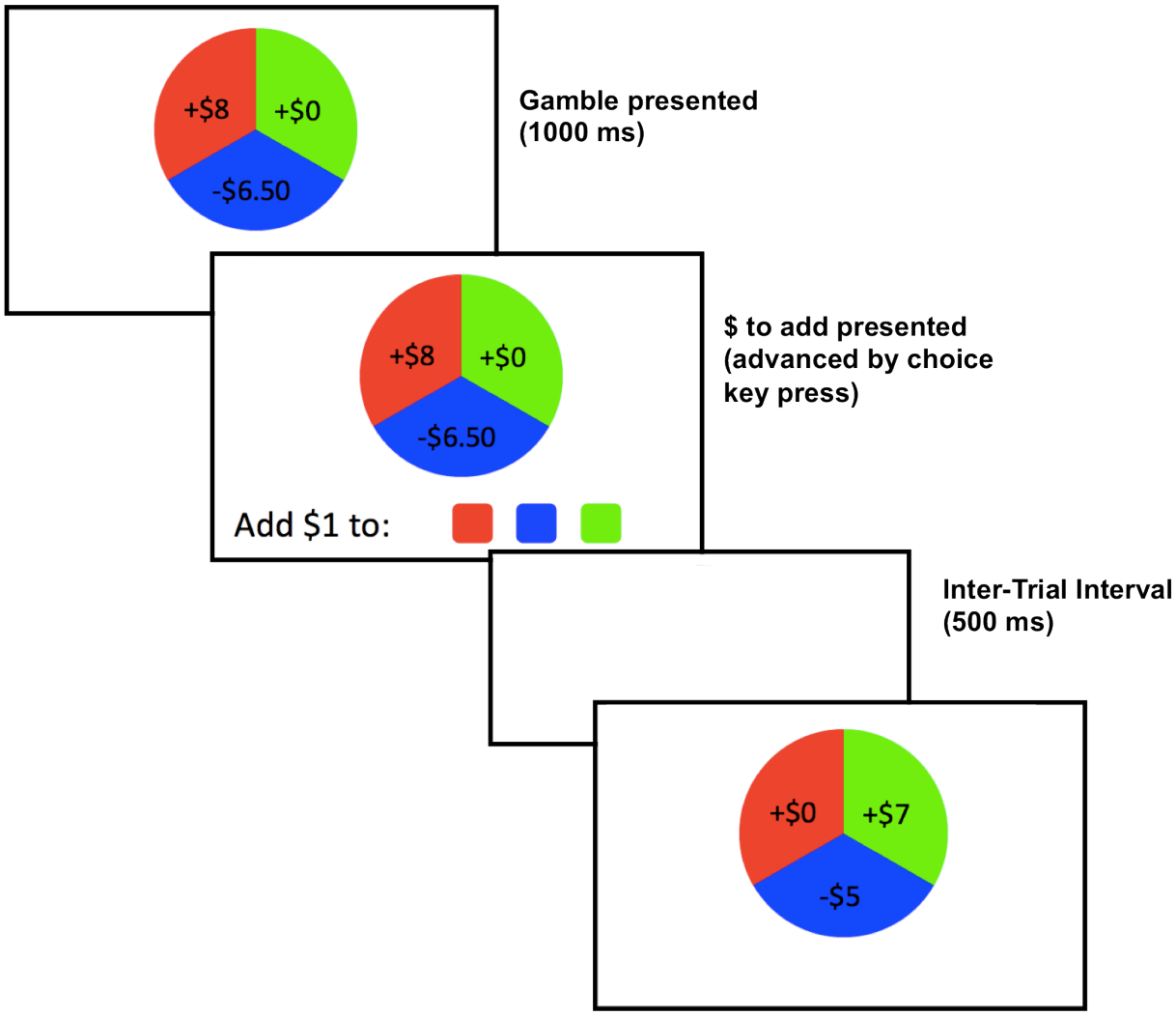
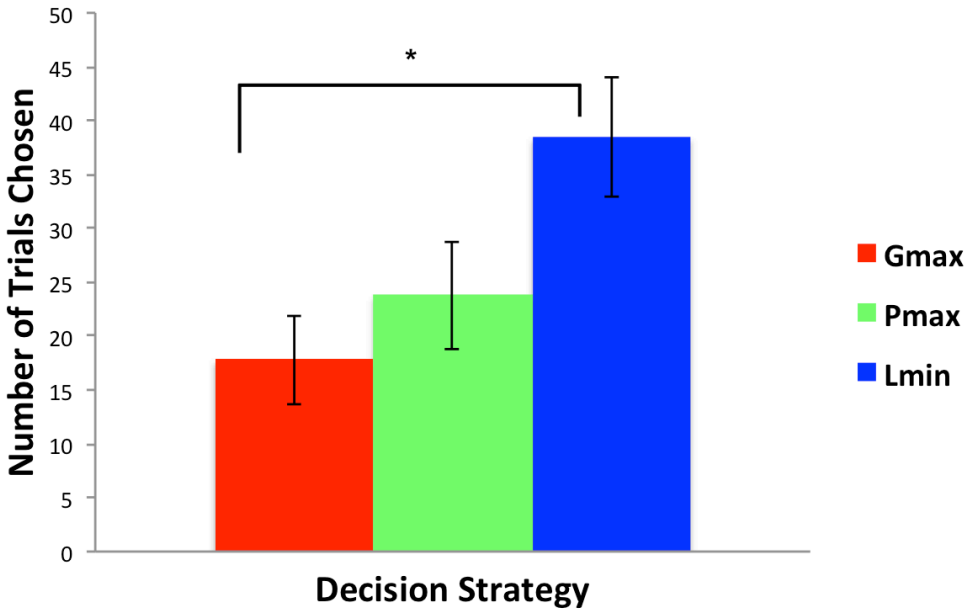


Figure 2. Differences in decision strategy frequency. Participants chose to use the loss-minimizing strategy significantly more often than the gain-maximizing strategy. Probability-maximizing did not differ significantly from either of the other two strategies.



V. General Discussion

The research presented in this dissertation helps to elucidate the neurobiology of adolescent decision-making when faced with the potential for both gain and loss. These studies provide evidence on behavioral, neural and neurochemical levels that adolescents are highly sensitive to potential losses and to changes in value more generally, and that these sensitivities are informed by both developmental and individual difference factors.

These findings suggest a more nuanced interpretation of the existing literature on adolescent reward sensitivity. The sensitivity to expected value observed in this work may underlie adolescent sensitivity to experienced reward, because adolescents may experience rewards as having greater subjective value than adults do. By only investigating tasks employing rewarding stimuli, prior researchers may have been viewing only the gain domain of adolescent sensitivity to value, which in fact extends into both the gain and loss domain.

Furthermore, these findings suggest that adolescents, like adults, are highly sensitive to losses, as predicted by Prospect Theory. Under conditions where adolescents are faced with the potential for both losses and gains, losses appear to "loom larger" in influencing adolescent behavior. Although inconsistent with the stereotype of adolescents as risk-takers because they believe themselves to be invulnerable to negative consequences, this finding is supported by evidence that adolescents do in fact perceive themselves as vulnerable to risk and make judgments about the costs and benefits of risky choices (see Reyna & Farley, 2006, Steinberg, 2007). The current research uses neuroimaging to expand this understanding of how adolescents experience potential negative outcomes, suggesting that neurodevelopmental differences may exist even when adolescents and adults display similar beliefs and behaviors. Future investigation and analysis of adolescent choice patterns during risky decision-making will allow

for more sophisticated modeling of adolescent decision-making. For example, the curvature of the value function can be assessed using the mixed gambles task, which can help to describe more precisely the extent to which potential gains and losses influence choice based on their magnitudes.

Finally, an important avenue of study is the extent to which social and affective conditions may affect the findings observed here. While the present studies were conducted in the "cold" (non-emotional) setting of the laboratory, most of the adolescent risk-taking that concerns researchers from a public health perspective (e.g., substance abuse, risky sexual behavior, reckless driving) occurs in "hot" (emotionally charged) contexts. It is possible that adding affectively arousing components to a choice (e.g. peer influences, heightened mood states) overwhelm the reward-sensitive regions of the adolescent decision-making system and lead to the increased risk-seeking behavior observed in naturalistic settings but not in the current experimental research. Similarly, the divergence between risk-avoidant and loss-sensitive behavior in "cold" settings and unhealthy risk-taking in "hot" ones has implications for the prevention of risky behavior in adolescents. The current data support the notion that adolescents are sufficiently aware of and capable of understanding the potential negative consequences of risk-taking (Steinberg, 2007). Instead, one possible avenue for intervention would be reducing the availability of affectively arousing conditions that may bias the otherwise successful adolescent decision-making system. For example, the presence of peers during a driving task has been shown to heighten risk-taking behavior and to elicit increased activation in reward-related brain regions (Chein et al., 2011, Gardner & Steinberg, 2005), but laws banning the presence of peers in the cars of young drivers have been shown to significantly decrease the fatal crash rates for 15-17 year-olds (McCartt et al., 2010).

These studies provide a valuable first step in developing a more complete picture of adolescent risk-taking. Adolescents are sensitive not only to reward but to value more generally, and individual differences in this sensitivity may play an important role in predicting real-world risk-taking. Furthermore, these studies demonstrate the value of investigating neurodevelopmental changes not only through functional neuroimaging, but also by beginning to characterize differences in neurotransmitter levels. Greater utilization of tasks that capture both gain and loss sensitivity, and of EBR to measure dopamine, will allow for a more nuanced understanding of the mechanisms underlying value representation in the adolescent brain and how that representation shapes real-world behavior. This understanding is an important first step towards the development and implementation of successful interventions and policies to prevent maladaptive adolescent risk-taking.

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