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Caudate responses to reward anticipation associated with delay discounting behavior in healthy youth



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ABSTRACT

Background: Choices requiring delay of gratification made during adolescence can have significant impact on life trajectory. Willingness to delay gratification can be measured using delay discounting tasks that require a choice between a smaller immediate reward and a larger delayed reward. Individual differences in the subjective value of delayed rewards are associated with risk for development of psychopathology including substance abuse. The neurobiological underpinnings related to these individual differences early in life are not fully understood. Using functional magnetic resonance imaging (fMRI), we tested the hypothesis that individual differences in delay discounting behavior in healthy youth are related to differences in responsiveness to potential reward.

Method: Nineteen 10–14 year-olds performed a monetary incentive delay task to assess neural sensitivity to potential reward and a questionnaire to measure discounting of future monetary rewards.

Results: Left ventromedial caudate activation during anticipation of potential reward was negatively correlated with delay discounting behavior. There were no regions where brain responses during notification of reward outcome were associated with discounting behavior.

Conclusions: Brain activation during anticipation of potential reward may serve as a marker for individual differences in ability or willingness to delay gratification in healthy youth.

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1. Introduction

Choices between immediate temptations and long-term goals abound in daily life and the ability to delay gratification improves long term outcomes. Understanding what governs adolescents' ability to delay gratification is of particular interest because decisions made during adolescence can have significant impact later in life. For example, choosing to use alcohol or other drugs during adolescence significantly increases risk for developing substance abuse (Grant and Dawson, 1997; Chambers et al., 2003). Furthermore, capacity to delay gratification in early childhood has been linked to adult health and well-being (Berman et al., 2013; Casey et al., 2011; Mischel et al., 2011; Schlam et al., 2012).

For a teenager, the decision to refrain from or use alcohol and other drugs is often a choice between long-term goals such as academic achievement and the short-term expected rewards of drug use. These expected rewards often include not only the pharmacologic effects of getting high or escaping negative affect, but also social approval from peers (Donovan, 2004). In comparison, the subjective value of long-term goals is diminished because future rewards are "discounted" as a function of their delay and expected probability of occurring. Individual differences in delay discounting are associated with obesity (Weller et al., 2008), substance abuse (Kirby et al., 1999), and other psychopathology (Alessi and Petry, 2003; Crean et al., 2000), suggesting that discounting may be a trans-disease process with relevance for many important public health challenges (Bickel et al., 2012).

Discounting of future rewards can be measured using tasks that ask a person to choose between a smaller immediate and a larger delayed reward. The comparison of each reward's subjective value requires accounting for both its magnitude and the delay to delivery (Ainslie, 1975). A number of fMRI studies have implicated ventral striatum, ventromedial prefrontal cortex, and cingulate cortex in tasks involving delay discounting choices (for review, see: Peters and Büchel, 2011), brain regions in which abnormalities have been reported across several psychiatric diagnoses including depression, anxiety, and substance abuse (Blackford and Pine, 2012; Koob and Volkow, 2009; Price and Drevets, 2009; Shin and Liberzon, 2009).

Studies in healthy adults have found some aspects of impulsivity to be associated with increased responsiveness to reward. For example, greater discounting of delayed rewards was positively correlated with brain activation in ventral striatum during receipt of reward in adults (Hariri et al., 2006), suggesting that individuals with very strong responsiveness to reward may be unable to resist the urge to pursue an immediately available reward. This interpretation is consistent with models of impulsivity that emphasize that strong approach behavior may outweigh potential consequences or lost opportunities for future rewards (Buckholz et al., 2010). Conflicting evidence, however, supports the hypothesis that increased impulsivity is associated instead with decreased ventral striatal function. Imaging studies have found decreased ventral striatal activation during reward tasks in adults and youth with ADHD in comparison to healthy controls with activation inversely

correlated with impulsivity (Scheres et al., 2007; Strohle et al., 2008). In studies of brain responses during discounting tasks in healthy adults, individuals who were more impulsive in terms of their intertemporal choice behavior showed lower response to larger delayed rewards relative to smaller sooner rewards in comparison to those who were less impulsive (Ballard and Knutson, 2009; Samanez-Larkin et al., 2011). Further support for the hypothesis that increased impulsivity may be related to diminished striatal function can be found in a rodent model where lesions in ventral striatum result in increased impulsivity (Cardinal et al., 2001). Improved understanding of the brain circuitry related to impulsive choice is needed to inform efforts to improve prevention and treatment of disorders related to impulse control such as substance abuse.

Given the heightened impulsivity of children and adolescents relative to adults (Spear, 2000; Steinberg et al., 2009) and differences in relative maturity of striatal and prefrontal circuitry (Casey and Jones, 2010; Somerville and Casey, 2010), there may be unique associations between neural response to reward and discounting behavior in this population that are altered in the course of development. In this study, we aimed to address the question of how individual differences in brain response to reward are related to delay discounting behavior in healthy youth.

We used a monetary incentive delay (MID) task as a probe for several reasons. First, the MID task does not require a choice between rewards, and thus provides an estimate of general reward responsiveness. Second, the MID task allows for a distinction between responses to anticipation of potential reward and notification of the reward receipt (Knutson and Greer, 2008). In the MID, the reward anticipation phase involves cueing of a potential reward opportunity and the preparation to take action to potentially obtain the reward. This anticipation of potential rewards may be more closely related to intertemporal choice behavior than responses to received rewards given that temporal choice decisions involve future potential rewards. Finally, by varying the magnitude of potential reward it is possible to separately model responses to presence or absence of reward and responses to the relative magnitude of rewards. An additional strength of the MID task is that striatal responses to reward cues show high reliability across time (Wu et al., 2014). We note that the present approach differs from studies in which scanning is performed during a temporal choice task. While such paradigms provide extremely useful information, they are difficult to interpret in terms of basic reward sensitivity because the anticipated rewards are already subject to temporal discounting, and the reward receipt often does not occur until weeks after the scanning session is completed.

We were most interested in individual differences in anticipatory reward responses because sensitivity to the magnitude of the reward may be particularly important for the ability to delay gratification. For instance, the subjective value of an extra \$50 delayed by 4 weeks will depend upon whether this option is being compared to a small immediate reward (e.g. \$10) or a very large one (e.g. \$1000). Previous work has demonstrated a reliable increase in activation in ventral striatum with increasing reward magnitude that correlates with self-reported

positive affect (Knutson and Greer, 2008) and work in humans and other animal models has shown that striatal activation and dopamine signaling are important for overcoming costs such as delay to reward receipt (Bjork et al., 2004; Wade et al., 2000; Wardle et al., 2011). In a recent study of brain responses during an intertemporal choice task, ventral striatal activation was shown to vary inversely with increasing discounting of future rewards (Ripke et al., 2012). The current study extends these results by examining the relationship of differing response to reward magnitude during a non-choice task with discounting behavior in healthy youth.

We tested the hypothesis that brain activation during anticipation and notification of potential reward would be associated with differences in discounting, and the hypothesis that differential responsiveness to increasing reward magnitude would be more strongly associated with individual differences in discounting behavior.

2. Methods

2.1. Participants

Twenty-eight healthy children aged 10–14 years participated in the current study. Exclusion criteria included: any current or past psychiatric or medical illnesses; meeting any DSM-IV diagnostic criteria for Attention-Deficit Hyperactivity Disorder; current or past use of psychoactive medications, current use of prescription medications, or using over-the-counter medication more than four times in the last month; lifetime use of alcohol, tobacco, or cannabis greater than five times, any use of other drugs; conditions that preclude MRI scanning (e.g. implanted electrical devices or metals, claustrophobia, or pregnancy); history of head injury with loss of consciousness; history of seizures; IQ less than 80 measured using Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999); and left-handedness. Screening for medical and psychiatric illness was completed using a semi-structured interview (KSADS, Kaufman et al., 1996) performed by trained lab personnel and reviewed by a child psychiatrist (MMB). Data from 9 participants were excluded due to: excessive motion during the scan ($n=4$), incidental findings on MRI ($n=2$), poor task performance ($n=1$), responses on the temporal discounting task being more than two standard deviations away from the mean of the rest of the sample ($n=1$), and not completing the MID task ($n=1$), resulting in a final sample of 19 (12 males, 7 females, mean age 12, $SD=1.4$). The study protocol was approved by the Institutional Review Board at Vanderbilt University and conformed to principles of the World Medical Association's Declaration of Helsinki. Participants provided assent and a parent provided informed consent prior to participation.

2.2. Behavioral measure of temporal discounting

Participants completed a computerized version of the Monetary Choice Questionnaire (MCQ; Fig. 1a; Kirby, 2009) implemented in E-Prime outside the fMRI scanner on a separate visit to the lab (mean time between study visits = 22.4 days). The MCQ is a measure of delay discounting

consisting of 27 choices between a smaller immediate reward (\$11–80) and a larger reward (\$25–85) delayed by 7–186 days. The procedure for estimating a participant's discounting function (k) using this task is detailed in an early study by Kirby et al. (1999). Because of the limited number of trials in this measure of discounting, estimation of k with this procedure results in selection of one of 10 possible values making it somewhat limited compared to other procedures (Kowal et al., 2007; Richards et al., 1999; Yi et al., 2010). For the primary measure of discounting behavior in this study, we used the proportion of choices in which the smaller sooner reward was selected. An advantage of the proportion score over other indices of discounting is that it uses a more straight-forward calculation that does not make assumptions about the hyperbolic shape of the discount function. Nevertheless, the proportion score was highly correlated with the slope of the hyperbolic discounting function, k , ($r=.92$, $p<.001$). Although it is not the most common measure of discounting, other groups have used proportion scores to estimate preference for immediate over delayed reward (Magen et al., 2008; Ersner-Hershfield et al., 2009).

2.3. Measurement of brain activation

As a probe for individual differences in responsiveness to reward, we used an event-related monetary incentive delay (MID) task (Fig. 1b; Knutson et al., 2000). Participants pressed a button as fast as possible in response to a target stimulus to earn monetary rewards. Specific cues indicated the value of a potential reward for each trial (\$0, \$1, or \$5). After the cue, which lasted 2500 ms, participants waited 2000–2500 ms for a target to appear and attempted to press a button while the target was visible. After a brief delay (946–2855 ms), a feedback screen lasting 2500 ms indicated the outcome (“Hit!” or “Miss!”) for each trial. Target duration (which varied from 170 to 400 ms in this sample) was determined during the session based on individual performance to keep success rate at 60%. If success rate dropped below this target percentage, 30 ms were added to target duration. If success rate rose above the target percentage, 30 ms were subtracted from the target duration. Participants completed 120 trials over four runs, each lasting six minutes, for a total of 48 trials with each gain cue (\$5 and \$1) and 24 trials with \$0 cues. This version of the task showed the dollar values available for each trial rather than an ambiguous cue to eliminate any learning effects (Samanez-Larkin et al., 2007; Wu et al., 2014). We included only gain (and not loss) trials in the task to increase the total number of trials per condition for greater statistical power. Participants were told that they would receive the money they won from the MID run with the greatest earnings (range: \$36–43) in addition to compensation for their time.

Images were acquired using a 3 T Phillips Intera Achieva MRI scanner (Phillips Medical Systems, Andover, MA). The experimental task was projected from behind on a mirror mounted on the head coil. Functional runs consisted of 168 dynamics collected over 28 slices, 4.5 mm thick with .45 mm gap, FOV = 240 mm × 240 mm, flip angle = 79, TR 2 s, and TE 35 ms.

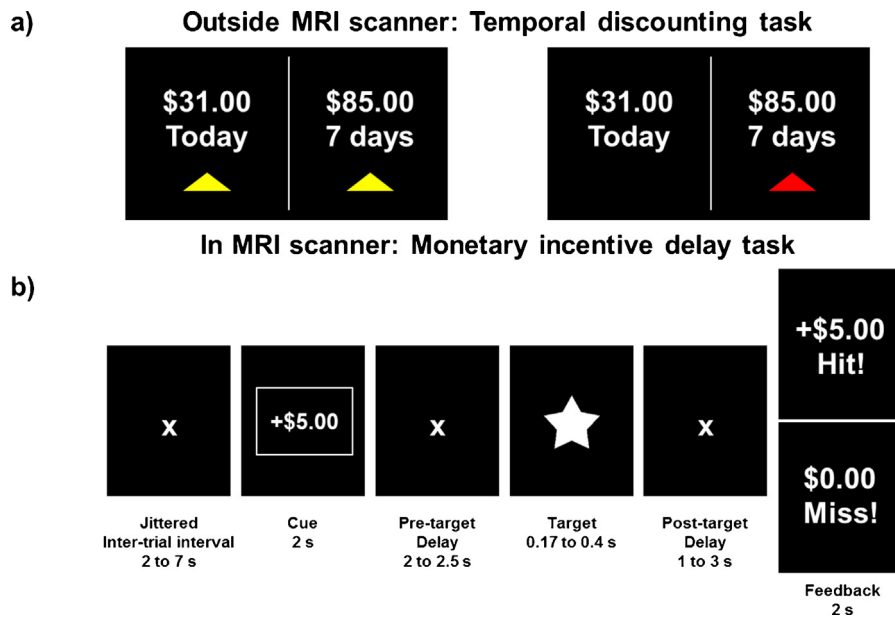


Fig. 1. Task description. (a) Participants completed a computerized version of the Monetary Choice Questionnaire (MCQ) outside the MRI scanner. This task consists of 27 choices between a smaller immediate and a larger delayed reward shown on a screen with yellow arrows under each option. After making a selection by pressing a button, the yellow arrows disappear and a red arrow appears, indicating the choice. Participants were told that there are no right answers and they should choose the option they would prefer to have. There was no time limit for this task. (b) During a separate visit to the lab, participants completed an MRI scanning session that included a Monetary Incentive Delay (MID) task in which they had opportunities to win \$0, \$1, or \$5 by pressing a button while a target appeared on the screen. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

2.4. Statistical analysis

Imaging data were analyzed using SPM8 (Wellcome Department of Cognitive Neuroscience, London, UK). During preprocessing, images were slice time corrected, realigned to the mean image, normalized to the SPM EPI template, and smoothed using an 8 mm full width half maximum Gaussian smoothing kernel. Motion during a single run for one participant and during two runs for another participant prevented the inclusion of these runs in the analysis. The data from the remaining runs for these 2 subjects were included and weighted accordingly (multiplied by a factor of $4/n$, where n is the number of runs of useable data).

A general linear model (GLM) was estimated using the following 10 regressors: 3 cue conditions (\$0, \$1, \$5), 1 regressor for target, 3 hit conditions (\$0, \$1, \$5), and 3 miss conditions (\$0, \$1, \$5). We first analyzed brain response to anticipation of potential reward and outcome notification. For anticipation, we conducted a repeated measures ANOVA with a single within-subject factor (magnitude) and tested for a main effect of magnitude. For notification, we conducted a repeated measures ANOVA with 2 within-subject factors (outcome and magnitude) and tested for a main effect of outcome. The observed pattern of task-based activation is similar to other reports using the MID task (Fig. 2). We then conducted a regression analysis with preference for immediate reward as a covariate within the task-relevant regions. We used this approach to ensure that we analyzed activation in task-relevant brain regions and to reduce the number of comparisons. To control for type 1 error, we used Monte Carlo simulation executed

in AlphaSim (<http://afni.nimh.nih.gov/afni/>) to determine a cluster threshold for family wise error correction to $p < .05$. Using a voxel-wise threshold of $p < .001$ and accounting for the intrinsic smoothness of the data, the cluster threshold was 80 voxels for the anticipation mask which included bilateral striatum, cingulate, brainstem, cerebellum, insula, visual, and motor cortex (59,904 voxels) and 70 voxels for the outcome mask which included bilateral striatum, medial prefrontal cortex, posterior cingulate, thalamus, medial temporal lobe, anterior parietal lobe, and precuneus (49,871 voxels, see Fig. 2). In a post hoc analysis to ensure that the effect was not driven by outliers, we extracted parameter estimates from the cluster where activation was significantly correlated with discounting behavior and display the scatterplot in Fig. 3b. For further analysis of magnitude effects, we performed post hoc tests of the correlation between discounting behavior and BOLD signal for the contrasts of \$5 vs. \$0, \$5 vs. \$1, and \$1 vs. \$0, using Bonferroni-corrected statistics.

Given that brain maturation occurs non-linearly and asymmetrically in VS and PFC, we expected that age might affect the results even in this rather narrow range of 4 years. Thus, age was entered into the GLM as an additional covariate to test for effects on the correlation of discounting behavior with brain activation during the MID task.

All statistical analyses outside SPM used SPSS 20. Normality was assessed using a Kolmogorov–Smirnov test. Descriptive statistics were used to summarize demographic data and means and standard deviations are reported. Pearson correlations were used to estimate the strength of the association between continuous variables. A paired t -test was used to compare reaction

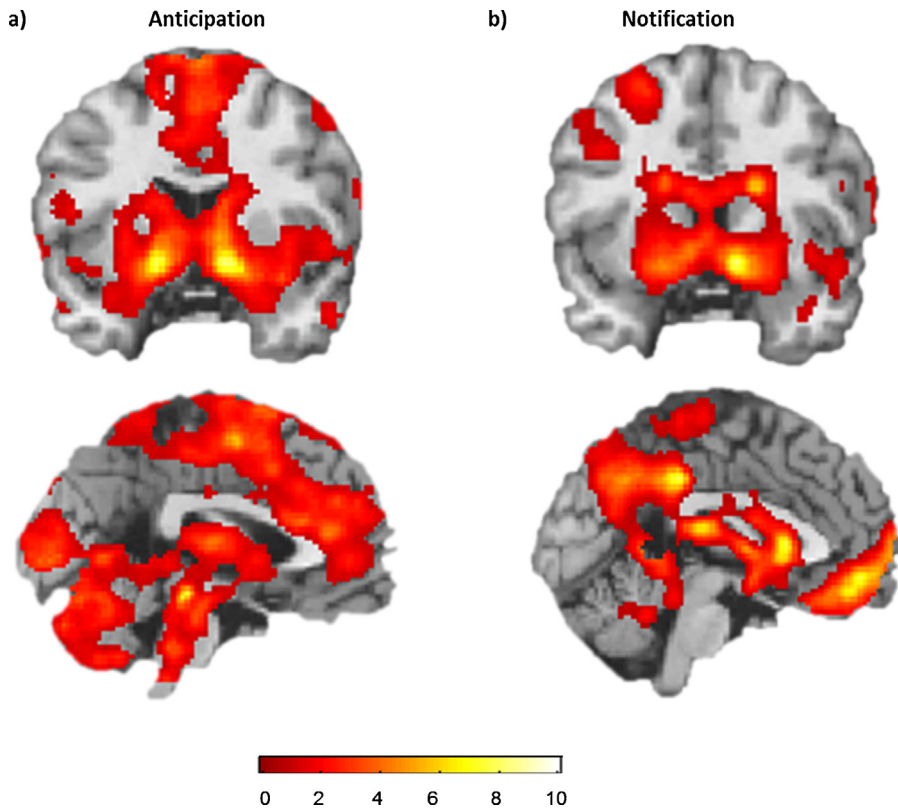


Fig. 2. Task based activation during monetary incentive delay task. Repeated measures ANOVA (FWE corrected $p < .05$) was used to identify task-related brain activation. (a) During anticipation of potential reward, the main effect of reward magnitude resulted in statistically significant activation of 59,904 voxels encompassing bilateral striatum, cingulate, brainstem, cerebellum, insula, visual, and motor cortex. (b) During notification of reward, the main effect of outcome resulted in statistically significant activation of 49,871 voxels encompassing bilateral striatum, medial prefrontal cortex, posterior cingulate, thalamus, medial temporal lobe, anterior parietal lobe, and precuneus. Coronal sections are located at $y = 8$ mm and sagittal sections are located at $x = 0$ mm. These clusters of task-based activation were used as regions of interest for the regression of discounting behavior.

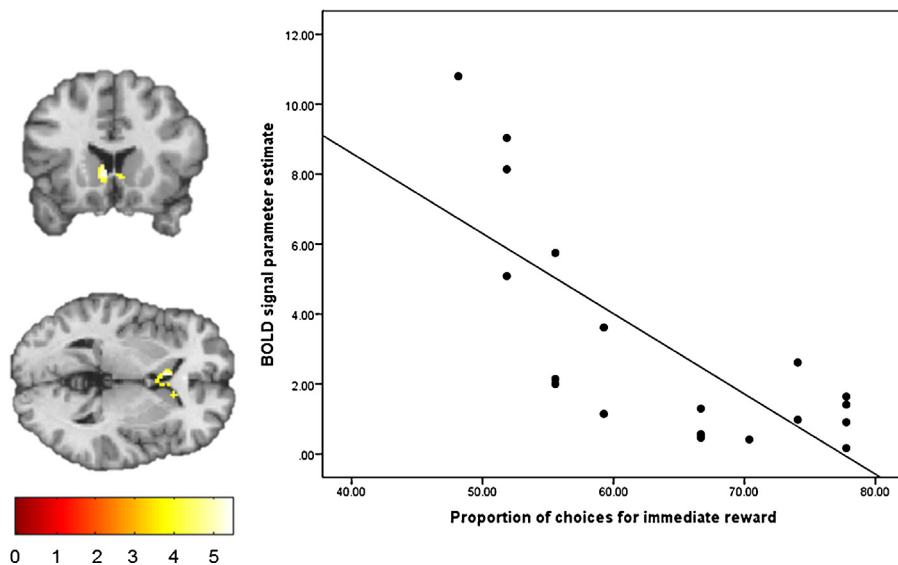


Fig. 3. BOLD signal change during anticipation of reward in left ventromedial caudate correlates with discounting behavior. (a) Regression of preference for immediate reward with BOLD signal change in response to potential reward cues versus no reward cues identified a single cluster in left ventromedial caudate of 155 voxels with peak $t = 5.49$ located at $x = -4$, $y = 18$, $z = 2$, where the relationship was statistically significant (FWE corrected $p < .05$). (b) BOLD signal parameter estimates for each participant were extracted from this cluster and plotted against discounting behavior.

times for immediate versus delayed choice on the MCQ which was completed outside the scanner. For analysis of effect of magnitude on response times, an ANOVA with repeated measures using a Huynh–Feldt correction was conducted with Bonferroni-corrected post hoc analysis.

3. Results

3.1. Temporal discounting and MID task behavior

Preference for immediate reward was normally distributed across this sample of 19 healthy 10–14 year-olds. ($Z = .71, p = .70$). The mean percentage of selections for the immediate reward on the monetary choice questionnaire was 64.1% ($SD \pm 10.5$), corresponding with a discount rate, $k = .03$ ($SD \pm .02$). Age was not correlated with preference for delayed reward ($r = -.08, p = .74$). Mean reaction time across all decisions made during the discounting task (performed outside the scanner) was 3283 ms ($SD \pm 1064$). Reaction time was similar for trials where the immediate reward was chosen compared to trials where the larger delayed reward was chosen ($t_{18} = -.65, p = .52$). In the MID task, there was a statistically significant effect of the magnitude of the reward on response times ($F_{(2,1457)} = 9.022, p < .001$), with \$5 trials having shorter mean response times than \$0 trials and \$5 trials having shorter mean response times than \$1 trials ($p < .017$). Across the sample, accuracy was not statistically different from our target rate of 60% ($t_{18} = -1.2, p = .25$), indicating that our adaptive target timing algorithm was effective.

3.2. Relationship between brain activation during anticipation of reward and discounting behavior

Within the region that showed a main effect for anticipation of gain (Fig. 2a), preference for immediate reward was significantly correlated with BOLD activation in left ventromedial caudate (155 voxels with peak location $-4, 18, 2, t = 5.49, p < .05$ corrected, Fig. 3a). Increased preference for immediate reward on the monetary choice questionnaire (MCQ) was associated with lower BOLD signal in left ventromedial caudate during anticipation of reward (Fig. 3b). Conversely, individuals with greater activation in this region during anticipation of potential reward were more likely to choose the larger delayed reward. There were no brain regions within our mask where preference for immediate reward was associated with statistically significantly greater brain activation during anticipation of reward.

The modulation of reward magnitude (\$5 vs. \$1 vs. \$0) in the MID task allows for examination of differences in brain activation in response to differing reward magnitudes. We considered whether the relationship between discounting behavior and BOLD signal was driven by response to any reward (\$5 and \$1 trials) compared to no reward (zero trials) or by an increased activation in response to larger reward (\$5) compared to smaller reward (\$1) trials. We hypothesized that individuals with a greater increase in BOLD signal to \$5 versus \$1 cues would be more likely to prefer to wait for the larger reward. To examine this

hypothesis, we tested for a statistically significant relationship between discounting behavior and BOLD signal for each of the following contrasts in SPM: \$5 vs. \$0, \$1 vs. \$0, and \$5 vs. \$1. The relationship was statistically significant for only the \$5 vs. \$0 contrast (119 voxels with peak $t = 4.42$ located at $-4, 16, 2$, FWE corrected $p < .017$).

Age was not associated with discounting behavior in this sample. However, given the importance of a potential relationship between age and brain activation in striatum, we considered whether the observed association between discounting and brain activation was affected by age. When age was entered into the regression model as a covariate, there was no change in the activation pattern or observed relationship with discounting behavior.

3.3. Relationship between brain activation during notification of reward and discounting behavior

An advantage of the MID task is the ability to distinguish anticipation of reward opportunity from notification of reward (Knutson and Greer, 2008). Work in adults demonstrating a positive relationship between preference for immediate reward and brain activation in ventral striatum used a reward notification task (Hariri et al., 2006). We therefore expected that there may be a different relationship between discounting behavior and brain responses during the anticipation and notification phases of the MID task. There were, however, no brain regions within our mask where temporal discounting behavior was statistically significantly associated with brain activation during notification of reward receipt.

4. Discussion

The current study sought to clarify the relationship between the ability to delay gratification and aspects of reward responsiveness in healthy youth. Individual differences in delay discounting behavior were associated with the level of activation in left ventromedial caudate during anticipation of potential reward. Youth who preferred a smaller immediate reward had lower responses in this region. Given existing models that conceptualize ventral striatal responses as reflecting immediate reward sensitivity (McClure et al., 2004) and developmental data that emphasizes the link between ventral striatum activation and approach/go behavior (Casey and Jones, 2010; Ernst et al., 2006), it may seem counter-intuitive that youth who are more willing to wait for a later reward would have increased striatal responses. However, it may prove useful to consider the responses in relation to the evaluation of the reward. Geier et al. (2010) provide evidence that difference in striatal responses can distinctly arise during reward evaluation versus other phases of reward tasks. In that study, young adults showed significantly greater ventral striatal responses during reward evaluation, even though teenagers showed greater responses during a subsequent motor preparation phase. It is possible that this maturational difference is similarly reflected here at the individual differences level, with the striatal responses explicitly reflecting a more “mature” reward evaluation process that helps optimize long-term outcomes (an effect

that appears to increase across adulthood e.g., [Samanez-Larkin et al., 2011](#)). Within this context, increased striatal responsiveness to potential reward may reflect a reward evaluation that could lead to a greater ability to make choices that maximize potential future rewards even when that requires waiting for the larger reward. Of course, the decision making process is complex and encompasses more than just striatal response, likely reflecting the interaction between approach and inhibition signals and a summation of these at the neural level. Further study of these interactions using tasks that can distinguish the role of prefrontal as well as striatal responses is needed.

Unfortunately, the MID task as applied here does not allow us to disentangle the reward evaluation and reward preparation phase, and similar issues of disentanglement arise in other studies. Nevertheless, it is clear that psychiatric conditions associated with higher impulsivity are often marked by decreased activation in the ventral striatum in response to reward-related stimuli. For example, decreased ventral striatal activation during reward anticipation has been seen in ADHD ([Scheres et al., 2007](#); [Strohle et al., 2008](#)) and alcohol use disorder ([Beck et al., 2009](#)), both of which are associated with heightened impulsivity, including steeper temporal discounting ([MacKillop et al., 2011](#); [Scheres et al., 2010](#); [Jarmolowicz et al., 2012](#)).

Ventral striatum, typically defined as the portion of striatum that is ventral to a line intersecting a point at the ventral corner of the lateral ventricle with a point at the termination of the internal capsule ([Mawlawi et al., 2001](#)), has been a focus of a great deal of recent work exploring developmental aspects of reward processing and the role of location in vulnerability for substance abuse. The precise location of the region where we found that activation in response to reward anticipation was associated with discounting behavior is too dorsal to be formally called “ventral striatum” and corresponds instead to a central region of the striatum which receives its primary projections from association cortices including ventromedial prefrontal cortex (vmPFC) and orbitofrontal cortex (OFC, [Haber and Knutson, 2011](#)). Activation in vmPFC is consistently linked to computation of value signals across temporal delays and commodities ([Ballard and Knutson, 2009](#); [Kable and Glimcher, 2007](#); [McClure et al., 2004](#); [Samanez-Larkin et al., 2011](#)) and anatomical studies show that this cortical region projects to the most medial portion of the caudate nearest the ventricle ([Haber and Knutson, 2011](#)). Neighboring portions of the caudate receive projections from OFC, an area that plays a critical role in relative reward processing ([Tremblay and Schultz, 1999](#)) and nuanced features of reward processing ([O’Doherty and Dolan, 2006](#)), including a sensitivity to temporal factors ([Zald, 2009](#)). Input from these regions is certainly relevant for maximizing reward and the current study suggests that individual variability in responses to reward may be linked to this valuation process. Given that activation measured using fMRI has been suggested to heavily reflect glutamatergic input to a brain region ([Logothetis and Wandell, 2004](#)) the activation observed in the current study may reflect increased input from these association cortices that promote better ability to delay gratification and wait for a larger later reward. Interestingly, a recent study found

that at the individual subject level, the location of the peak activation during a temporal discounting task shifted from ventral to dorsal with increasing self-reported impulsivity ([Onoda et al., 2011](#)).

Another possible interpretation of the primary finding in the current study is related to overcoming costs to obtain reward. Dopamine signaling is important for overcoming costs such as effort expenditure and delay to reward receipt ([Bjork et al., 2004](#); [Treadway et al., 2012](#); [Wade et al., 2000](#); [Wardle et al., 2011](#)). While striatal activation is not a proxy for dopamine signaling, the responsivity of this ventral caudate region to potential rewards may scale with a willingness to overcome costs in order to maximize long term attainment of rewards. Such an enhanced sensitivity would allow individuals to remain focused on long-term goals in the face of immediate temptation.

We hypothesized that sensitivity to increasing reward magnitude in the anticipation reward phase would be associated with stronger associations with discounting behavior, however in the current sample, increased sensitivity to individual reward magnitudes did not appear to be associated with individual differences in discounting behavior in healthy adolescents. Interestingly, a recent study found that for adolescents, affective ratings do not vary with reward magnitude ([Jarcho et al., 2012](#)) in contrast to studies in adults where both affective ratings and brain activation increase with increasing reward magnitude ([Knutson and Greer, 2008](#)). While the present data are certainly consistent with [Jarcho et al. \(2012\)](#), we must note that the \$5 vs. \$0 contrast showed a significant contrast with discounting while the \$1 vs. 0 did not reach statistical significance. This suggests that some degree of sensitivity to reward magnitude may contribute to the observed association, but that its contribution is at best relatively modest. The small sample size and the limited range of potential reward values in the present study may have been insufficient to capture a specific impact of reward magnitude sensitivity. Visual inspection of the pattern of mean percent signal change for each individual participant suggests that some individuals did show an approximately linear increase in mean signal with increasing reward magnitude, while others showed a significant increase from \$0 to \$1, then no change from \$1 to \$5, and others showed no difference between \$0 and \$1, but an increase from \$1 to \$5. Further examination of individual differences in sensitivity thresholds to varied reward magnitude may prove useful in understanding differences in decision making and may shed light on neurobiological vulnerability for psychiatric illness.

It should be noted that while the MID task has been widely used as a measure of brain response to opportunity for reward, it has produced findings in developmental contexts that contradict those of other tasks. During anticipation of reward, adolescents sometimes show lower activation in the striatum during anticipation of reward with the MID task ([Bjork et al., 2004, 2010](#)), but increased activation relative to adults during reward receipt using other paradigms (e.g. [Ernst et al., 2005](#); [Galvan et al., 2006](#); [Geier et al., 2010](#); [Van Leijenhorst et al., 2010](#)). It is possible, therefore, that the finding observed here is unique to the monetary incentive delay task and further investigation of

the role of specific task features in eliciting particular brain activation patterns is needed. In addition, the MID task used in the current study included only gain trials which may affect the salience of positive cues given that the only comparison is to zero cues rather than loss cues.

Recent reviews of the developmental reward literature propose several hypotheses to explain the differences in findings in different tasks (Jarcho et al., 2012; Richards et al., 2013; Ripke et al., 2012). Differences between tasks in the predictability of reward magnitudes on each trial may help explain contradictory findings (Ripke et al., 2012). Unlike the MID task where potential reward outcome values and cue are linked and made explicit to the participant, in other tasks reward outcomes are variable and the cue-magnitude link is not explicit. In the MID task the value of the reward is known at the time of the action. In these types of tasks, adolescents consistently show lower activation than adults. In tasks where the outcome is variable or not pre-determined, adolescents show greater striatal activation than adults (for further review of the effect of task differences in developmental response to rewards, see Richards et al., 2013). Studies that directly compare within-subject differences in responses to these two different task types would help to clarify some of the discrepancies in the literature regarding developmental aspects of reward response.

We found no statistically significant relationship between delay discounting behavior and brain activation during notification of reward outcome. This finding differs from previous work in healthy adults where greater preference for immediate reward was associated with greater striatal activation during notification of reward outcome in a guessing task (Hariri et al., 2006). We considered whether the relatively small sample size in the current study may have limited the power to detect a relationship between discounting behavior and brain activations in response to notification of reward outcome (given the fewer number of comparisons that can be made for outcome relative to anticipation). To address this possibility, we lowered the statistical threshold and still found no relationship between discounting behavior and brain activations during notification of reward outcome. Differences in the age of the samples and in the tasks used to elicit reward related brain activation may explain the discrepancy in this finding. Given the known relationships between age and discounting behavior (Steinberg et al., 2009) and age and brain activation during reward processing (Casey and Jones, 2010; Ernst et al., 2006) we included age in the analysis as a covariate to assess for age effects and found no statistically significant relationship between age and discounting behavior or brain activation patterns. The absence of age related differences may be a result of the small size of the sample and narrow age range. The limited age range of the current study and the lack of an adult comparison group do not allow for direct conclusions to be drawn about age effects and may have obscured inferences about how these data relate to previous work in adults. Direct comparison of responses in adolescents and adults using the same paradigm would be necessary to definitively determine whether and how adolescents differ from adults in the relationship of discounting behavior and brain responses to notification of reward outcome.

Adolescents are consistently more likely than children or adults to engage in risky behavior, raising the question of whether they have adequate cognitive capacity to weigh options and make advantageous decisions (Steinberg, 2007). In fact, the ability to weigh the costs of risky decisions has been shown to be similar in adults and adolescents when cognitive control is engaged (Ernst et al., 2011; Ernst and Fudge, 2009; Geier and Luna, 2009; Smith et al., 2011) but in emotionally charged contexts such as those when reward are at stake, greater sensitivity to reward may overwhelm these inhibitory mechanisms resulting in poor decisions (Casey et al., 2011). The current study did not specifically examine brain activation related to these self-control mechanisms which are likely to play a role in discounting behavior (Figner et al., 2010). In addition to differences in activation patterns in particular brain regions, structural and functional connectivity between regions is likely to play a large role in determining individual differences in discounting behavior. Recent studies using diffusion tensor imaging to investigate how individual differences in discounting related to differences in white matter integrity found that increased white matter integrity is associated with less impulsive responding (Christakou et al., 2011; Peper et al., 2012). This finding along with emerging work using transcranial magnetic stimulation of dorsolateral prefrontal cortex to alter discounting behavior (Essex et al., 2012) supports the idea that regulation of reward choice by inhibitory control regions is highly relevant for understanding discounting. Given that development of prefrontal cortex is not yet complete by adolescence, strategies to improve the engagement of top-down cognitive control during reward decisions may be particularly important in this age group (Jarcho et al., 2012).

A potential limitation of the current study is the use of a hypothetical rather than an incentive-compatible discounting task. Several studies have compared responses to hypothetical and real monetary reward conditions (Johnson and Bickel, 2002; Locey et al., 2011; Scheres et al., 2008). When the reward magnitude and duration of delay are similar, behavioral responses do not differ significantly between real and hypothetical tasks. It should be noted, however, that behavior observed during tasks using small rewards (e.g., 5–10 cents) and short delays (30–60 s) does not correlate with larger sums delayed over longer periods for either hypothetical or real conditions (Scheres et al., 2008). In a study of brain activation in response to hypothetical versus real rewards, Kang et al. (2011) found that the same brain regions were activated, but with greater intensity to real versus hypothetical rewards. In the current study, the discounting task was performed outside the scanner. In the MID task performed in the scanner, participants played for real money, thus we do not expect that any differences in hypothetical versus real discounting procedures would alter the observed result.

5. Conclusions

Exploring reward processing and its relationship to decision-making in children and adolescents is particularly important given the increase in risk taking associated with this developmental stage (Spear, 2000). Finding ways to

enhance the appeal of a delayed outcome may be critical for efforts to promote motivation toward long-term goals such as finishing school rather than the immediate temptation to engage in potentially dangerous behavior such as drug and alcohol use. Further study of the interaction between age, discounting behavior, and brain activation during reward paradigms as well as during delay discounting tasks is warranted to inform prevention efforts in youth at-risk for pathology related to poor impulse control. Studies that assess interventions aimed at increasing ability to delay gratification may be especially relevant for promoting healthy development in at-risk populations.

Conflicts of interest

Dr. Cowan reports the following potential conflicts: Within the past 3 years, Dr. Cowan has received publication royalties from Lippincott Williams and Wilkins, consultant income from the Southwest Michigan First Life Science Fund and the University of West Alabama, and research and salary support from Shire Pharmaceuticals and Novo Nordisk for projects not overlapping with this report.

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