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Longitudinal study of striatal activation to reward and loss anticipation from mid-adolescence into late adolescence/early adulthood

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Abstract

Adolescent risk-taking behavior has been associated with age-related changes in striatal activation to incentives. Previous cross-sectional studies have shown both increased and decreased striatal activation to incentives for adolescents compared to adults. The monetary incentive delay (MID) task, designed to assess functional brain activation in anticipation of reward, has been used extensively to examine striatal activation in both adult and adolescent populations. The current study used this task with a longitudinal approach across mid-adolescence and late adolescence/early adulthood. Twenty-two participants (13 male) were studied using the MID task at two time-points, once in mid-adolescence (mean age = 16.11; SD = 1.44) and a second time in late adolescence/early adulthood (mean age = 20.14; SD = .67). Results revealed greater striatal activation with increased age in high- compared to low-incentive contexts (incentive magnitude), for gain as well as for loss trials (incentive valence). Results extend cross-sectional findings and show reduced striatal engagement in adolescence compared to adulthood during preparation for action in an incentive context.

Keywords

Reward; Striatal; Longitudinal; Development; fMRI; Monetary Incentive Delay Task (MID)

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1. Introduction

Adolescence is a time of heightened risk-taking, which in part is attributed to adolescents' sensitivity to rewards shown through both behavioral and brain studies (e.g., Galvan, 2010; Luciana, 2010; Luna et al., 2012, Casey et al., 2008; Ernst et al., 2011). Whether and how this sensitivity changes across adolescence within individuals remains to be better understood. Many excellent recent reviews address developmental changes in adolescent reward processes (e.g., Galvan, 2010; Luciana, 2010; Luna et al., 2012, Casey et al., 2008; Ernst et al., 2011). In brief, some studies find less striatal activation in adolescents than in adults (Bjork, et al., 2004; 2010), supporting the hypothesis of striatal hypo-sensitivity to rewards during adolescence (Blum et al., 1996, 2000; Bjork et al., 2004), while other studies show the reverse (Ernst et al., 2005; Galvan, et al, 2006; Van Leijenhorst, et al., 2010), supporting the hypothesis of adolescent hypersensitivity to rewards (Chambers, Taylor, & Potenza, 2003). Various factors may contribute to these discrepant findings (for reviews see Galvan, 2010; Richards, Plate, Ernst, 2013), such as age at time of testing, type of baseline period used, and/or type of task administered (e.g., capturing incentive-related anticipation of action, or anticipation of outcome). All previous developmental studies have been cross-sectional (Richards et al., 2013), and cross-sectional studies are known to introduce biases into studies of development (e.g., statistical effects brought about by socio-demographic differences between age groups; e.g., Evans & Rooney, 2011, page 202). We conducted the first longitudinal study examining neural responses to a reward paradigm in healthy subjects across adolescence.

To this aim, we selected one of the most commonly-used reward tasks, the monetary incentive delay (MID) task, which was designed to probe striatal function (Knutson, Fong, Bennett, Adams, & Hommer, 2003). This task has four major advantages, relative to other reward-processing tasks. First, it is a simple paradigm, which was designed explicitly to emulate reward tasks used in non-human primates (e.g., Schultz, Apicella, Scarnati, & Ljungberg, 1992). Thus, this task has clear translational value. Second, this is the only task that has been used in more than a single study of reward-related age differences across adolescence in striatal function, and the available cross-sectional findings appear consistent across multiple studies (Bjork, et al., 2004; 2010; Cho et al., 2013). Third, it is a robust task for examining age-related changes as shown by high test-retest reliability in adults (Wu, Samanez-Larkin, Katovich, & Knutson, in press); thus, we can attribute change over time to development across adolescence. Fourth, this paradigm has been carefully designed to equate performance across individuals, such that the task generates similar levels of monetary gain across study participants. Based on previous data using the MID task (e.g., Bjork et al., 2010), we predicted increased striatal activation with age, such that late adolescents/young adults would show higher striatal activation compared to mid-adolescents. In addition, we did not expect to detect age-related changes in how striatal function codes gain vs. no-loss anticipation. Although striatal activation is commonly found to be greater for gain trials than loss trials (e.g., Bjork et al., 2004; 2010; Cho et al., 2013; Guyer et al., 2006; and Knutson et al., 2003), studies with the MID task have not shown an effect of age on these analyses (no valence-by-age interactions; Bjork et al., 2004; 2010;

Guyer et al., 2006). Therefore, we predicted greater activation for gain trials than loss trials, with no influence of age on this effect of valence.

2. Method

2.1. Participants

Twenty-two participants (13 male) were studied at two time points, once in mid-adolescence (Time-1: mean age = 16.11; SD = 1.44; age-range 13.75–18.25), and a second time in late adolescence/early adulthood (Time-2: mean age = 20.14; SD = .67, age range 18.33–20.92). The time interval between sessions averaged 4 years (mean = 4.03 years; SD = 1.26; range = 2.25–6.05 years). Participants were recruited from a longitudinal study of temperament and affect regulation (See Fox et al., 2001; and Henderson et al., 2004 for demographic details of cohort). A subset of the data presented here at Time-1 (mid-adolescence) has already been used in a previous publication (Guyer et al., 2006). Psychiatric diagnoses were assessed at both time points, in mid-adolescence using the Schedule for Affective Disorders and Schizophrenia for School Aged Children–Present and Lifetime Version (KSADS; Kaufman et al., 1997), and in late adolescence/early adulthood using the Structured Clinical Interview for DSM Disorders (SCID; Ventura, et al, 1998). Both measures were administered by experienced clinicians. Six participants met criteria for an Axis I diagnosis (internalizing and/or externalizing disorders [Time-1: 1 comorbid and 2 internalizing; Time-2: 1 comorbid, 3 externalizing, and 1 internalizing). All behavioral and brain activation analyses were conducted with and without participants with diagnoses. Analyses with these participants removed were still significant. Findings with and without these participants are shown in the Results section. The current study received IRB approval from the institutional review board. All participants and their parents provided written informed assent/consent to participate in the study.

2.2. Measures and Tasks

2.2.1. MID task (Knutson, Adams, Fong, & Hommer, 2001)—This task was identical to the MID task used previously in other studies of children and adolescents (e.g., Guyer et al., 2006). The task consisted of two runs of 72 contiguous 6-second trials. Each trial began with the presentation of a cue (presented for 250 ms), followed by a delay period (crosshair fixation point presented for 2000–2500 ms), a response target (presented for 160–260 ms), and lastly a feedback stimulus (1650 ms) indicating gain, loss, or no change, and the current cumulative dollar amount (see Figure 1). Participants were required to press a button as soon as a target appeared. Cues included 4 categories, 1) circle cues (64 trials), indicating potential monetary gain (reward trials); 2) square cues (64 trials) indicating potential monetary loss (punishment trials); 3) 16 neutral trials (triangle cues); and 4) 48 “surprise” trials. Magnitude of incentive values was indicated by horizontal lines inside the circles and squares: one line for $0.20 (32 trials), two lines for $1.00 (32 trials), and three lines for $5.00 (32 trials). Two other types of trials, 16 neutral trials (triangle cues), and 48 “surprise” trials were also included. However, these trials were not analyzed because of their ambiguous nature (for example, neutral trials could be experienced as positive as a no-loss trial, or negative as a no-gain trial). The order of trials was fully randomized within each run. Participants were informed that they would receive the earned cumulative dollar

amount. Participants completed a practice block (72 trials) at the start of the scan, which served two purposes. First, it minimized learning effects on performance during scanning. Second, it provided an estimate of a participant's performance, which was used to set the target duration time and thus the difficulty level of run 1 of the actual task (to approximate ~66% accuracy rate in run 1). Five levels of difficulty were available, based on the target duration: 1 [easiest] = target duration range of 233–333 ms, 2 = 216–316, 3 = 200–300, 4 = 183–283, 5 [most difficult] = 166–266). Performance on run 1 was then used to set the difficulty level (1–5) for run 2 (approximating a 66% accuracy rate in run 2). This procedure was applied so that all participants experienced roughly the same level of success across the task. Participants received the total dollar amount accumulated during the task (mean = $38.12, SD = 20.14) and this gain was added to the compensation for study participation.

2.2.2. Post-Task Debriefing—A brief post-task questionnaire was administered. Participants were asked to rate each picture (MID cue image) according to how much they liked it on a scale from −5 to 5, with −5 indicating that they disliked it very much, 0 indicating a neutral rating, and 5 indicating that they liked it very much.

2.3. Data Analyses

2.3.1. Behavioral data analysis—Behavioral task performance analyses consisted of three separate 2(Age: mid-adolescence vs. late adolescence/early adulthood) × 3(Incentive Salience: high, medium, and low) × 2(Valence: gain vs. loss) repeated-measures ANOVAs for performance accuracy, reaction times (RT), and debriefing. Task difficulty change and time-of-testing were entered as covariates for performance accuracy and RT. Post-task debriefing data were analyzed to capture how attractive participants perceived each MID cue to be.

2.3.2. fMRI data acquisition and analysis—Scanning occurred in two General Electric Signa 3 tesla magnets (Time-1: all data acquired on scanner-A; Time-2: 17 participants tested on scanner-A and 5 participants tested on scanner-B). A Cedrus (SanPedro, CA) Lumina response box recorded behavioral data. MID stimuli were projected onto a screen at the foot of the scanner bed and viewed with mirrors mounted on the headcoil. Head movement was constrained by the use of foam padding. Functional scans were acquired with the following sequence parameters. Each brain volume consisted of 30 interleaved slices 4mm thick acquired in the sagittal plane using a T2*-weighted echo planar sequence with a repetition time (TR) of 2500ms, echo time (TE) of 23ms, and flip angle of 90°. Voxel dimension was 3.75 × 3.75 × 4.0mm. Matrix size was 64 × 64mm, and field of view (FOV) was 24cm. To allow for signal stabilization, four acquisitions were obtained before task onset. A high-resolution structural image was also acquired for each participant using a T1-weighted standardized magnetization prepared spoiled gradient recalled echo sequence: 1241mm slices, TR of 8100ms, TE of 32ms, flip angle of 15°, matrix size of 256 × 256mm, and FOV of 24cm.

Analysis of Functional and Neural Images (AFNI) software was used to analyze fMRI data (Cox, 1996). Standard preprocessing of echo planar data included slice time correction, motion correction, and spatial smoothing with a 6mm full-width half-maximum smoothing

kernel. A despiking algorithm was then applied to the data on a voxel wise basis to smooth out deviations in signal > 2.5 SD from the mean, followed by a band-pass filtering algorithm to smooth cyclical fluctuations in signal (either > 0.011 or < 0.15s) that were not temporally indicative of a hemodynamic response. Each participant's data were converted to percentage signal change using each participant's voxel wise time series mean as a baseline.

Preprocessed time series data for each individual were analyzed by multiple regression (Neter, Kutner, Machtsheim, Wasserman, 1996). The regression model consisted of event-related regressors, six regressors modeling effects attributable to residual motion (using the motion correction factors in the x, y, and z planes and in the yaw, pitch, and roll dimensions), and two regressors modeling baseline and linear trends for each of the two runs. Event-related regressors included cues, signaling trial type (large, medium, and small potential gain; large, medium, and small potential loss; neutral and surprise trials), delay fixation, target, and feedback. The event times began with the onset of the cue, which lasted 250 ms and were modeled as an instantaneous event with the gamma-variate function (Cohen, 1997).

This study focused on within-individual developmental changes in striatal responses to incentives. Because of our a priori hypotheses, we used a region of interest (ROI) approach. Striatal anatomical ROIs were generated using Talairach anatomical boundaries provided by AFNI, to define voxels that fell within each ROI after spatial normalization (Talairach and Tournoux, 1988). Means of β-coefficients across the voxels of each ROI (dorsal caudate, ventral caudate, putamen, globus pallidus, and nucleus accumbens) were then exported separately into SPSS (SPSS, Chicago, IL). Because previous studies have shown developmental difference in activation between high and low incentive values (e.g., Bjork, et al., 2010), and because low motivation to respond provides a cleaner control condition than no motivation to respond (i.e., neutral trials), our main contrasts of interest were high-incentive value vs. low-incentive value in mid-adolescence at Time-1 and late adolescence/early adulthood at Time-2. ROI mean values of percent BOLD signal change, for each participant were then entered into SPSS (SPSS, Chicago, IL) to conduct analyses of age differences across and within regions (repeated-measures ANOVA). Of note, we did not analyze neural activation to the feedback events because we used the original MID task, which did not include a temporal jitter between cue and feedback stimuli, thus making it difficult to isolate feedback-specific neural activation.

2.3.3. Data Analysis—Variance in age at Time-1 (mid-adolescence; SD = 1.44) was noticeably larger than variance in age at Time-2 (late adolescence/early adulthood; SD = .67). This difference was addressed by adding the [Time-2 – Time-1] age gap as a covariate to all analyses.

Time-2 fMRI data were acquired on two different but similar 3T Siemens scanners: 17 participants tested on scanner-A and 5 participants tested on scanner-B. All Time-1 fMRI data were acquired on scanner A. Because Time-2 scanning was done on two scanners, t-tests compared Time-2 data collected on scanner-A with Time-2 data collected on scanner-B, for all regions of interest (ROIs; dorsal caudate, ventral caudate, putamen, globus pallidus, nucleus accumbens) for the high- minus low-incentive value contrasts. Results

revealed no significant differences in mean percent signal change between scanners, thus we included data from both scanners in our analyses. This strategy to test for potential scanner differences is in line with other studies (e.g., Bitter, Mills, Adler, Strakowski, & DelBello [2011]; Schmahl et al. [2006]). Additionally, we added Scanner as a covariate to our brain data ANOVA model.

At both Time-1 and Time-2, practice block performance was used to set the target duration (i.e., difficulty level of task) for all trials in run-1, and, in turn, run-1 performance was used to set the target duration of trials in run-2. Therefore, it is possible that participants played an easier or harder game at Time-2 than Time-1. We compared Time-1 and Time-2 task difficulty level using repeated-measures ANOVA. This analysis revealed greater task difficulty level at Time-2 (mean = 3.65, SD = .99) than Time-1 (mean = 2.68, SD = 1.31), $t(19) = -3.09$, $p = .006$). Thus, task difficulty change (Time-2 task difficulty – Time-1 task difficulty) was entered as a covariate in subsequent behavioral and brain activation analyses.

A-priori t-tests were conducted on all measures (neural and behavioral) to test for sex differences. Since no significant sex differences emerged, sex was not entered as a covariate in subsequent analyses.

A 3-way repeated-measures ANCOVA was used to test the effects of Age (mid-adolescents, late adolescents/young adults), Region (dorsal caudate, ventral caudate, putamen, globus pallidus, nucleus accumbens), and Valence (gain, loss) on BOLD activation to high-incentive vs. low-incentive. Covariates of nuisance included time-of-testing interval, task-difficulty change, scanner, and performance accuracy. We used the high-incentive vs. low-incentive contrast rather than each incentive value compared to neutral (triangle) activation because of the ambiguous nature of the neutral cue. The neutral cue could be experienced as “no gain” (negative valence) or “no loss” (positive valence). The use of “a small gain” to contrast with high gain trials and “a small loss” to contrast with high loss trials provided cleaner comparisons. Furthermore, using the high-incentive vs. low-incentive contrast also added the benefit of sparing us one degree of freedom, and thus more power in the ANOVA model because we did not have to include incentive value as a factor. This method of comparing a high value vs. a low value of incentive or risk is in line with a number of other studies (e.g., Ernst et al., 2005; Jarcho et al., 2012; and Van Leijenhorst et al., 2010). Region was included as a factor to determine regional specificity of developmental patterns within the striatum. To determine whether the effects of Age were specific to striatal regions, or occurred more generally throughout the brain, additional analyses were conducted for two control regions. As in previous work (Guyer et al., 2006), the control regions were the primary visual cortex [Brodmann area (BA) 17] and the primary motor cortex (BA 4), using an ROI approach with the same level of stringency as that used for the striatal analyses. Interactions between Age and ROI (Region) on the high- vs. low-incentive BOLD signal were the effects of primary interest, and only if these effects were significant were post-hoc contrasts conducted.

For completeness, we also present whole-brain analyses. The whole brain statistical threshold was based on a combination of alpha-level ($p<.005$) and cluster-size thresholds

(determined by Monte Carlo simulations; for p<.05, k=588) to yield a cluster-corrected results.

Lastly, we conducted a number of preliminary Pearson correlations to examine whether striatal activation correlated with behavioral data (performance accuracy, RT, and debriefing measure) differently for mid-adolescents than late adolescents/early adulthood.

3. Results

3.1. Behavioral Data

To determine whether performance measures changed with age, two separate 3 (Incentive Value: high, medium, low) × 2 (Valence: gain vs. loss) × 2 (Age: mid-adolescents, late adolescents/young adults) repeated-measures ANOVAs were conducted for performance accuracy and reaction time (RT; for correct trials) with task difficulty change and time-of-testing interval between mid-adolescence and late adolescence/early adulthood added as covariates (see Table 1 for means and SDs for all behavioral variables).

Accuracy results revealed a trend-level main effect of Valence, $F(1,16) = 3.93$, $p = .07$, $\eta^2 = .20$, and a significant Age-by-Valence effect, $F(1,16) = 6.18$, $p = .02$, $\eta^2 = .28$ [effect increased slightly when excluding subjects with clinical diagnoses: $F(1,11) = 7.10$, $p = .02$, $\eta^2 = .39$; see Table 2 for means and SDs]. Main effects of Age and Incentive Value were not significant. Post-hoc analyses (Bonferroni corrected) revealed reduced accuracy on loss trials relative to gain trials only for late adolescents/young adults, $F(1,16) = 7.83$, $p = .01$, $\eta^2 = .33$ (see Figure 2). No difference in accuracy for gain vs. loss was found for mid-adolescents. This suggests that late adolescents/young adults might have been less careful, or more distracted for loss trials than gain trials relative to when they were mid-adolescents. No other main effects or interactions were found to be significant.

Results for RT revealed no significant changes from mid-adolescence to late adolescence/early adulthood. No significant or trend-level main effects or interactions were found for RT (see Table 1).

Additionally, to determine whether subjective values changed with age, a similar repeated-measures ANOVA as above was conducted on a debriefing measure of incentive salience, in which participants rated how much they liked the cues (−5 to +5 Likert scales). Results revealed a main effect of Valence, $F(1,19) = 432.24$, $p < .001$, $\eta^2 = .96$, and a Valence-by-Incentive Value interaction, $F(2,38) = 62.01$, $p < .001$, $\eta^2 = .76$. Bonferroni-corrected contrasts revealed that gain trials were rated as more positive than loss trials and that these differences were greatest for high incentive trials and least for low incentive trials ($p <$ or $= .001$). However, we did not find any significant age effects (see Table 2 for means and SDs).

Lastly, we conducted exploratory Pearson correlations between debriefing data and both performance accuracy and RT (see Table 2). For both mid-adolescence and late adolescence/early adulthood, greater perception of loss (debriefing measure) was associated with decreased performance accuracy (medium loss and small loss, respectively), however, after correcting for multiple comparisons, this effect was no longer significant. No other effects were found.

3.2. fMRI Data

A 5 (Region: dorsal caudate, ventral caudate, putamen, globus pallidus, nucleus accumbens) × 2 (Age: mid-adolescents, late adolescents/young adults) × 2 (Valence: gain, loss) repeated-measures ANOVA was conducted on the high-incentive minus low-incentive contrast. These analyses controlled for individual variability in time-of-testing interval, task-difficulty change, scanner, and performance accuracy differences between mid-adolescents and late adolescents/young adults. Results revealed no main effects of Age, Valence, or Region and no significant three-way interaction, but did reveal a significant two-way interaction of Age-by-Region, $F(4,56) = 2.67$, $p = .04$, $\eta^2 = .16$ [Statistical significance but not effect size on the Age-by-Region effects decreases slightly when excluding participants with clinical diagnoses: $F(4,36) = 2.38$, $p = .07$, $\eta^2 = .21$; see Figure 3]. Since Valence had no significant main or interaction effects, we averaged brain activation across gain and loss trials for post-hoc tests, and examined the Age effect on each region separately. Contrasts revealed greater activation at Time-2 (late adolescents/young adults) than Time-1 (mid-adolescents), but only for the dorsal caudate, $F(1,21) = 4.68$, $p = .04$, $\eta^2 = .18$ (Bonferroni corrected for multiple comparisons). All other regions showed no effects of Age.

Two additional repeated-measures ANCOVAs were conducted on the primary visual cortex (BA 17) and the primary motor cortex (BA 4) to test for general brain changes in mean percentage signal change across Age. Results revealed no Age effects on either region (see Figure 4), suggesting that the increased activation in the dorsal caudate reflected a specific response to reward and loss, rather than a general effect across the brain.

Additionally, we conducted exploratory Pearson correlations analyses between striatal activation and behavioral measures, including performance accuracy, RT, and debriefing measures (see Table 2). For mid-adolescence, nucleus accumbens activation, averaged across gain and loss trials, increased as performance accuracy increased. However, this effect was no longer significant after controlling for multiple comparisons (see Table 2). Nevertheless, to prevent striatal activation differences from being conflated by performance accuracy, i.e., to ensure effects were not due to individual differences in task difficulty, we controlled for performance accuracy within the ANCOVA model (see methods). Additionally, results revealed that mid-adolescents, who experienced losses as being more salient (debriefing measure), showed greater brain activation (averaged across gain and loss trials) for dorsal caudate, ventral caudate, nucleus accumbens, globus pallidus, putamen, and BA4. Interestingly, this pattern of effects was not evident at T2, for late adolescence/early adulthood. However, these effects were no longer significant after controlling for multiple comparisons (putamen and BA4 are trend level, $p < .10$).

Lastly, for completeness, we also conducted a whole-brain analysis on the main (high- vs. low-incentive) contrast. For this analysis, significant results were limited to those surpassing a combination of two criteria. These criteria included a statistical threshold on the activation differences in high- vs. low-incentive ($p < .005$) and a subsequent threshold regarding the extent of the cluster that was beyond the size that could be found randomly 5% of the time ($k=588$). Consistent with previous studies, e.g., Guyer et al. (2006), we found greater striatal activation in high vs. low incentive value at both T1 in mid-adolescents and at T2 in late

adolescents/early adults, averaging across gain and loss trials (see Table 3). In regard to main effects of age, results revealed significant age effects (collapsing across trial valence and incentive value) only in the left precentral gyrus (see Table 3).

4. Discussion

The current study was conducted to clarify age-related changes in striatal activation to incentives by adopting a longitudinal approach rather than the traditional cross-sectional design. Findings support previous studies suggesting increased incentive-related striatal activation from mid-adolescence to late adolescence/early adulthood in the cue-anticipation-for-action stage of the MID task (Bjork, et al., 2004; 2010). Furthermore, results also indicate that this developmental increase in striatal response was similar for reward and punishment conditions. Finally, findings were specific to the dorsal striatum since no age-related change was detected in regions of the ventral striatum, or, more generally, in primary sensory-motor cortical areas.

In recent years, at least 15 published fMRI studies have compared striatal function in adolescents and adults (review, Richards et al., 2013; see page 983 for a table depicting task differences), all using cross-sectional designs. A number of these studies showed increased striatal activation with age (Blum et al., 1996,2000; Bjork et al., 2004), while others showed decreased activation with age (Ernst et al., 2005; Galvan, et al, 2006; Van Leijenhorst, et al., 2010). These discrepancies may be due to differences in task requirements (e.g., the presence or absence of a decision making), or the nature of the incentive anticipation (e.g., incentive-related action anticipation or outcome anticipation). However, since the previous studies all used cross-sectional designs, they are vulnerable to various biases (e.g., statistical effects brought about by socio-demographic differences between age groups) that are minimized using longitudinal designs. We conducted the first longitudinal work examining neural responses to a reward paradigm in healthy subjects across adolescence. To this aim, we used the MID task because it is a simple paradigm that requires relatively few trials and is thus appropriate for use with pediatric samples, but still requires a motor response and thereby allows for more in depth interpretation of the brain data. In the future, additional longitudinal studies of adolescence should be conducted with paradigms showing decreased striatal activation with age, such as the wheel of fortune task (e.g., Ernst et al. 2005), in an effort to determine if inconsistent findings of age effects relates to differences across the reward paradigms used in each study. Since the current findings replicate cross-sectional patterns for the MID task in adolescence, the current data provide convincing evidence that striatal function increases across adolescence in the specific stage of reward processing (i.e., anticipation of action) probed by the MID task.

The second finding indicated that the development of striatal reactivity did not differ between gain and loss contexts. As with the first set of findings on age effects, this second set of results is also consistent with previous studies that examined developmental differences in brain responses to reward vs. punishment in the incentive-anticipation stage (e.g., Bjork et al., 2010). However, a relatively large body of work suggests a behavioral sensitivity that is enhanced to appetitive stimuli and diminished to aversive stimuli in adolescents relative to adults, in humans (e.g., Cauffman et al., 2010) and animals (e.g.,

Spear and Varlinskaya, 2012; for a review see Ernst, Daniele, & Frank, 2012). One potential explanation for these discrepant findings, as discussed by Bjork et al. (2010), may be the motivational salience of the task. More specifically, Bjork and colleagues suggest that tasks that emulate real-world situations, with more entertaining or more salient rewards relative to the rather mundane rewards utilized in the MID task, might yield different results. However, this interpretation is not supported by our exploratory correlational effects. We show that striatal activation (averaged across gain and loss trials) increases with greater scores on the subjective ratings of the loss cues in mid-adolescence (for dorsal caudate, ventral caudate, nucleus accumbens, globus pallidus, and putamen). These findings suggest that the absence of clear gain- vs. loss-condition difference on striatal activation in the present work might be in part due to individual differences in the subjective value of potential loss. In short, the discrepancy between these bodies of works examining the developmental trajectories of appetitive and aversive stimuli is an area of research that needs to be carefully addressed using paradigms sufficiently powered to examine this specific question.

Finally, the striatal region that was most sensitive to developmental differences in this study was located relatively more dorsally compared to other studies of reward processing, including those using the MID task (e.g., Bjork et al., 2010). However, the majority of studies on reward processes report the engagement of all components of the striatum, including nucleus accumbens, caudate, and putamen, to various degrees. The dorsal striatum is typically associated with motor function, including the formation of stimulus-response learning, particularly through instrumental learning processes that involve goal-directed behavior (e.g., Everitt & Robbins, 2005). This is especially relevant to the MID task, which uses a standard design for the study of instrumental learning. The dorsal striatum, although not reported specifically in prior developmental MID studies, was part of the striatal clusters whose activation differed between adults and adolescents (J. Bjork, personal communication). The importance and functional meaning of the regional dissociation between ventral and dorsal striatal findings remains to be ascertained.

Overall, the findings of this study need to be considered in light of the following caveats. First, brain activation data were collected using two different scanners, and second, we included participants with and without clinical diagnoses. Even though analyses showed no effects of scanner or clinical diagnosis, these factors may have increased error variance, thereby potentially reducing effect sizes. Furthermore, the gap between T1 and T2 testing varied across participants. Even though we controlled for this variable in our analyses, results should be interpreted with caution. Additionally, this study included 22 participants. A larger sample size would provide more power to detect additional potential age-related changes. Lastly, the current study only assessed two time periods (mid-adolescents and late adolescents/early adults), and could not segregate participants more finely as a function of age. A larger sample would allow for more discrete analyses of age, and thus a finer-grained developmental assessment of striatal activation. Therefore, future studies should incorporate larger samples with a wider age range and more repeated assessments to allow for the use of more sophisticated analytic methods, such as mixed-model regression, and thus the examination of more complex developmental questions. Despite these limitations, the present study provides longitudinal data needed to confirm the findings reported previously using cross-sectional designs. More specifically, this longitudinal study supports previous

cross-sectional studies showing hypo-sensitivity to reward in mid-adolescence compared to late adolescence/early adulthood in the anticipation for action stage of processing.

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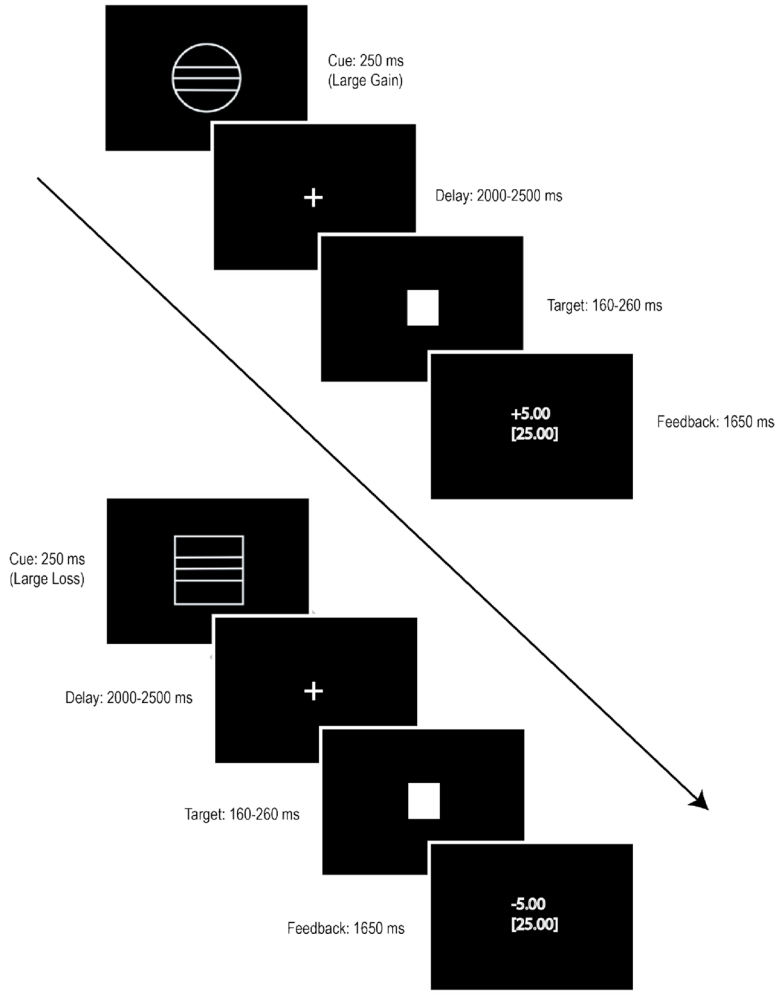

Figure 1.
Monetary incentive delay (MID) task showing large gain and large loss trials.

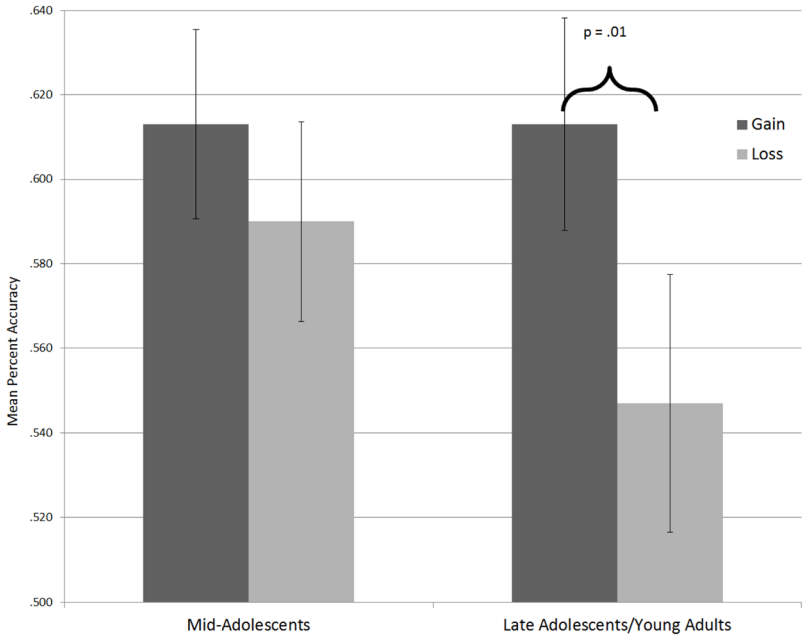

Figure 2.

Mean performance accuracy values for Valence-by-Age interaction (error bars = Standard Errors).

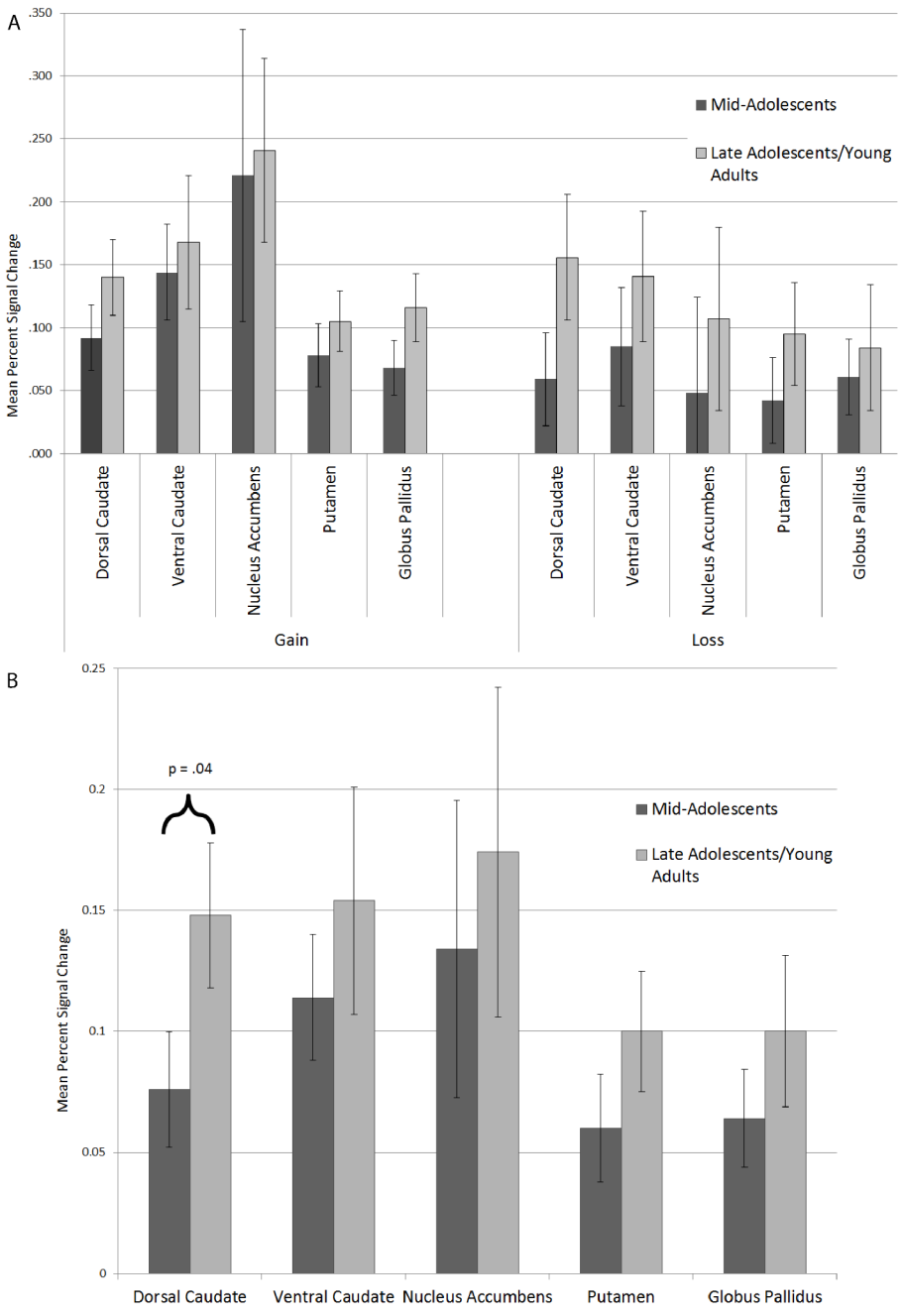

Figure 3.

Mean Age-related differences in percent signal change (high incentive activation – low incentive activation) for striatal ROIs. A) Activation for gain and loss separately (3-way interaction not significant); B) Activation averaged across gain and loss trials (Age-by-Region interaction significant). All error bars are SEs.

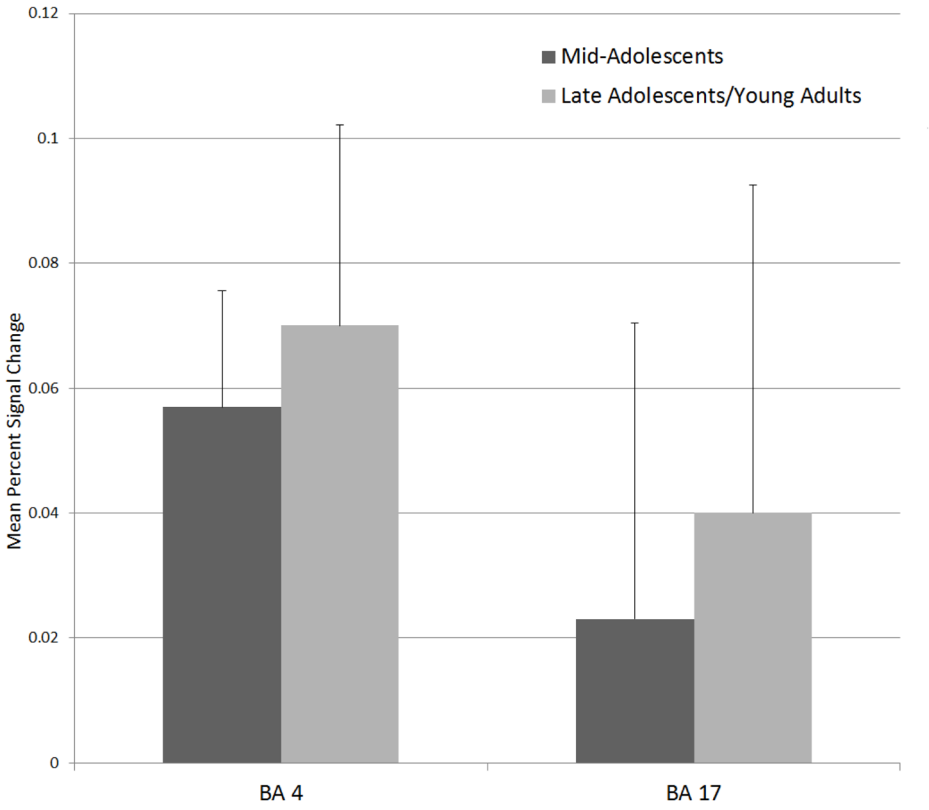

Figure 4.

Mean Age-related differences in percent signal change (high incentive activation – low incentive activation) for primary visual cortex ROI and motor cortex ROI, i.e., control regions, averaged across gain and loss trials (error bars = SE). Results revealed no significant Age effects.

Table 1

Means and SDs for behavioral and brain activation data.

	Mid-Adolescence		Late Adolescence/Early Adulthood	
	Mean	**SD**	**Mean**	**SD**
Brain Data (% Signal Change for high-low incentive contrast)				
Dorsal Caudate Loss	.07	.15	.15	.21
Dorsal Caudate Gain	.09	.11	.14	.13
Ventral Caudate Loss	.08	.20	.12	.22
Ventral Caudate Gain	.13	.17	.19	.26
Nucleus Accumbens Loss	.03	.31	.07	.33
Nucleus Accumbens Gain	.21	.49	.28	.39
Putamen Loss	.05	.15	.09	.17
Putamen Gain	.08	.11	.12	.11
Globus Pallidus Loss	.07	.13	.09	.20
Globus Pallidus Gain	.07	.10	.12	.11
BA 17 Loss	−.00	.23	−.01	.27
BA 17 Gain	.07	.24	.07	.30
BA 04 Loss	.03	.12	.05	.14
BA 04 Gain	.08	.19	.09	.15
Behavioral Data				
RT Gain Small (ms)	239.94	33.16	229.22	43.91
RT Gain Medium (ms)	249.10	32.42	233.02	46.33
RT Gain Large (ms)	236.93	36.86	224.49	40.30
RT Loss Small (ms)	249.16	36.62	239.20	68.62
RT Loss Medium (ms)	245.13	33.81	232.89	44.12
RT Loss Large (ms)	233.84	26.95	231.23	50.07
RT Neutral (ms)	267.47	39.79	250.36	44.14
Accuracy Gain Small (%)	.60	.11	.61	.16
Accuracy Gain Medium (%)	.63	.14	.59	.13
Accuracy Gain Large (%)	.60	.16	.63	.16
Accuracy Loss Small (%)	.55	.18	.53	.16
Accuracy Loss Medium (%)	.60	.11	.54	.17
Accuracy Loss Large (%)	.62	.13	.58	.16
Accuracy Triangle (%)	.46	.15	.57	.17
Debriefing Data (rating −5 to +5)				
Gain Small	2.86	1.62	2.43	1.36
Gain Medium	3.90	.89	3.33	1.71
Gain Large	4.95	.22	4.67	.91
Loss Small	−2.52	1.60	−2.33	1.46
Loss Medium	−3.62	1.12	−3.57	.93
Loss Large	−4.95	.22	−4.52	1.33

	Mid-Adolescence		Late Adolescence/Early Adulthood	
	Mean	**SD**	**Mean**	**SD**
Triangle	−.25	1.52	.24	1.14

Table 2

Exploratory correlation table showing associations between brain activation (across gain and loss trials) and behavior measures, including reaction times, performance accuracy, and debriefing data. Values are Pearson Correlations. Significance values are not corrected for multiple comparisons. Brain data is based on the high incentive vs. low incentive contrast.

Mid-Adolescence

	Brain Data							**Debriefing Data**						
	Dorsal Caud.	**Vent. Caud.**	**Nucl. Accum.**	**Glob. Pal.**	**Putam.**	**BA 17**	**BA 04**	**Gain Small**	**Gain Med.**	**Gain Large**	**Loss Small**	**Loss Med.**	**Loss Large**	**Neutral**
Behavioral Data														
Reaction Times														
Gain Small	.15	−.21	−.19	.10	.06	.15	−.13	**.27**	.07	.43*	−.13	−.21	−.19	.35
Gain Medium	−.16	−.30	−.27	−.03	−.002	.07	−.05	.11	**.09**	.33	.04	−.12	−.17	.43
Gain Large	−.25	−.38	−.33	−.20	−.15	.01	−.16	.30	.13	**.29**	.01	−.28	−.06	.59**
Loss Small	.04	−.11	−.05	.11	.13	.01	.007	.44*	.20	.23	**−.31**	−.51*	−.21	.44
Loss Medium	.18	.02	−.04	.20	.17	.12	.03	.32	.19	.36	−.22	**−.39**	−.30	.41
Loss Large	−.21	−.33	−.30	−.15	−.18	−.12	−.30	.41	.23	.27	−.24	−.42	**.14**	.51*
Neutral	.07	−.19	−.008	.11	.18	.15	−.07	.34	.27	.23	−.22	−.36	−.31	**.35**
Performance Accuracy														
Gain Small	−.26	.10	.02	−.24	−.26	−.06	−.10	**−.15**	.009	−.04	−.02	−.11	.04	.13
Gain Medium	.25	.01	−.16	.26	.22	.08	.09	−.30	**−.24**	.005	.12	.17	−.20	−.48*
Gain Large	.30	.17	−.001	.34	.25	.04	.12	−.49*	−.40	**−.14**	.28	.44*	−.13	−.51*
Loss Small	.32	.25	**.45***	.02	.04	.24	.13	.06	−.11	.30	**−.12**	−.26	−.06	−.22
Loss Medium	.23	−.03	−.003	.16	.08	.24	.30	−.64**	−.71**	.10	.40	**.47***	−.10	−.50*
Loss Large	.36	.16	.09	.29	.31	**.46***	.36	−.32	−.35	.31	.22	.10	**−.21**	−.29
Neutral	−.31	−.11	−.36	−.13	−.13	.03	−.17	.03	.01	−.07	.22	−.17	.25	**.38**
Debriefing (+5 to −5)														
Gain Small	−.08	.04	.22	−.08	.008	−.04	−.11							
Gain Medium	−.21	.02	.09	−.18	−.09	−.20	−.15							
Gain Large	.10	−.02	.03	−.11	−.10	.20	.06							
Loss Small	−.14	−.32	**−.51***	−.11	−.10	.24	.05							

Mid-Adolescence

	Brain Data							**Debriefing Data**						
	Dorsal Caud.	**Vent. Caud.**	**Nucl. Accum.**	**Glob. Pal.**	**Putam.**	**BA 17**	**BA 04**	**Gain Small**	**Gain Med.**	**Gain Large**	**Loss Small**	**Loss Med.**	**Loss Large**	**Neutral**
Loss Medium	.02	−.17	−.32	−.008	−.05	.22	.04							
Loss Large	**−.60****	**−.43***	**−.43***	**−.64****	**−.71****	−.22	**−.70****							
Neutral	**−.50***	**−.44***	−.33	−.35	−.33	−.25	**−.46****							

Late Adolescence/Early Adulthood

	Brain Data							**Debriefing Data**						
	Dorsal Caud.	**Vent. Caud.**	**Nucl. Accum.**	**Glob. Pal.**	**Putam.**	**BA 17**	**BA 04**	**Gain Small**	**Gain Med.**	**Gain Large**	**Loss Small**	**Loss Med.**	**Loss Large**	**Neutral**
Behavioral Data														
Reaction Times														
Gain Small	.16	.12	.15	.08	.16	.04	−.03	**.44**	.37	.44	−.41	−.44	−.44	−.22
Gain Medium	.14	.08	.11	.01	.11	−.02	−.03	.47*	**.44**	.42	−.44	−.37	−.42	−.07
Gain Large	.08	−.004	.02	−.03	.03	−.02	−.10	.48*	.52*	**.35**	−.38	−.23	−.35	−.08
Loss Small	−.03	−.14	−.10	−.09	−.10	−.14	−.21	.47*	.40	−.19	**−.31**	−.24	−.19	−.16
Loss Medium	.12	.04	.02	.02	.04	.06	−.01	.48*	.44	−.33	−.35	**−.32**	−.33	−.07
Loss Large	−.001	−.13	−.04	−.10	−.09	−.11	−.22	.45*	.30	−.14	−.38	−.19	**−.14**	−.14
Neutral	−.02	−.03	.03	.03	−.07	.06	−.02	.19	−.04	.31	−.20	−.005	.31	**−.18**
Performance Accuracy														
Gain Small	−.03	.05	.08	−.12	−.004	−.02	−.09	**−.30**	−.45*	.22	.06	.09	.22	−.16
Gain Medium	−.11	−.20	−.18	−.17	−.18	−.14	−.13	−.07	**−.10**	.30	.14	.09	.30	−.31
Gain Large	.03	−.19	−.41	−.11	−.20	.12	.06	−.07	.08	**.04**	.32	.07	.04	.12
Loss Small	.12	.12	.12	−.04	.002	.02	.05	−.40	−.21	−.13	**.47***	.55*	.13	.17
Loss Medium	−.12	−.04	−.05	.11	.01	.04	.10	−.48*	−.43	−.15	.41	**.10**	.15	−.03
Loss Large	.14	.40	.41	.22	.34	.03	**.45***	−.65**	−.37	.01	.54*	.08	**−.01**	.07
Neutral	.15	.09	−.07	.13	.12	.21	.13	−.37	.05	.21	.46*	.42	−.21	**.36**
Debriefing (+5 to −5)														
Gain Small	.06	−.23	−.18	−.11	−.22	.14	−.16							
Gain Medium	.18	−.02	−.08	.05	−.08	.12	−.003							

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Late Adolescence/Early Adulthood

	Brain Data							**Debriefing Data**						
	Dorsal Caud.	**Vent. Caud.**	**Nucl. Accum.**	**Glob. Pal.**	**Putam.**	**BA 17**	**BA 04**	**Gain Small**	**Gain Med.**	**Gain Large**	**Loss Small**	**Loss Med.**	**Loss Large**	**Neutral**
Gain Large	.23	.17	.24	.11	.08	.04	.04							
Loss Small	.02	−.01	−.28	.09	.06	−.05	.15							
Loss Medium	−.12	−.10	−.30	−.04	−.16	−.11	−.17							
Loss Large	−.18	−.11	−.19	−.08	−.01	−.06	−.02							
Neutral	.38	.20	−.12	.12	.09	.41	.40							

*
< or = .05;

**
< or = .01

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Table 3

Whole-brain results. The whole-brain statistical threshold was based on a combination of alpha-level (p<.005) and cluster-size thresholds (determined by Monte Carlo simulations; for p<.05, k=588) to yield cluster-corrected results.

Region	X	Y	Z	Statistical Value	Volume
High - low incentive value contrast, collapsing across gain and loss for time 1 (t-scores)					
Right Caudate	12	6	9	6.42	17075
Right Anterior Cingulate	11	44	6	5.74	1146
Right Medial Frontal Gyrus	9	22	32	5.06	2455
Left Insula	−27	18	11	5.92	2994
Right Precentral Gyrus	32	−6	39	4.79	2239
Right Precentral Gyrus	11	−12	62	4.44	1488
Right Precentral Gyrus	35	−10	59	4.78	805
Left Precentral Gyrus	−47	−11	49	5.21	2205
Left Occipital	−18	−64	23	6.74	3594
Right Occipital	27	−65	28	4.94	1377
Right Cerebellum	7	−50	−8	3.83	590
Right Brainstem	18	−23	−6	4.31	944
High - low incentive value contrast, collapsing across gain and loss for time 2 (t-scores)					
Left Caudate	−12	9	4	8.80	194661
Right Medial Temporal Gyrus	46	−26	0	4.86	760
Left Dorsolateral PFC	−32	33	36	4.50	627
Time 1 – time 2, collapsing across valence and incentive level (t-scores)					
Left Precentral Gyrus	−38	−3	52	4.16	618