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Candy and the brain: neural response to candy gains and losses

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Abstract Incentive processing is a critical component of a host of cognitive processes, including attention, motivation, and learning. Neuroimaging studies have clarified the neural systems underlying processing of primary and secondary rewards in adults. However, current reward paradigms have hindered comparisons across these reward types as well as between age groups. To address methodological issues regarding the timing of incentive delivery (during scan vs. postscan) and the age-appropriateness of the incentive type, we utilized fMRI and a modified version of a card-guessing game (CGG), in which candy pieces delivered postscan served as the reinforcer, to investigate neural responses to incentives. Healthy young adults 22–26 years of age won and lost large and small amounts of candy on the basis of their ability to guess the number on a mystery card. BOLD activity was compared following candy gain (large/small), loss (large/small), and neutral feedback. During candy gains, adults recruited regions typically involved in response to monetary and other rewards, such as the caudate, putamen, and orbitofrontal cortex. During losses, they displayed greater deactivation in the hippocampus than in response to neutral and gain feedback. Additionally, individual-difference analyses suggested a negative relationship between reward sensitivity (assessed by the Behavioral Inhibition/Behavioral Activation Scales) and the difference between high- and low-magnitude losses in the caudate and lateral orbitofrontal cortex. Also within the striatum, greater punishment sensitivity was positively related to the difference in activity following high as compared to low gains. Overall, these results show strong overlap with those from previous monetary versions of the CGG and provide a baseline for future work with developmental populations.

Keywords Basal ganglia · Reward

How we react to, seek out, avoid, or anticipate rewarding and aversive stimuli in our environment influences a host of cognitive and behavioral processes essential to everyday life. Understanding the basic functional mechanics of how gains and losses are processed in healthy adults is a critical first step before investigating how these processes change over the course of typical development, or how abnormalities in these processes manifest in child and adult onset psychopathology (Barch & Dowd, 2010; Bjork, Smith, & Hommer, 2008; Forbes et al., 2006; Gotlib et al., 2010; Knutson, Bhanji, Cooney, Atlas, & Gotlib, 2008). A rich literature has established the neurocircuitry involved in reward and punishment processing in animals and humans (Haber & Knutson, 2010). The animal literature has focused on primary rewards (i.e., food and liquids), but the human neuroimaging literature has more frequently focused on secondary rewards (i.e., money) that have value based on their ability to procure other rewards. However, monetary rewards may be less appropriate for examining the development of reward processing in young children, who may not yet understand the value of such abstract rewards and the exchange rate between specific amounts of money and desired goods. As such, the goal of the present study was to validate the modification of a gambling task using candy that is appropriate for use across a wide age range, including very young children.

Decades of work in animals and humans have established the roles of the striatum, orbitofrontal cortex (OFC), prefrontal cortex (PFC), and other regions of the limbic system in incentive processing (Haber & Knutson, 2010). The majority of human studies investigating gain/loss processing have utilized

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secondary monetary rewards and have reported consistent patterns of activity during receipt of monetary gains versus loss or no-gain events (Delgado, Locke, Stenger, & Fiez, 2003; Elliott, Newman, Longe, & Deakin, 2003; Galvan et al., 2005; Knutson, Fong, Adams, Varner, & Hommer, 2001; O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001). Specifically, regions of the dorsal and ventral striatum, along with medial portions of OFC, display greater functional responses to reward events than to loss and/or baseline, as well as greater responses to larger versus smaller rewards (Elliott et al., 2003; Galvan et al., 2005; Knutson et al., 2001; Knutson, Fong, Bennett, Adams, & Hommer, 2003; Knutson, Westdorp, Kaiser, & Hommer, 2000; Santesso et al., 2008; Simon et al., 2010). Moreover, patients with neuropsychiatric illnesses characterized in part by a lack of experienced pleasure, such as depression and schizophrenia, display reduced striatal activation during reward processing (Dowd & Barch, 2012; Forbes et al., 2006; Knutson, Bhanji, Cooney, Atlas, & Gotlib, 2008). This relationship between hedonic capacity and striatal reward response also extends to healthy populations in which, again, individuals with greater reward responsivity (measured by Behavioral Activation Scale [BAS] total score), reduced behavioral inhibition (Behavioral Inhibition Scale [BIS] total score), and fewer anhedonic symptoms (Chapman Anhedonia Scales) display greater striatal activity during reward events (Dowd & Barch, 2012; Simon et al., 2010).

There is less consensus regarding regions that respond maximally to receipt of punishment/loss. Some studies have reported increased response to punishment/loss in regions such as the hippocampus, amygdala, and insula (Anderson et al., 2003; Camara, Rodríguez-Fornells, & Münte, 2008; Elliott, Friston, & Dolan, 2000; Phelps & LeDoux, 2005; Small et al., 2003). However, other studies have found increased responses in these regions to *both* punishment/loss *and* reward as compared to neutral events, possibly indicating encoding of salience rather than valence alone (Elliott et al., 2000; Elliott et al., 2003). The evidence is also mixed as to which regions of OFC and PFC respond maximally to losses; some studies have reported a lateral/medial punishment/reward distinction within the OFC, in which lateral regions showed increased response to punishment/loss events (Kringelbach & Rolls, 2004; O'Doherty, Kringelbach, et al., 2001; O'Doherty, Rolls, Francis, Bowtell, & McGlone, 2001), while others have reported greater response to reward in both lateral and medial PFC (Bjork et al., 2004; Elliott et al., 2003; Kim, Shimojo, & O'Doherty, 2006, 2011; O'Doherty, Kringelbach, et al., 2001; Sescousse, Redoute, & Dreher, 2010; Simon et al., 2010).

Monetary rewards are advantageous in many ways: They lend themselves to manipulation of amount without overwhelming concerns of satiation, are simple to deliver in a scanner via visual cue, and allow the participant to obtain any number of other goods that he or she desires with the money earned during the task. However, significant and systematic differences may exist in how monetary incentives are processed/valued across development. Specifically, monetary rewards may be less salient and may be more difficult to value for children, who have less life experience with money and less developed abstract reasoning/mathematical skills than do adults. Thus, the subjective value of a given amount of money likely changes from childhood through adolescence and into adulthood. Some innovative investigators have utilized token economies (systems in which points/tokens earned during the task are later exchanged for prizes) to reduce such developmental confounds (Geier & Luna, 2012). While this approach is clearly effective for adolescent populations, preschool and school-aged children may have difficulty with such an abstract system of exchange. Token economies require the participant to understand the exchange rate between points and prizes (e.g., 15 points = 1 prize) and to associate a given trial's outcome with the subjective value of a prize. Moreover, enough points to obtain another whole prize are not typically won/lost on each individual trial, meaning that a given trial's derived value is equivalent only to a portion of a prize. This requires the child to maintain a representation of accumulated earnings across trials and to evaluate the current trial's outcome in the context of a total sum. Given the complexity of such secondary paradigms and developmental differences in abstract reasoning ability, children's attention/motivational drive may be better captured when more immediate/tangible rewards (i.e., candy) are employed that can be directly represented on screen during the scan.

Primary rewards offer an opportunity to investigate incentive processing without as many concerns regarding how age may interact with the processing of abstract incentives. Primary-reward paradigms have utilized a host of incentives, including liquids (sweet, bitter, and/or salty solutions delivered in scanner), candy (delivered postscan), food odors (pleasant and unpleasant, delivered in scanner), and even erotic pictures (displayed in scanner), among others (Achenbach & Rescorla, 2003; Clithero, Reeck, Carter, Smith, & Huettel, 2011; Kim et al., 2011; Kringelbach, O'Doherty, Rolls, & Andrews, 2003; Levy & Glimcher, 2011; O'Doherty, Rolls, et al., 2001; Sescousse et al., 2010). Such studies in adults have yielded patterns of activation largely similar to those reported in monetary paradigms. Specifically, greater responses to the delivery of rewarding (e.g., juice, chocolate milk), as compared to neutral, solutions are found in regions such as the caudal OFC, medial OFC, basal ganglia, and anterior insula, where activity is related to the subjective pleasantness of the consumed liquid (Frank et al., 2008; Kobayashi et al., 2004; Kringelbach, de Araujo, & Rolls, 2004; Kringelbach et al., 2003; O'Doherty, Rolls, et al., 2001; O'Doherty, Deichmann, Critchley, & Dolan, 2002). Responses to "punishing" solutions such as saline and quinine

also echo responses to monetary loss. Regions of lateral OFC, anterior cingulate cortex (ACC), hippocampus, amygdala (AMY), and insula (INS) display increased response to the delivery of punishing solutions. Again, results are also mixed regarding the medial/lateral OFC distinction for reward and punishment response when using primary rewards (Frank et al., 2008; O'Doherty, Rolls, et al., 2001; O'Doherty et al., 2002; Sescousse et al., 2010; Zald, Lee, Fluegel, & Pardo, 1998).

Also, a handful of studies have directly compared responses to primary and secondary rewards that help to generalize from the literature on monetary reward processing in adults to suggest the potential utility of using more primary rewards in young child populations (Chib, Rangel, Shimojo, & O'Doherty, 2009; Clithero et al., 2011; Kim et al., 2011; Levy & Glimcher, 2011; Sescousse et al., 2010). Once again, similar patterns of responses are found in striatal and insular regions when primary and secondary rewards are employed. Of note is a potential dissociation within the OFC in terms of responses to these two types of rewards. A meta-analysis conducted by Kringelbach and Rolls (2004), including both primary- and secondary-reward studies, suggested a posterior/anterior distinction in OFC response to primary versus more abstract rewards, respectively. This posterior/anterior distinction has been further supported by work directly comparing primary (erotic pictures) and secondary (money) rewards (Sescousse et al., 2010). However, some evidence has also supported the opposite pattern (Kim et al., 2011).

Although the literature reviewed above suggests that primary and secondary rewards modulate many of the same neural systems, a number of challenges are encountered when adapting primary-reward paradigms for use in developmental populations in ways that would allow for clear conceptual and/or empirical comparisons to the existing monetary reward literature. First, the logistical characteristics of the paradigms historically used to deliver the two incentive types have often differed. In secondary paradigms, a trial's outcome is signaled via a visual cue indicating the size and valence (gain/loss) of the outcome—a lump sum of money to be delivered postscan. In primary paradigms, participants traditionally directly experience/consume the incentive in-scanner—that is, tasting a sweet liquid/smelling a pleasant odor. Second, the intrinsic properties of primary/secondary rewards often make comparisons problematic. This difference is most apparent in the punishment/loss domain, where directly consuming or experiencing something aversive (e.g., quinine/saline solution or unpleasant odor) may elicit different psychological and neural responses than does losing something appetitive (e.g., money or tokens). Other hindrances include difficulty in manipulating the magnitude of primary rewards (e.g., delivery of larger liquid rewards can be uncomfortable and potentially dangerous, especially in children) and satiation/habituation, in which the value of an incentive can decrease throughout the experiment.

To address these challenges, we developed a modified version of the card-guessing game (CGG), a task in which *monetary* gains/losses have traditionally been employed, and used fMRI to investigate how healthy adults respond to gains and losses of candy as a means of validating this paradigm before moving to its use in a developmental population (Delgado, Nystrom, Fissell, Noll, & Fiez, 2000). We felt that a paradigm in which primary rewards did not have to be consumed in-scanner would be most comparable to current secondary paradigms, would allow us to investigate responses to primary rewards without concerns regarding delivery timing, increased head motion, and choking hazards, and would be the simplest to implement from a logistical standpoint. Moreover, candy readily lends itself to developmental questions, children would not need to consume liquids in the scanner (a choking hazard associated with increased motion), and very young children might find it easier to comprehend differing amounts candy displayed on screen, as compared to differing amounts of money or points aggregated across trials and then later exchanged for prizes. As such, we believe that results from this paradigm will provide a baseline describing functional responses to candy rewards and losses in healthy young adults that can be used to inform future studies investigating these processes in developmental and other special populations, as well as directly comparing the responses to different reward types.

As our modification of the CGG uses a primary reward (candy) but delivers the reward out of the scanner, we hypothesized that our results would provide a bridge between the responses reported in studies using primary and secondary rewards. We expected to see reward- and loss-related modulation of BOLD activity in regions of the striatum, amygdala, and OFC, as reported in previous studies using the CGG and other secondary-reward paradigms (Cox, Aizenstein, & Fiez, 2008; Delgado et al., 2003; Delgado et al., 2000; Delgado, Stenger, & Fiez, 2004; Forbes et al., 2010; May et al., 2004; Tricomi, Delgado, McCandliss, McClelland, & Fiez, 2006; Tricomi, Delgado, & Fiez, 2004). What was less clear was whether, within the OFC, we would see a more anterior or posterior pattern of activity, which the literature suggests might in part relate to the type of reward used (primary vs. abstract). Additionally, we expected that individuals with greater reward responsivity and hedonic tone would display greater striatal activity during reward feedback, replicating findings in the extant literature (Dowd & Barch, 2012; Simon et al., 2010).

Method

Participants

A total of 21 young adults participated in this study. One participant was excluded from the analysis on the basis of a history of major depressive disorder (assessed via self-report on the Adult Behavior Check List; Achenbach & Rescorla, 2003). The remaining 20 participants included ranged in age from 22 to 26 years (mean age = 23.95, *SD* = 1.353; eight males, 12 females). The participants were healthy and free of any major medical disorder, did not report a past history of any mental disorder, had not taken psychotropic medications within the past two weeks, and were nonsmokers. They were recruited via posted advertisements at Washington University and were not given any instructions/restrictions regarding food or beverage consumption. All of the participants gave informed consent, and the Washington University in St. Louis Institutional Review Board approved the study.

Procedure

The experiment was conducted over the course of two separate in-person sessions: a behavioral session, followed by a neuroimaging session. In the behavioral session, participants completed several individual-difference questionnaires (see below) and a demographic form. Additionally, participants completed a behavioral probabilistic reward task based on those of Pizzagalli, Jahn, and O'Shea (2005) and Tripp and Alsop (1999) that is not addressed in these analyses. The participants then returned on a different day (within three weeks of the behavioral session) to complete the neuroimaging session. During this fMRI session, they completed the Beck Depression Inventory (BDI; Beck, Steer, & Brown, 1996), out-of-scanner practice for the neuroimaging task, and an in-scanner CGG based on that of Delgado et al. (2000) and Delgado et al. (2004), followed by a postscan questionnaire.

Individual-difference measures Participants were administered the following individual-difference measures during the behavioral session: (1) the Behavioral Inhibition Scale and Behavioral Activation Scale (BIS/BAS; Carver & White, 1994), (2) the Chapman Anhedonia Scales (CS; Chapman, Chapman, & Raulin, 1976), and (3) the Snaith–Hamilton Pleasure Scale (SHPS; Snaith et al., 1995). As the Chapman scales (both the physical and social components) were strongly correlated with the SHPS, a composite variable, *hedonics* (HED), was created by reverse-coding the physical and social components of the CS, computing *z* scores for the two reverse-coded CS scales and the SHPS, and then summing the three *z* scores, such that a higher HED value indicated that an individual was more hedonic. A subset of the participants also completed the Positive Affect and Negative Affect Scales (PANAS; Watson, Clark, & Tellegen, 1988), but these measures were not included in further analyses. Descriptive statistics and pairwise correlations between the individual-difference measures can be found in Supplementary Tables 1–2.

Card-guessing game Participants were told that they would play a CGG in which they were to guess the number on a mystery card (represented by a "?") to potentially win or lose candy, on the basis of whether or not that guess was correct. The type of candy incentive, M&Ms or Skittles, was determined by the participant's preference, indicated during study enrollment (the visual feedback did not differ by candy types). The participants were told that potential card numbers ranged from 1 to 9 and that they should indicate whether they thought that the mystery card number was more or less than 5 by pressing one of two buttons with either the left or the right thumb. Participants were required to make their guess while the mystery card "?" was displayed onscreen (2,000 ms). If no response was made, the "?" was replaced by a fixation cross for the remaining duration of that missed trial. If a guess was made, feedback was displayed for 2,000 ms immediately following the buttonpress. Feedback included the actual number on the card, a message of "Great Job!" and a green up arrow for gain trails, a message of "Sorry" and a red down arrow for loss trials, and a picture of the number of candy pieces gained or lost (see Fig. 1).

Participants could gain or lose both large and small amounts of candy on the basis of their guess and the number on the card. Participants received a high gain (four candies) if their guess was "above 5" and the number was 8 or 9, or if their guess was "below 5" and the number was 1 or 2. They received a low gain (two candies) if their guess was "above 5" and the number was 6 or 7, or if their guess was "below 5" and the number was 3 or 4. Conversely, participants received a high loss (two candies) if their guess was "above 5" and the number was 1 or 2, or if their guess was "below 5" and the number was 8 or 9. They received a low loss (one candy) if their guess was "above 5" and the number was 3 or 4, or if their guess was "below 5" and the number was 6 or 7. Finally, if the number 5 was displayed, no candy was gained or lost, and the feedback on these neutral trials included the card number, "Next Trial" and two dash marks (see Fig. 1). The computer program was designed so that if the trial was meant to be—for example—a high-gain trial, the program adapted the card number to the participant's choice, to ensure the appropriate outcome for that trial type. On the basis of previous research, a 2:1 ratio of gain to loss amounts was used, such that participants added four and two pieces of candy to their total on high- and low-gain trials, respectively, and lost one and two pieces from their total on

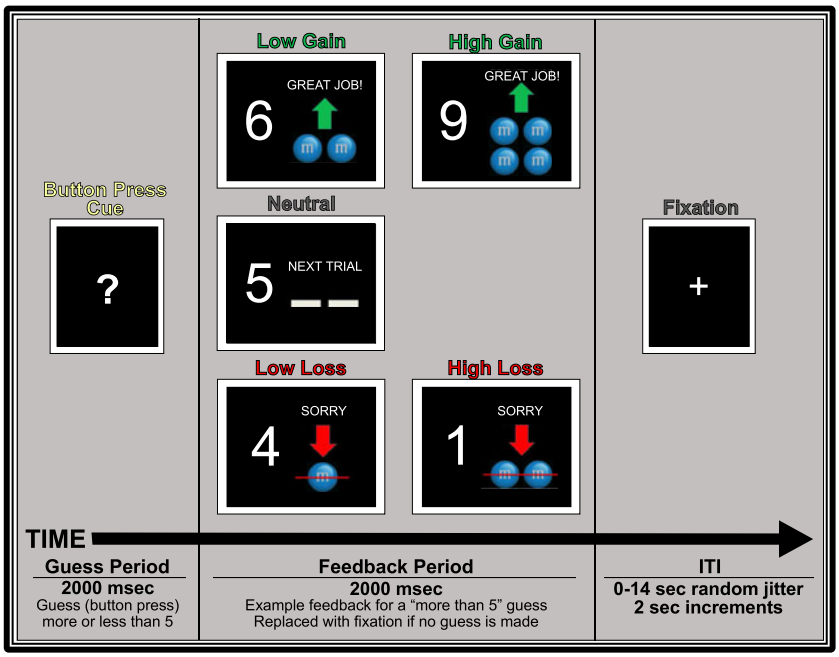

Fig. 1 Timing of the card-guessing game: Example of possible feedback types following a "more than 5" guess. Each trial lasted 4 s in total. The cue to make a guess (?) was displayed for up to 2 s. Feedback (including the number on the mystery card, an arrow denoting gain/loss or dashes for no gain/loss, and the amount of candy exchanged) was presented as soon as a guess was made and lasted for 2 s. A fixation cross was presented for any remaining portion of the 4 s. The intertrial intervals (ITIs) lasted from 0 to 14 s, with a random jitter in 2-s increments. If a guess was not made during the 2-s cue to make a guess, a fixation cross was presented for 2 s in place of the feedback

low- and high-loss trials, respectively. This ratio was used to prevent frustration with the task and to maintain engagement, as well as to ensure that the participants received candy at the end of the task (Tversky & Kahneman, 1981). The participants were told that they would receive a lump sum of candy at the conclusion of the experiment reflecting the net amount of candy earned during the task.

To ensure that all participants understood the task, written instructions were presented on a computer using PsyScope software, followed by actual task practice, prior to entering the fMRI scanner (Cohen, MacWhinney, Flatt, & Provost, 1993). All trial types were experienced during the practice task, and participants were told that any candy earned during the practice would be added to their candy total. This served as a candy endowment to offset any initial losses during the in-scanner task.

In-scanner trials were presented in a fixed order with a rapid event-related design, using PsyScope software on a Macintosh computer for both stimulus presentation and data collection (Cohen et al., 1993). The computer selected a card number on each trial following the participant's guess, depending on the predetermined trial type. Determining the card number shown after the participant's buttonpress ensured that the guess, predetermined trial type (gain, loss, or neutral), and card numbers were always congruent and that there were no "correct/incorrect" guesses. This is the standard procedure with the CGG and ensures that all participants experience roughly the same events in the scanner (i.e., no one by chance gets a disproportionate amount of high-gain trials). The task was divided into six blocks, each lasting 5 min and containing eight potential instances (if the participant made a guess for all trials) of the five trial types—high/low gain/loss and neutral—delivered in a fixed pseudorandom order, such that each participant experienced the same order of events. On average, participants failed to make a response on four trials over the course of the entire scanning session. Each trial lasted 4,000 ms (see Fig. 1), followed by an intertrial interval (ITI) of 0–14,000 ms that was randomly jittered in 2,000-ms increments. All participants completed the six scan blocks, and no data were excluded due to excessive head movement (excessive motion was defined by a mean voxel-wise standard deviation, mode 1,000 normalized, of greater than 15 for a given blood oxygenation level dependent [BOLD] run). Participants were given $50 as compensation for their time along with 150 M&Ms/Skittles at the end of the scanning session, regardless of performance.

fMRI data acquisition and processing

Imaging data were collected using a 3-T TIM TRIO Siemens whole-body system and included a T1 (sagittal acquisition, TE = 3.16 ms, TR = 2,400 ms, FOV = 256 mm, flip angle = 8°, one acquisition, 176 slices, 1 × 1 × 1 mm voxels) image and functional images collected with a 12-channel head coil using a standard gradient-echo EPI sequence sensitive to BOLD contrast (T2*) (TR = 2,000 ms, TE = 27 ms, FOV = 384 mm, flip = 77°). During each functional run, 150 whole-brain volumes were acquired, consisting of 36 contiguous axial images with isotropic voxels (4 mm^3) acquired parallel to the anterior–posterior commissure plane. Two functional runs of 160 TRs (~11 min total) were acquired while participants rested with eyes closed.

The fMRI data were preprocessed using in-house Washington University software. Prior to preprocessing, the first four frames of each run were discarded to allow for signal stabilization. The data were then (1) reconstructed into images and normalized across runs by scaling the whole-brain signal intensity to a fixed value and removing the linear slope on a voxel-by-voxel basis to counteract any effects of drift (Bandettini, Jesmanowicz, Wong, & Hyde, 1993); (2) corrected for head motion using rigid-body rotation and translation correction algorithms (Friston, Jezzard, & Turner, 1994; Snyder, 1996; Woods, Cherry, & Mazziotta, 1992); (3) registered to Talairach (Talairach & Tournoux, 1988) space using a 12-parameter linear (affine) transformation; and (4) smoothed with an 8-mm full-width-at-half-maximum Gaussian filter.

Estimates of functional activation during each of the five trial types (high/low gain/loss and neutral) were obtained by using a general linear model (GLM), also incorporating regressors for linear trend and baseline shift to estimate the hemodynamic response function for each trial type. The task analyses used a GLM approach that did not assume a specific hemodynamic response shape. While it is possible that developmental effects could mostly be explained by differences in magnitudes of activation, it is also likely that development would interact with BOLD response over time. Thus, we felt that using an unassumed (FIR type) approach would provide the most information without imposing assumptions regarding the shape of the hemodynamic response that might bias future investigations. For each trial type, neural responses at ten time points (20 s) were estimated relative to baseline fixation, in order to provide adequate temporal resolution of the hemodynamic response. We felt that this approach provided the best balance between the cost of power and the benefit of a more complete picture of the hemodynamic response. The task was designed to focus on trial outcomes and did not allow for the dissociation of anticipation and receipt of feedback. Although time courses were estimated beginning with trial onset, participants were quick to make a response (the mean reaction time was 521.8 ms, standard deviation 91.4 ms), and thus feedback onset occurred well within the first time point on average for each participant. These estimates were then entered into group-level analyses treating subjects as a random factor. We also computed an assumed response shape GLM for each participant for use in the individual-difference analyses, since this type of GLM provided us with a single beta estimate for each condition. This GLM included the same five trial types (and regressors for linear trends and baseline shifts across runs) and used the Boynton function (Boynton, Engel, Glover, & Heeger, 1996).

fMRI data analysis

To examine the influence of the valence (gain vs. loss) and magnitude (low vs. high) of feedback, we performed a voxel-wise repeated measures analysis of variance (ANOVA) with three within-subjects factors: Outcome Valence (two levels: gain, loss), Outcome Magnitude (two levels: high, low), and Time Point within trial (the ten frame estimates for each trial type, beginning at trial onset). We then followed up this analysis with an additional repeated measures ANOVA to identify regions where activation was related to salience (i.e., responses to gain/loss were similar and different from neutral) rather than the valence and/or magnitude of feedback. Because there was only one level of neutral feedback, neutral trials were not included in the first ANOVA. The second ANOVA included Time Point and Condition (gain [both high- and low-gain trials], neutral, and loss [both high- and low-loss trials]) as within-subjects factors.

In the analyses described above, we focused on regions showing interactions with time point within trials, given our use of unassumed (FIR type) GLMs. When appropriate, post hoc ANOVAs were performed within all significant regions identified by the ANOVAs described above. For these post hoc analyses, the mean percent signal change across each region was extracted for each of the ten estimated time points. This was done for each applicable condition, and then post hoc ANOVAs were run comparing two trial types (e.g., gain vs. neutral) over the ten time points.

To focus our results, these two voxel-wise ANOVAs were conducted within an anatomically defined a priori mask developed by S. M. Beck and colleagues (Beck, Locke, Savine, Jimura, & Braver, 2010). This mask (see Supplemental Fig. 1) covered an a priori network of regions implicated in reward processing that were hand-drawn in Talairach space on the basis of anatomical landmarks and previously published functional coordinates, including the dorsal and ventral striatum, ventral tegmental area, substantia nigra, amygdala (AMY), orbitofrontal cortex (OFC), ventromedial prefrontal cortex (VMPFC), and insula (INS) (S. M. Beck et al., 2010). ANOVA results within the a priori mask were corrected for multiple comparisons using a combined p-value/cluster-size threshold ($p < .005$ and 21 voxels) determined using AlphaSim simulations (smoothing = 2 voxels, 1,000 iterations, voxels in mask = 5,332) to provide a false-positive rate of $p < .05$ for the whole mask (Forman et al., 1995; McAvoy, Ollinger, & Buckner, 2001).

To reduce redundancy across the two ANOVA results, all significant regions identified in the first ANOVA were converted to a binary mask. This mask was then applied to the second ANOVA prior to thresholding. The remaining voxels were subjected to the same multiple-comparison correction criteria ($p < .005$ and 21 voxels). Regions identified in each of the two ANOVAs were then partitioned such that peaks of activity were considered separate regions if they were more than 10 mm apart, as measured by a peak-splitting algorithm (Kerr, Gusnard, Snyder, & Raichle, 2004; Michelon, Snyder, Buckner, McAvoy, & Zacks, 2003).

We also conducted exploratory voxel-wise whole-brain analyses, which were corrected for multiple corrections using a *p*-value/cluster-size threshold ($p < .0013$ and 17 voxels) determined by Monte Carlo simulations, in order to provide a whole-brain false-positive rate of $p < .05$, and partitioned such that peaks of activity were considered separate regions if they were more than 12 mm apart according to the same peak-splitting algorithm (Kerr et al., 2004; Michelon et al., 2003). Whole-brain results are reported and discussed in the supplementary materials. We felt that the combination of threshold and cluster size provided a good balance between detecting small regions showing strong effects and larger regions with subtler task-related activity differences.

Individual-difference data analysis

To identify regions where task activation was related to reward/punishment sensitivity and hedonic tone, individual-difference measures of reward sensitivity (BAS total score), loss sensitivity (BIS total score), and hedonics (HED) were each correlated separately with magnitude estimates from the assumed GLMs. Magnitude estimates used in the correlation analyses included differences between each of the four individual trial types and neutral (e.g., HG–NU). Additionally, differences between the high and low trial types for both loss and gain (HL–LL and HG–LG) were included on an exploratory basis. Functional regions identified by the correlations within the mask were thresholded using a *p*-value/cluster-size threshold ($p < .005$ and 26 voxels) in order to provide a false-positive rate of $p < .01$. To identify potential multivariate outliers, Mahalanobis D^2 scores were computed for each resultant region using the individual-difference measure and imaging contrast of interest as independent variables. No participant passed the $p < .001$ threshold required for multivariate outliers for any region. To further test the robustness of the reported effects, correlations were computed again within the regions identified in the voxel-wise correlations without participants whose multivariate outlier score was less than $p < .05$. All discussed correlations remained significant ($p < .05$) when these participants were removed from the analyses.

Results

We started the analysis using an ANOVA with Valence (gain, loss), Magnitude (high, low), and Time Point (ten time points within-trial estimate; Time Point 1 corresponding to the onset of the buttonpress cue) as within-subjects factors.

Effects of valence

Regions identified as displaying a Valence × Time Point interaction within the reward mask included areas of the insula, lateral OFC, caudate, putamen, amygdala, and hippocampus (Table 1 and Figs. 2 and 3). All of these regions other than the hippocampus showed greater activation during gain than loss trials. The hippocampus showed less *de*activation for gain than for loss trials. Planned within-region post-hoc ANOVAs involving all trial types, including neutral trials that were not included in the original ANOVA, indicated that activity was greater in gain than in neutral trials in the lateral OFC region, but that neutral trials did not differ significantly from loss trials. In addition, neutral trials elicited greater activity than did loss trials in dorsal putamen regions and the insula. However, neutral-trial activity did not differ significantly from gain or loss in the remaining regions (including ventral putamen, caudate, thalamus, amygdala, and hippocampus), as is shown in Table 1, Fig. 3, and Supplemental Figs. 2–3. This result was surprising, as graphs depicting time courses particularly for the caudate/putamen regions seemed to indicate a difference between neutral and either gain or loss peak activation in several of these regions.

Table 1 Valence × Time Point interaction regions

Region of Activation	Laterality	Talairach Coordinates			Pattern
		x	*y*	*z*	
Activation					
Lateral orbitofrontal cortex BA 47	R	42	26	–9	G > N = L
Insula BA 13	R	35	–5	16	G = N > L
Dorsal putamen	R	27	–13	10	G = N > L
Dorsal putamen	R	24	5	9	G = N > L
Dorsal putamen	L	–26	–13	10	G = N > L
Dorsal putamen	L	–23	3	11	G = N > L
Putamen/caudate	L	–17	9	4	G > L
Putamen/caudate	R	15	9	5	G > L
Ventral putamen	L	–23	–2	–3	G > L
Ventral putamen	R	22	–1	–7	G > L
Ventral putamen	R	30	–13	–4	G > L
Thalamus	L	–8	–8	18	G > L
Amygdala	L	–18	–5	–13	G > L
Caudate body	L	–15	7	17	G > L
Caudate body	R	15	12	15	G > L
Caudate body	L	–6	3	6	G > L
Deactivation					
Hippocampus	L	–26	–17	–11	L > G

These regions displayed a Valence × Time Point interaction within the a priori reward mask. Post hoc analyses detailed in the Methods section were performed on each region. Regions in which activation during neutral trials did not significantly differ from activity during either gain or loss trials are noted as showing either G > L or L > G patterns of activity. BA = Brodmann area; L = left; R = right; G = gain; N = neutral; L = loss

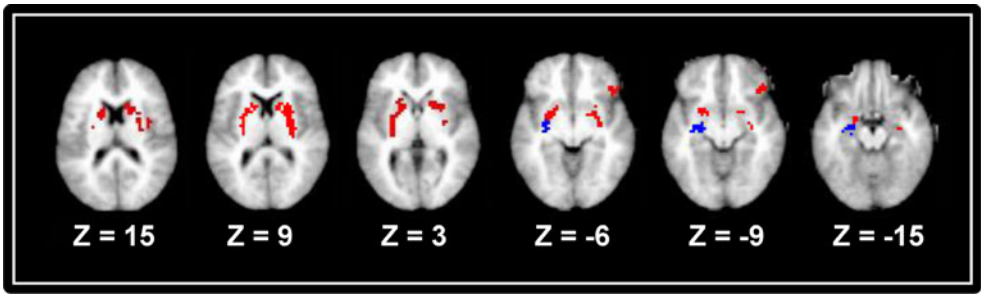

Fig. 2 Regions of interest (ROIs) identified as showing a significant Valence × Time Point interaction within the a priori reward mask. In the online figure, red = ROIs with greater activation during gain than loss trials, and blue = ROIs with greater deactivation during loss than gain trials

To further investigate the relationship between neutral and gain/loss activation within the striatum, we performed exploratory post hoc paired *t* tests designed to specifically test for differences in peak activation between the neutral condition and the gain and loss conditions. Percentages of signal change for individual trial types (neutral, gain, loss) were averaged for Time Points 4 and 5 (the time points corresponding to the peak response across all regions included in these analyses) within each caudate and putamen region identified in the analyses described above (Valence × Magnitude ANOVA). Because of the exploratory nature of these post hoc tests, uncorrected *p* values are reported. Interestingly, the relationship between neutral and gain/loss activation differed along the rostral–caudal axis of the striatum. Specifically, within the caudate and more rostral putamen/caudate regions, neutral-trial activity did not differ from loss activation, but did differ from gain. Within the caudal putamen regions, neutral-trial activity significantly differed from loss-trial activity, while it did not differ from gain-trial activity (*p* values are reported in Supplementary Table 3).

Effects of magnitude and the interaction of valence and magnitude

No regions displayed a significant two-way interaction between magnitude and time point or a three-way interaction between valence, magnitude, and time point within the a priori anatomical mask.

Effects of salience

The ANOVA above identified regions where activity differed depending on the valence of the trial outcome. However it is possible that some regions encode salience rather than the valence of feedback. In these regions, we would expect to see similar patterns of activity to feedback of different valences (gain/loss) that would differ significantly from the response to neutral feedback. To identify such regions, we conducted an additional voxel-wise ANOVA within our a priori mask that included the neutral condition. Thus, this ANOVA used condition (gain, loss, or neutral) and time point as within-subjects factors. However, no significant regions unique to the Condition × Time Point interaction were found within the a priori reward mask.

Individual-difference results

To evaluate whether individual differences in task-related activity were related to individual differences in reward/punishment sensitivity or hedonic tone, magnitude estimates for the difference between the trial types and neutral (e.g., HL–NU) and the difference between high and low trials within gain/loss (e.g., HG–LG) were correlated with BAS, BIS, and HED within the a priori reward mask. Only contrasts with significant correlations ($p < .01$, corrected for multiple comparisons using a combination of *p* value and cluster size [$p < .005$, $n = 26$]) are reported.

Behavioral activation system (BAS) correlations Interestingly, reward sensitivity (BAS total score) was most strongly correlated with loss-related activity, and not with gain-related activity as hypothesized (Table 2A and B, Supplementary Figs. 4–6). Specifically, low-loss trial activity showed a positive correlation with BAS in a region of inferior frontal gyrus (49, 19, –1). A positive correlation was also found between BAS and the difference between low-loss and neutral-trial activity (LL–NU) within the right caudate and a portion of the right lateral OFC. The same lateral OFC and caudate regions displayed a negative correlation between BAS and the difference between high- and low-loss trial activity (HL–LL; Supplementary Fig. 5). Specifically, as BAS increased, so did the difference in activity between low-loss and neutral trials, and the difference in activity between high and low loss decreased with increasing BAS scores in these lateral OFC and caudate regions.

Behavioral inhibition system (BIS) correlations Mirroring the BAS correlation results, punishment sensitivity (BIS) was most strongly associated with gain-trial activity, and no significant correlations were found with loss related activity (Supplementary Figs. 4 and 6, Table 2C and D). Portions of the insula, caudate, and putamen displayed a positive correlation between BIS and the difference between high- and low-gain trial activity (HG–LG), indicating that individuals with increased punishment sensitivity show greater neural

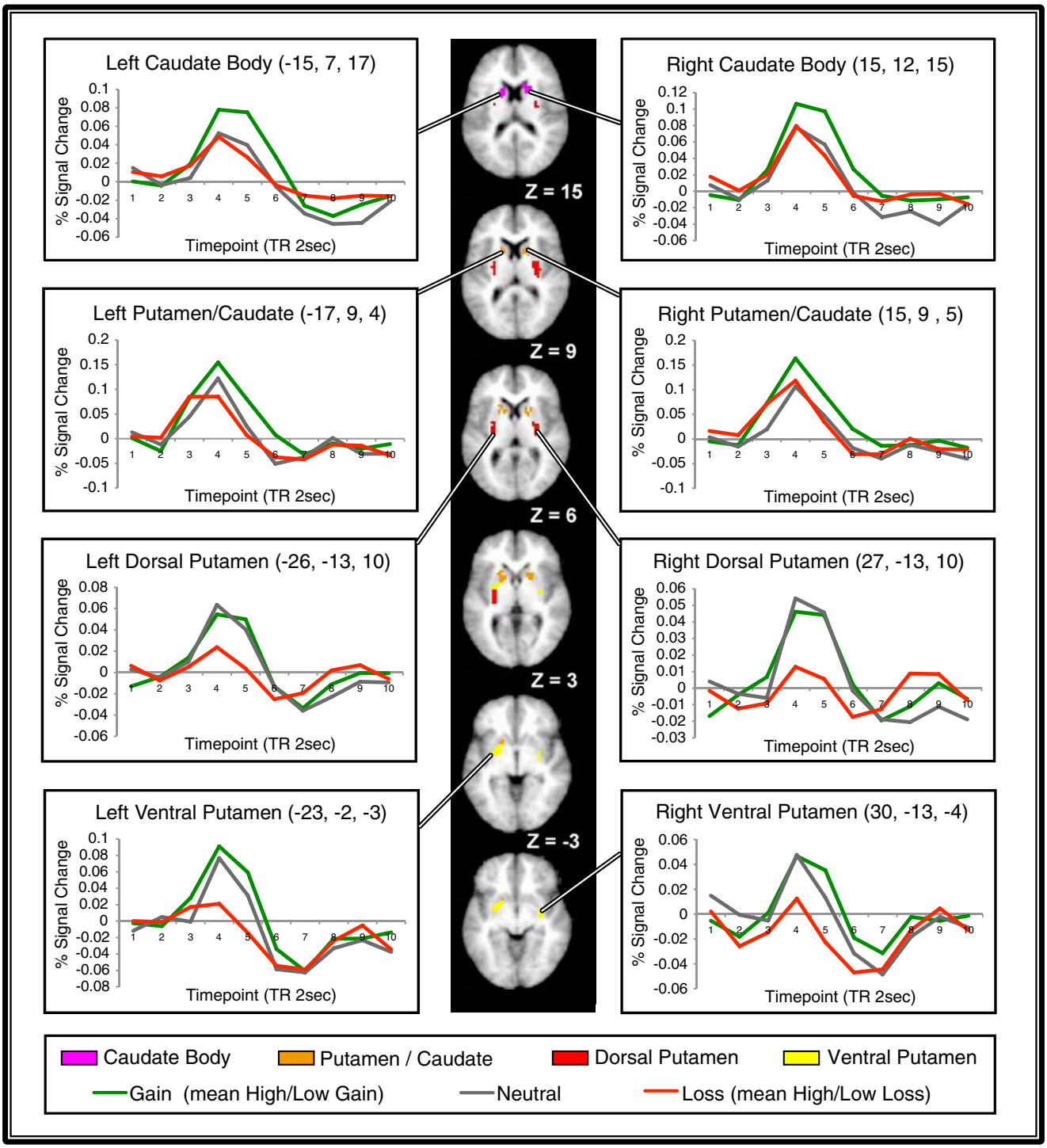

Fig. 3 Valence × Time Point interaction: Representative time courses of striatal regions displaying a rostral/caudal distinction in response to neutral feedback. Caudate regions, as well as rostral putamen/caudate regions, show greater activation following gain feedback as compared to neutral and loss feedback. Dorsal and ventral putamen regions display greater activation following gain and neutral feedback as compared to loss feedback

responses to high-gain than to low-gain trials, while those with lower punishment sensitivity showed the opposite relationship.

Several regions, including the left caudate and bilateral putamen, showed both a significant negative correlation between BAS and HL–LL and a positive correlation between BIS and HG–LG. The BIS correlation did not remain significant within the insula region when a potential outlier was excluded (Supplemental Fig. 6).

Table 2 Individual-difference correlations

Region of Activation	Laterality	Talairach Coordinates		
		x	*y*	*z*
A) LL–NU Positive Correlation With BAS				
Inferior frontal gyrus BA 47	R	46	19	–1
Caudate body	R	11	7	13
B) HL–LL Negative Correlation With BAS				
Putamen	L	–22	–3	9
Caudate body	R	11	10	11
Inferior frontal gyrus BA 47	R	50	18	–1
Putamen	L	–29	1	–2
Caudate body	L	–14	3	17
Putamen	R	28	–12	9
Claustrum	R	35	–11	0
Putamen	L	–33	–17	0
Putamen	R	24	1	6
Superior temporal gyrus BA38	R	37	2	–9
Insula BA13	L	–34	–23	16
Insula BA13	R	41	–3	7
Lateral globus pallidus	L	–13	3	4
Claustrum	L	–33	10	3
Putamen	R	21	1	–8
Caudate body	L	–18	11	12
Claustrum	R	33	8	8
Inferior frontal gyrus BA 47	R	50	33	–2
Putamen	R	24	15	–5
C) HG–LG Positive Correlation With BIS				
Putamen	R	23	2	8
Claustrum	R	38	–8	8
Putamen	L	–19	1	12
Caudate body	L	–12	7	8
Insula BA 13	R	39	–4	–3
Insula BA 13	L	–36	9	6
D) Overlap Between HG–LG With BIS and HL–LL With BAS				
Insula**	R	38	–7	2
Putamen	L	–21	0	10
Putamen	R	23	0	7
Caudate body	L	–13	5	10

(A) Regions displaying a significant correlation between BAS and the difference between low-loss and neutral trial activity (LL–NU). (B) Regions displaying a significant correlation between BAS and the difference between high-loss and low-loss trial activity (HL–LL). (C) Regions displaying a significant correlation between BIS and the difference between high-gain and low-gain trial activity (HG–LG). (D) Regions showing a positive correlation between HG–LG and BIS, along with a negative correlation between HL–LL and BAS. L = left; R = right;]BA = Brodmann area; HG = high gain; LG = low gain; NU = neutral; HL = high loss; LL = low loss; BAS = BAS total score, a measure of reward sensitivity from the BIS/BAS (Behavioral Activation/Inhibition) Scales; BIS = BIS total score, a measure of loss sensitivity from the BIS/BAS Scales. ** The correlation between HG–LG and BIS was nonsignificant when a within-region-of-interest correlation was conducted excluding the participant with the lowest BIS score.

Hedonics correlations No regions showing a significant correlation between the hedonics composite variable (HED) and any task conditions were found within the a priori reward mask.

Discussion

The goals of this study were to develop a paradigm using primary rewards congruent with current secondary-reward paradigms, and then to establish baseline responses in healthy young adults for use in future investigations of gain/loss processing in developmental populations. To do this, we modified a version of the CGG, which previously had utilized monetary incentives, to employ small candy pieces (consumed out of scanner) as reinforcers. This modification allowed us to modulate both incentive valence (gain, loss, neutral) and magnitude (high, low) similarly to previous monetary studies.

Valence effects

Consistent with the secondary-reward literature, we observed strong valence (gain vs. loss) effects in regions of the dorsal (caudate body/putamen) and ventral (ventral putamen) striatum, lateral OFC, insula, thalamus, hippocampus, and amygdala (Cox et al., 2008; Delgado et al., 2003; Delgado et al., 2000; Delgado et al., 2004; Elliott et al., 2003; Estle, Green, Myerson, & Holt, 2007; Kim et al., 2011; Knutson et al., 2001; O'Doherty, Rolls, et al., 2001; Tricomi et al., 2006; Tricomi et al., 2004; Valentin & O'Doherty, 2009; Zald et al., 1998). All regions except the hippocampus displayed greater activation during gain feedback than during loss feedback, with bilateral putamen displaying the most extensive effects. Dorsal striatal activation, particularly the caudate, is the most consistently reported valence effect observed in studies using the CGG. Feedback-modulated responses in this region are expected, given that the CGG requires a timely buttonpress that the participant believes will impact the type of feedback that he or she receives (gain vs. loss) and the dorsal striatum's involvement in the goal-directed action component of reward-processing/decision-making (O'Doherty et al., 2004; Tricomi et al., 2004).

We also observed an interesting dissociation between responses to neutral feedback in the caudate body/rostral putamen and more caudal portions of the putamen. In caudate and rostral putamen regions, activation was similar to neutral and loss feedback, and less than activation to gain responses, while in more caudal putamen regions, neutral and gain responses were similar and greater than loss responses. This pattern of activity may indicate a reduced

response during loss trails in the caudal putamen, as opposed to an increased response to gain/neutral feedback, and vice versa in more rostral regions. It is important to note that our analyses investigating these effects were exploratory; however, this pattern of activation was remarkably consistent, both between hemispheres and within the given structures. Studies investigating functional dissociations within the striatum have traditionally focused on comparisons between the dorsal and ventral striatum, with less evidence for a rostral/caudal distinction in function (Joel, Niv, & Ruppin, 2002; O'Doherty et al., 2004). However, functional connectivity studies have reported distinct patterns of connectivity for the caudate and more caudal putamen, with the caudate displaying positive functional relationships with frontal control regions (e.g., DLPFC and ACC), while the putamen displayed positive functional connections with cortical regions involved in movement (Barnes et al., 2010; Di Martino et al., 2008). How these patterns of connectivity relate to our findings is unclear, and future work will be needed to determine whether this result is replicable and how it relates to dissociations in function across basal ganglia subregions.

We also observed valence effects in the ventral putamen, as have been seen in previous CGG studies using monetary incentives (Delgado et al., 2003; Delgado et al., 2000; Delgado et al., 2004). We did not, however, observe valence effects in the nucleus accumbens. Other CGG studies have also shown ventral striatal activity in the ventral putamen/pallidum but not in the accumbens (Cox et al., 2008; Delgado et al., 2003; Delgado et al., 2000; Delgado et al., 2004; Forbes et al., 2010; May et al., 2004; Tricomi et al., 2004). While the ventral striatum, including the ventral putamen, is involved in representation of incentive value, the nucleus accumbens may be maximally sensitive to anticipation/prediction of rewards or to when reward information can be used to alter behavior (Delgado, Miller, Inati, & Phelps, 2005; Knutson et al., 2001; O'Doherty et al., 2004; Tricomi et al., 2004). Additionally, this is a very small region, and possibly there could have been significant between-subjects variability in accumbens morphology within our sample. Another explanation of the absence of nucleus accumbens activity could be the pseudorandom structure of the CGG, which is ideal for isolating responses to task feedback independent of learning effects.

In addition to finding no valence effects in the accumbens, most adult studies using the CGG have not reported valence effects in the OFC, although a recent article with a larger sample (n = 28) reported valence effects in regions of medial OFC (Cox et al., 2008; Delgado et al., 2003; Delgado et al., 2000; Delgado et al., 2004; Forbes et al., 2010; Tricomi et al., 2006; Tricomi et al., 2004; Wilbertz et al., 2012). It is surprising that few adult CGG studies have reported OFC activation, considering the role of the OFC in incentive processing and given that studies with younger participants have reported both medial and lateral OFC valence effects (Forbes et al., 2010; May et al., 2004). Unlike other adult CGG studies, we found a significant effect of valence in the lateral OFC, such that activity to high-gain trials was greater than activity to either neutral or loss trials. May and colleagues also reported increased response to reward in lateral OFC, using a monetary version of the CGG in children and adolescents (May et al., 2004). Reward-processing studies frequently report a lateral/medial OFC distinction in activity patterns, with greater response to punishment in lateral regions and greater response to reward in medial regions (Kringelbach, 2005; Kringelbach & Rolls, 2004). However, some studies have suggested that this lateral/medial relationship may rely at least in part on whether the gain/loss feedback leads to behavioral change (Breiter, Aharon, Kahneman, Dale, & Shizgal, 2001; Elliott et al., 2000; Elliott et al., 2003; Kringelbach, 2005; Kringelbach & Rolls, 2004). As our task was specifically designed such that behavior could not be used to influence task feedback, it is not entirely clear why we (and May et al., 2004) found gain-related responses in lateral OFC, although this may reflect some more general property of value processing in response to gain (Elliott et al., 2003; Kringelbach, 2005; Kringelbach & Rolls, 2004; O'Doherty, Kringelbach, et al., 2001).

Also of interest is the posterior position of our lateral OFC region. As noted above, there is evidence in the literature that more abstract rewards, such as money, elicit activation in more anterior portions of OFC, while primary rewards elicit activation in more posterior portions of OFC (Kringelbach & Rolls, 2004; Sescousse et al., 2010). However, we did not have clear hypotheses regarding whether we would observe valence effects in posterior versus anterior OFC, given of our combination of elements from secondary- and primary-reward tasks (timing of reward delivery and reward type, respectively). Interestingly, studies using monetary CGGs have reported valence effects in anterior portions of the OFC, while in our candy version, valence effects were observed more posteriorly (Forbes et al., 2010; May et al., 2004). Thus, our results are generally consistent with an anterior–posterior gradient of secondary (abstract) to primary rewards in OFC responses. However, the OFC is a difficult region of the brain to image, and the signal within our sample was much stronger in posterior than in more anterior portions of the OFC. Thus, these OFC results should be interpreted as a positive finding regarding valence effects in posterior OFC, but not as a strong null finding regarding anterior OFC response to primary-like rewards, as their absence could reflect reduced signal quality.

Other regions identified as showing significant valence effects in our candy version of the CGG, including regions of the amygdala, hippocampus, thalamus, and insula, have mixed support from other monetary CGG studies. Regions of thalamus are constantly identified in CGG studies, but support is mixed as to whether the thalamus shows general responsivity to the task (e.g., main effect of time) or to

valence-specific effects (Delgado et al., 2003; Delgado et al., 2000; Delgado et al., 2004; Forbes et al., 2010; May et al., 2004; Tricomi et al., 2006). Studies that have reported thalamic valence effects have shown greater activity to reward than to loss feedback, in line with our results (Delgado et al., 2003; Tricomi et al., 2006). We also observed greater activation to gain than to loss trials in the amygdala. This result is consistent with a hypothesized role for the amygdala in processing affectively salient stimuli. However, surprisingly, previous CGG studies have not reported modulation of amygdala activity as a function of valence (Elliott et al., 2003; Forbes et al., 2010; Knutson et al., 2001; Sescousse et al., 2010). We observed greater *de*activation in the hippocampus to loss than to gain events, but again, previous CGG studies have not shown hippocampal modulation. Insula regions have been identified in several CGG studies (e.g., Delgado et al., 2000; Delgado et al., 2004), but only one study reported significant valence effects (Tricomi et al., 2006). In this prior study, the insula region displayed greater activation to loss than to reward, the opposite pattern of activity we report. However, our insula region (35, –5, 16) was located anterior and medial to the region identified by Tricomi et al. (2006). The majority of CGG studies have focused on effects of valence within the striatum, whereas we chose to focus on regions within a much larger a priori mask. It is possible that previous CGG studies failed to find valence effects in regions such as the amygdala and hippocampus simply because the effects fell outside of a priori regions of interest, and thus were subjected to a higher statistical threshold.

Magnitude effects

Other groups using the CGG have found interactions between valence and magnitude particularly within the caudate (Delgado et al., 2003; Elliott et al., 2000). Unlike these other studies, we did not find a significant interaction between feedback valence (gain, loss) and magnitude (high, low) within the dorsal striatum, although we did observe significant valence effects in the caudate. A possible explanation for this result could be that the difference between the high- and low-magnitude conditions was not large enough to elicit significantly different striatal responses between high and low trials, or that the effect size is small in this paradigm, and more trials would be needed to detect such a relationship. Importantly, particularly for future between-group developmental studies, it is possible that healthy young adults who receive monetary compensation for their time are not engaged sufficiently by winning or losing a few small candies to elicit parametric modulation of the BOLD response by outcome "value," though it is possible that such differences in amounts of candy would be more salient in younger children.

Individual-difference effects

We observed a relationship between task-related activity in several striatal/insular regions and individual differences in reward and punishment sensitivity (BIS/BAS total scores), but failed to identify any regions showing task activity related to our hedonics composite score (Carver & White, 1994). Interestingly, BAS scores were related to loss rather than to gain responses. Specifically, bilateral regions of the caudate displayed a negative correlation between BAS and the difference in response to high-loss and low-loss feedback. This correlation was related to reduced response to low-loss feedback in individuals with lower BAS total scores. The right caudate region also displayed a positive correlation between BAS and the difference in responses to low-loss and neutral feedback. This correlation was related to both decreased response to low-loss and increased response to neutral feedback in individuals with lower BAS scores. Similar correlations with BAS and task activity were found within a region of right lateral OFC that also displayed greater response to high-gain feedback than to low-gain, neutral, and loss feedback in the main analyses. Again, individuals with increased reward sensitivity showed reduced differences between different levels of loss.

Our individual-difference results are a bit counterintuitive, given evidence that reward sensitivity (BAS) is traditionally thought to relate to processing of appetitive stimuli, and punishment sensitivity (BIS) to relate to aversive processing. However, some evidence has linked BAS with negative affect following significant events (Carver, 2004). Our results suggest that individuals who are more sensitive to reward show reduced responses to low losses within the striatum, potentially suggesting a heightened sensitivity to minor losses. In contrast, they also suggest that individuals more sensitive to punishment show increased response to the best gain option and less response to the worst gain option, potentially suggesting more sensitivity to the relative "bad" versus "good" options within available gains. Given that most of the previous studies examining individual differences in punishment and reward sensitivity have used monetary rewards, it will be important to directly compare these individual relationships for monetary versus more primary rewards in future studies.

Also of note are our null findings involving the composite hedonics variable HED. Although other studies have reported negative relationships between striatal activation during reward and anhedonia in control samples, it is possible that we simply did not have enough power and/or that our nonclinical population did not have enough variance in hedonic tone to detect this relationship (Dowd & Barch, 2010, 2012).

Limitations and future directions

Although we observed results that were largely consistent with those of other CGG studies, interpretation of results that differed from those of monetary studies would be strengthened by future within-subjects studies designed to directly compare responses to candy and monetary incentives. Because we were interested in designing a paradigm appropriate for use across a wide developmental spectrum, we chose to use small amounts of candy delivered postscan as an incentive. While we believe that this paradigm has promise for developmental applications, it is by no means the only option, and is not entirely free of potential developmental confounds. Studies utilizing and directly comparing responses to other incentive types (e.g., food odors, liquid rewards, and even social rewards) and structures (e.g., token economies), while they are perhaps more difficult to implement for developmental questions, are certainly warranted to empirically evaluate which methods are best designed to address developmental incentive-processing questions.

We chose to focus our individual-difference analyses on self-report measures of reward/punishment sensitivity, but interesting individual differences within task behavior that we did not investigate may influence group-level task responses. For example, interesting individual differences are likely to exist in how the neutral condition is interpreted (positively, as successfully avoiding loss; negatively, as failing to obtain a gain; or maybe as a combination of the two, depending on what feedback has recently occurred). Also, although this task was explicitly designed to elicit responses to gain/loss that were independent of any ongoing learning, it is possible that some individuals did try to adjust their behavior in an organized attempt to obtain more gains. Studies with larger and more diverse samples would be better designed to investigate these questions.

Future studies will also be needed to determine the influence of the timing of reward delivery (in-scanner vs. postscan) on incentive processing. In-scanner ratings of hedonic and/or affective response to the different feedback types/amounts would also have strengthened our interpretations and ensured that participants were actively engaged in the task over the course of the entire experiment. Thus, our results are an important first step in establishing methods for delivering primary rewards in a manner congruent with traditional monetary studies, but validation in larger, more diverse samples will be needed for both our individual-difference and valence effects.

Conclusions

We aimed to create a modified version of the CGG that would both be appropriate for developmental populations and allow for more direct comparison with secondary-reward paradigms. As hypothesized, we observed differential activity to gain and loss feedback in the striatum, amygdala, and OFC. Unlike other monetary CGG studies, a posterior OFC region displayed valence-dependent activation in our task. This finding potentially supports an anterior/posterior distinction in OFC response to abstract/primary rewards, but poor anterior OFC signal quality could also explain these null results. Overall, our results show strong continuity with previous studies using both primary and secondary rewards, and provide an important baseline for use of this paradigm with child and other special populations.

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