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Dorsal striatum responses to reward and punishment: Effects of valence and magnitude manipulations

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The goal of this research was to further our understanding of how the striatum responds to the delivery of affective feedback. Previously, we had found that the striatum showed a pattern of sustained activation after presentation of a monetary reward, in contrast to a decrease in the hemodynamic response after a punishment. In this study, we tested whether the activity of the striatum could be modulated by parametric variations in the amount of financial reward or punishment. We used an event-related fMRI design in which participants received large or small monetary rewards or punishments after performance in a gambling task. A parametric ordering of conditions was observed in the dorsal striatum according to both magnitude and valence. In addition, an early response to the presentation of feedback was observed and replicated in a second experiment with increased temporal resolution. This study further implicates the dorsal striatum as an integral component of a reward circuitry responsible for the control of motivated behavior, serving to code for such feedback properties as valence and magnitude.

Rewards play an important role in motivated behavior. The hedonic properties of a potential reward can lead to approach behavior and a sense of pleasure after consumption, serving to reinforce such behavior (Schultz, 2000). Thus, it is important to consider how the human brain perceives different properties of a salient stimulus, such as valence and magnitude. The striatum is one of several regions implicated by previous research in the processing of reward-related information. Activity in the striatum has an important role in detecting the presence of an affective stimulus (Apicella, Ljungberg, Scarnati, & Schultz, 1991; Hikosaka, Sakamoto, & Usui, 1989; Hollerman, Tremblay, & Schultz, 2000), its predictability (Berns, McClure, Pagnoni, & Montague, 2001; Pagnoni, Zink, Montague, & Berns, 2002; Schultz, Tremblay, & Hollerman, 1998), and the valence—reward or punishment—associated with such a stimulus (Breiter, Aharon, Kahneman, Dale, & Shizgal, 2001; Delgado, Nystrom, Fissell, Noll, & Fiez, 2000). The striatum, therefore, seems to be in a position to influence and guide behavior by coding the affective properties of a stimulus. To exert such a function, the striatum should also have the capacity to rank feedback according to magnitude or preference. Accordingly, when presented with feedback, the striatum should parametrically order its response in accordance with the valence and magnitude of the feedback.

As was previously discussed, a variety of data strongly supports the involvement of both the dorsal and the ventral striatum in a circuit responsible for detecting a reward-related stimuli and further detecting its valence. Less is known, however, about how the striatum responds to other stimulus properties, such as magnitude. The literature has shown that magnitude manipulations affect activity in other areas implicated in a potential reward circuitry—mostly, the prefrontal cortex and the amygdala. For example, a correlation exists between the speed at which rats run down a runway to retrieve a reward and the magnitude of such a reward (Crespi, 1942). After amygdala lesions, rats become insensitive to reductions in the reward amount (Salinas, Packard, & McGaugh, 1993). In monkeys, enhancement of activity was observed in the dorsolateral prefrontal cortex during the memory phase of a visual-memory task for trials associated with a large versus a small reward (Leon & Shadlen, 1999). The orbital frontal cortex, an area heavily implicated in emotion (Bechara, Damasio, & Damasio, 2000; Grant, Contoreggi, & London, 2000; Rolls, 1999, 2000), is also affected by changes in magnitude. In humans, for example, the orbital frontal cortex was active in a paradigm in which participants chose between small likely rewards and large unlikely rewards (Rogers et al., 1999) and in a reversal learning paradigm in which different magni-

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tudes of reinforcement were given (O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001).

One area that receives projections from both the frontal cortex (Haber, Kunishio, Mizobuchi, & Lynd-Balta, 1995; Middleton & Strick, 2000) and the amygdala (Groenewegen, Wright, Beijer, & Voorn, 1999) is the striatum, where magnitude effects and even investigations of magnitude manipulations have been less frequently reported. Recently, Hassani, Cromwell, and Schultz (2001) showed that monkey striatal neurons fire more vigorously for preferred rewards, suggesting that some ranking based on preference may occur in the striatum. In a clever paradigm, Breiter et al. (2001) found higher ventral striatum activity associated with higher outcomes in a "wheel of fortune" like task. A more direct measurement of the effects of magnitude in the striatum was done by Knutson, Adams, Fong, and Hommer (2001), who scanned participants while they anticipated rewards and punishments that varied in amounts. The study showed that ventral striatum activity was associated with anticipation of larger rewards, whereas the dorsal striatum was activated while both rewards and punishments of larger magnitude were anticipated. Although in this study magnitude changes in the striatum were looked at, the primary focus was on the effects of magnitude in the anticipatory phase. Thus, more research is needed to fully understand how the striatum responds to the actual delivery of rewards and punishments of different magnitudes.

In a previous study, we developed a gambling task (card-guessing paradigm) in which participants were asked to guess the value of a card (Delgado, Nystrom, et al., 2000). A correct guess yielded a monetary reward, whereas an incorrect guess led to a monetary punishment. Using an event-related design, we observed differential responses to reward and punishment feedback in the striatum, where the hemodynamic response for rewards was significantly higher than that for punishments in the 6- to 9-sec time window after feedback presentation. In this paper, we will further examine the previously observed dissociation of valence in the striatum by studying how the response is affected by the magnitude of the outcome. In our first experiment, we used a modified version of the card-guessing paradigm to measure striatal activity following the delivery of monetary rewards and punishments that varied parametrically. The outcomes were either a large ($4.00) or small ($0.40) monetary reward or a large ($2.00) or small ($0.20) monetary loss. The primary goal was to replicate the differences in activation according to valence and to go beyond prior studies by varying the magnitude of the outcome—thus providing further evidence that the striatum influences or guides motivated behavior by processing the motivational properties of a stimulus.

In our previous study (Delgado, Nystrom, et al., 2000), we also observed a differential response to punishments and rewards that evolved within 3 sec of feedback presentation. The rapidity of this response caused us to question its reliability. Although it is likely that the presentation of a surprising and affective stimulus (e.g., a bear appearing from nowhere) causes fast, immediate cognitive and physiological responses, our understanding of the properties of the hemodynamic response limits any possible interpretation. Hence, a secondary goal of this research was to determine whether an early response (of less than 3 sec) to a feedback could be replicated and further characterized temporally. This was accomplished by examining the activation detected within 3 sec of feedback presentation in the first experiment and by running a second experiment with increased temporal sampling.

EXPERIMENT 1

Method

Participants. Twenty right-handed volunteers participated in this study (11 females, 9 males). The participants were mostly graduate and undergraduate students drawn from the University of Pittsburgh (average age = 22.9 years, *SD* = 3.26). Two participants were removed from all analysis because of excessive motion during their scan sessions. The participants were asked to fill out a brief questionnaire to ensure that they had prior experience with gambling but were not abusive or excessive in such behavior (i.e., have you played cards for money: not at all, less than once a week, or once a week or more). The questionnaire was based on the South Oaks Gambling Screen (Lesieur & Blume, 1987). Information about any family history of gambling was not acquired. All the participants gave informed consent according to the policies of the Institutional Review Board at the University of Pittsburgh.

Cognitive task. The paradigm involved a series of 144 interleaved trials, divided into nine runs of 16 trials each. Each trial lasted 15 sec and began with the presentation of a visually displayed card projected onto a screen. The card had an unknown value ranging from 1 to 9, and the participant was instructed to make a guess about the value of the card. A question mark appeared in the center of the card, indicating that the participant had 2.5 sec to guess whether the card value was higher or lower than the number 5. The participant pressed the left or the right button of a response unit to indicate his or her selection. After the choice-making period, a number appeared in the center of the card for 500 msec, followed by an arrow that was also displayed for another 500 msec. The appearance of a green arrow pointing upward indicated that the participant had correctly guessed the card value. A large green arrow corresponded to a large reward of $4.00. A smaller green arrow indicated a small reward of $0.40 (Figure 1A). The appearance of a red arrow pointing downward indicated that the participant had incorrectly guessed the card value, leading to a penalty of $2.00 if the arrow was large and a $0.20 penalty if the arrow was small. Unlike our previous design (Delgado, Nystrom, et al., 2000), there was no neutral condition, and the number 5 never appeared as the value of a card. Therefore, there were four types of trials (large and small reward and large and small punishment). The same gain-to-loss ratio as that from our previous design was kept (2:1), in accordance with classic decision-making literature suggesting that the impact of negative outcomes, such as losses, is larger than that of positive outcomes, such as gains (Kahneman & Tversky, 1979; Tversky & Kahneman, 1981). For trials in which a response was not made on time, the feedback was a pound sign (#), and such trials were excluded from all analyses. After the 3.5-sec period between presentation of the response cue (question mark) and the reward/punishment outcome, there was an 11.5-sec delay before the onset of the next trial. An experimental session, therefore, consisted of 144 trials of 15 sec

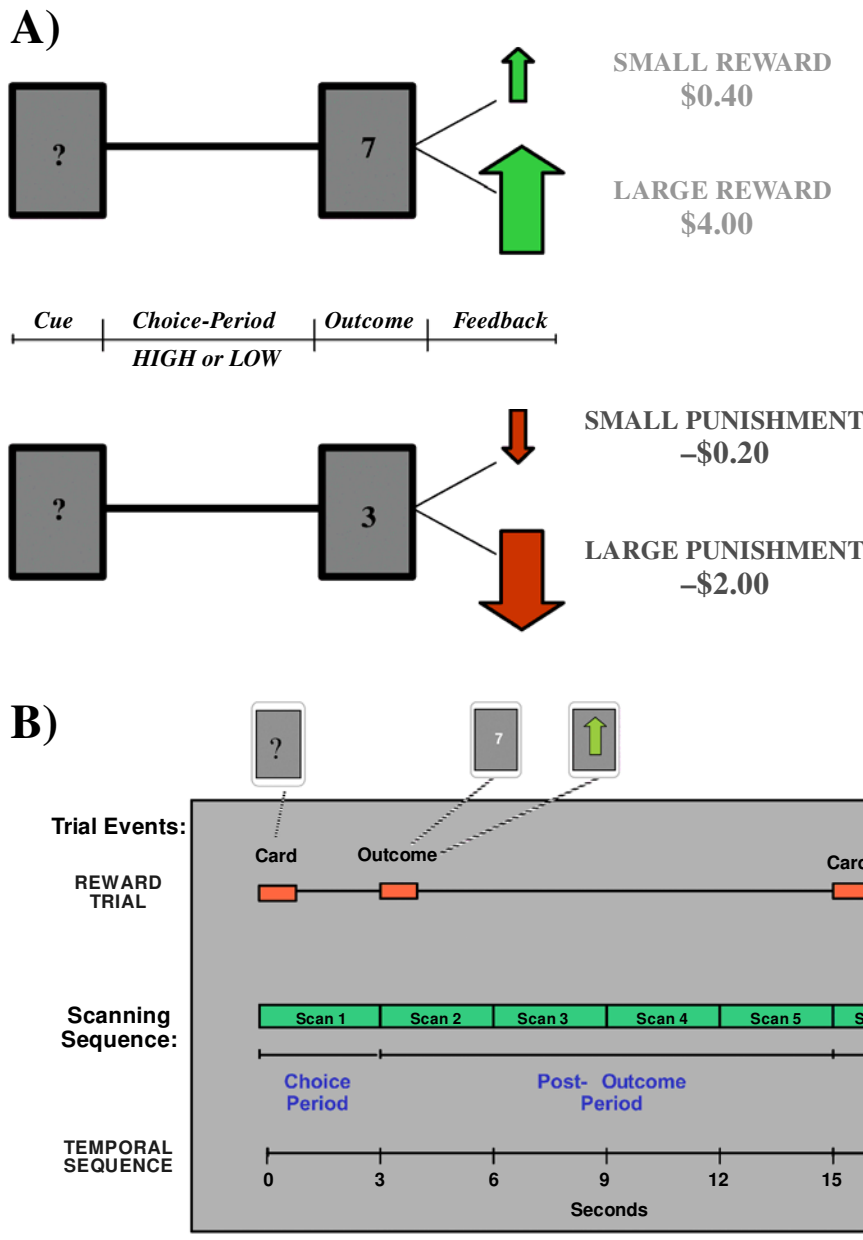

Figure 1. (A) Description of task and events in card-guessing paradigm: large reward, small reward, large punishment, and small punishment. The sequence of events is depicted in the timeline, where cue (presentation of a question mark) is the first event, followed by the choice-making period, during which the participants were asked to guess whether the value of the presented card was higher or lower than 5. After a choice was made, the value of the card was revealed (outcome), and this was followed by reward or punishment feedback that varied according to magnitude. (B) Temporal and scanning sequence of events in one trial. A single trial consisted of five scans of 3 sec each (total, 15 sec). Analysis was performed during the postoutcome period (T2–T5).

each (Figure 1B). Stimulus presentation and behavioral data acquisition were controlled by a Macintosh computer with PsyScope software (Macwhinney, Cohen, & Provost, 1997).

Unbeknownst to the participant, the outcome of each trial was predetermined to be of a specific valence and magnitude. Card values were selected only after the participant had indicated his or her guess on each trial. Each participant performed 36 trials of each condition. The nine runs were broken down into three groups: Group A had more reward trials during the beginning of the task, whereas Group B had more punishment trials and Group C was evenly matched. This allowed for counterbalancing of runs across participants to help minimize effects of scanner drift. The participants were told they could keep the final sum of monetary outcomes at the end of the experiment, although they were not given information regarding cumulative earnings throughout the session.

Data acquisition and analysis. A conventional 1.5-T GE Signa whole-body scanner and standard RF coil were used to obtain 20 contiguous slices (3.75 × 3.75 × 3.8 mm voxels) parallel to the

AC-PC line. Structural images were acquired in the same locations as the functional images, using a standard T1-weighted pulse sequence. Functional images were acquired using a two-interleaved spiral pulse sequence (TR = 1,500 msec, TE = 34 msec, FOV = 24 cm, flip angle = 70°; Noll, Cohen, Meyer, & Schneider, 1995). This T2*-weighted pulse sequence allowed 20 slices to be acquired every 3 sec. Images were reconstructed and corrected for motion with AIR (Woods, Cherry, & Mazziotta, 1992), adjusted for scanner drift between runs with an additive baseline correction applied to each voxel-wise time course independently, and were detrended with a simple linear regression to adjust for drift within runs. Structural images of each participant were coregistered to a common reference brain (Woods, Mazziotta, & Cherry, 1993). Both statistical maps created in analysis and the reference brain were transformed to standard Talairach stereotaxic space (Talairach & Tournoux, 1988), using AFNI software (Cox, 1996). Functional images were then globally mean-normalized to minimize differences in image intensity within a session and between subjects and were smoothed, using a three-dimensional Gaussian filter (4-mm FWHM) to account for between-subjects anatomic differences. Peak activity of each region of interest was reported using Talairach coordinates (Talairach & Tournoux, 1988).

A repeated measures three-way analysis of variance (ANOVA) was performed on the entire set of coregistered data, with participants as a random factor. Within-subjects factors included valence (reward or punishment), magnitude (large or small), and time (the postoutcome period: four sequential 3-sec scans in a trial of 15 sec, referred to as T2–T5). The first scan (T1 period) represented the choice-making period and was not included in the analysis. Comparisons of interest included interactions of each factor (magnitude and valence) with time (T2–T5), because these should consistently capture differences in the time course of the blood oxygen level dependent (BOLD) response associated with each trial type. Special focus was given to the three-way interaction between magnitude, valence, and time [$F(3,51) = 4.81$, $p < .005$]. Our previous work (Delgado, Nystrom, et al., 2000) supports the assumption that changes in our selected variables (e.g., valence) can be better characterized by examining activity over the duration of a single trial (e.g., time). Regions of interest (ROIs) consisting of five or more contiguous voxels were selected, as a precaution against Type 1 errors (Forman et al., 1995). Inferences were therefore made on regions defined by strength of effect ($p < .005$) and size (5 or more voxels). To confirm and extend the ANOVA findings, post hoc one-tailed t tests were performed at specific time points, using event-related time series data for each ROI, to provide fMRI mean intensity value for each condition for Time Periods T1–T5. The focus of these analyses was Time Point T4, which occurred in the 6 to 9 sec time window after the presentation of a reward. This was the time period in which the biggest differentiation between reward and punishment had been observed in the previous study, as well as the period in which the difference should be most pronounced due to the hemodynamic lag, which usually results in a peak of activity 4–6 sec after presentation of an event (Kwong et al., 1992). A secondary analysis, motivated by prior results, was performed to further investigate any response at Time Point T2 (during the initial 3 sec when the reward was presented).

Results

I. Interaction of time, magnitude, and valence. The main comparison of interest was the three-way interaction between magnitude and valence over time (Table 1). Areas identified by this analysis [$F(3,51) = 4.81$, $p < .005$] were the left angular gyrus, which decreased in activity, the left lingual gyrus, which initially showed a decrease in activation followed by an increase, and the left dorsal striatum, where the activity was localized to the caudate nucleus.

The activation in the left caudate nucleus was characterized by the previously observed pattern of sustained activation for a reward event, as opposed to a decay below baseline for punishment events (Delgado, Nystrom, et al., 2000). The critical difference between reward and punishment was observed 6 sec after the presentation of the feedback, when a typical hemodynamic response would be expected. A differential response between valences was observed when the outcome magnitude was small (Figure 2A) and when it was large (Figure 2B). Thus, irrespective of magnitude, the left dorsal striatum differentiated between reward and punishment.

In addition, the magnitude of an outcome, as indicated by the three-way interaction, did influence the response of the caudate nucleus (Figure 3). The highest activation was associated with the large reward trials, followed by the small reward trials. The lowest activation was associated with large punishment trials, whereas small punishment trials were slightly higher. One-tailed, paired t tests were performed post hoc to determine whether the four conditions (large and small reward and large and small punishment) significantly differed during the 6- to 9-sec time window after the outcome (Time Point T4). Large reward was higher than small reward [$t(17) = 2.25$, $p < .05$]. Similarly, small punishment was higher than large punishment [$t(17) = 2.07$, $p < .05$]. Small reward was significantly higher than small punishment [$t(17) = 2.91$, $p < .01$], and large reward was higher than large punishment [$t(17) = 6.04$, $p < .0001$]. Thus, a parametric ordering according to magnitude of the outcome was observed in the left caudate nucleus.

The inverse pattern was observed during the initial 3 sec after the feedback was presented (Time Point T2). Large punishment produced the highest activation, and it was significantly higher than large reward [$t(17) = 4.42$, $p < .001$]. Although small punishment was of a higher order than small reward, the two conditions were not differentiated at Time Point T2 [$t(17) = 0.2$, $p = .58$]. The parametric order of this early response, therefore, was almost the complete inverse of the later response that occurred at the 6- to 9-sec time window, although the differences between the conditions were less robust.

Activity in the other two ROIs identified by this contrast was marked by decreases in activation from the onset of the trial. The left angular gyrus showed a decrease from the onset of the trial, with large reward events showing a sharper decrease then all other events at later time points, before its eventual return to baseline at the end of the trial. The left lingual gyrus showed an initial decrease in activ-

Table 1
Interaction of Magnitude, Valence, and Time

Region of Activation	Brodmann Areas	Talairach Coordinates			Average F Ratio
		x	y	z	
Left angular gyrus	39	−38	−62	35	5.71
Left caudate nucleus		−11	12	7	5.94
Left lingual gyrus	18	−3	−56	3	5.31

Note—$p < .005$.

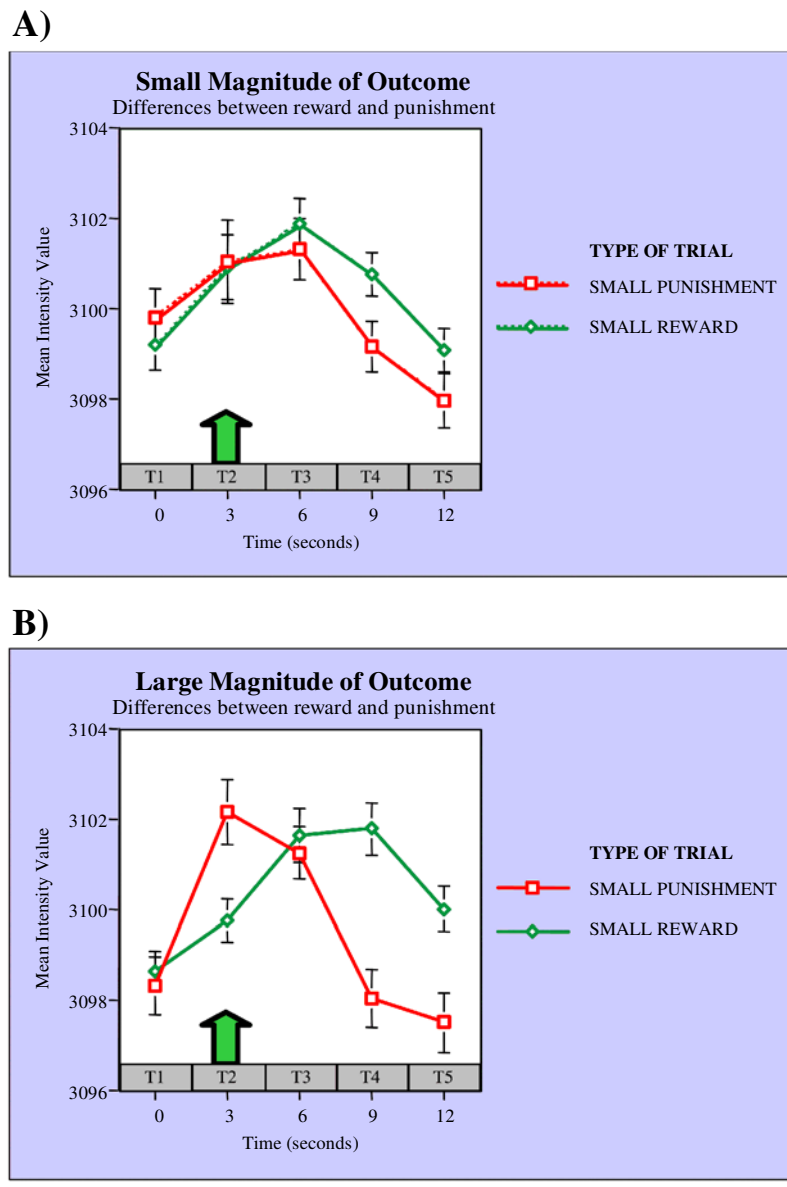

Figure 2. Time series for left caudate nucleus showing that irrespective of magnitude, the dorsal striatum differentiates between reward and punishment. There was an increase in activation at the onset of the trial that was sustained when a reward was received and that decayed when a punishment was received, during both the small magnitude comparison (A) and the large magnitude comparison (B). Standard error bars were calculated on a per participant basis across both time and conditions. The fMRI mean intensity value is displayed on the *y*-axis, whereas the temporal frame of a trial, 15 sec per trial, is displayed in the *x*-axis (time in seconds). The green arrow represents the onset of the feedback arrow (reward or punishment) according to the temporal frame of the trial (3 sec after the onset of the trial). The scan progression (T1–T5) is also displayed above the time scale (gray boxes), and each data point in the graph represents one scan acquisition or time point.

ity, followed by a sharp increase after Time Point T2. The pattern of activation following the increase was highest for large reward and next highest for large punishment, followed by small reward and small punishment trials (at Time Point T4). This ROI appeared to be coding the size of the visual stimulus (the large arrows), followed by either color or orientation (green or red or pointing up or down). The lingual gyrus may extract details from the presented visual stimulus, and indeed, it has been linked with identification of such stimuli as landscapes and buildings (Takahashi & Kawamura, 2002). However this suggestion deserves future research, since at the onset of the trial,

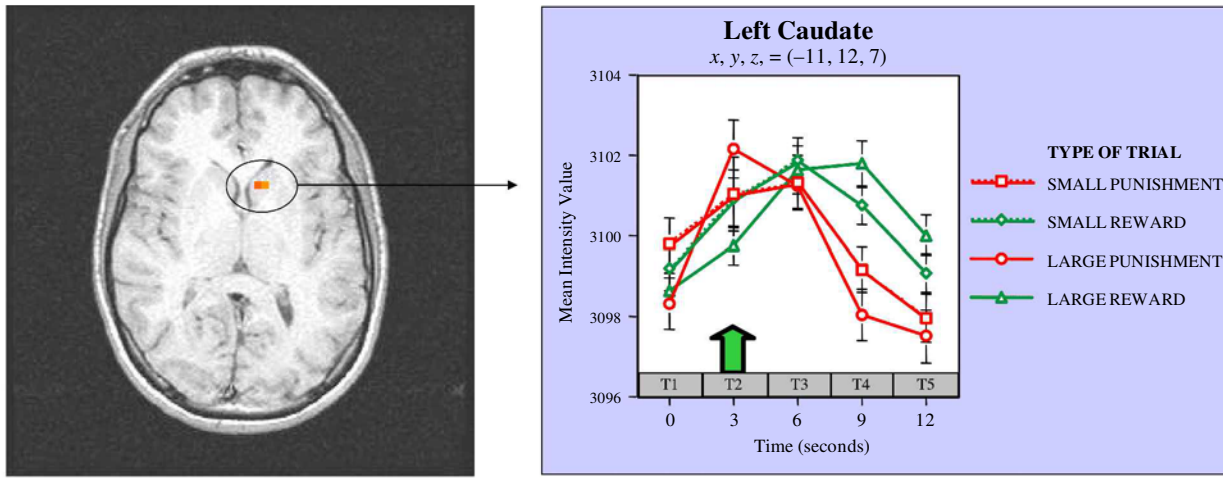

Figure 3. Activation of the left caudate nucleus (dorsal striatum) identified by a three-way interaction of magnitude, valence, and time. During the 6- to 9-sec time window after the delivery of a feedback (Time Point T4), a parametric ordering was observed, since the largest activation was large reward, followed by small reward, then small punishment, and finally large punishment. The inverse ordering was observed during the initial 3 sec after the feedback was presented (Time Point T2), during which an early response to large punishment was higher than that to large reward.

there was a decrease in activation and the literature of BOLD fMRI has yet to fully provide an understanding of what such decreases from the onset of trials signify.

II. Interaction of time and magnitude. Regions that varied with magnitude over time are listed in Table 2 [$F(3,51) = 4.81, p < .005$]. Activation was observed in the cuneus and the lingual gyrus, where the large magnitude trials had a higher signal than did the small trials. A similar pattern was observed in the parahippocampal gyrus: The activation showed an increase when feedback was revealed, and large reward events had the highest signal. The overall pattern observed in these regions suggests that the activity was driven mostly by the size of the arrows, although an effect of valence (such as an influence of reward in the parahippocampal gyrus) cannot be discounted.

III. Interaction of time and valence. A contrast of the brain regions activated over time that differed according to valence yielded the ROIs shown in Table 3 [$F(3,51) = 4.81, p < .005$]. The largest effects were observed in the bilateral dorsal striatum and the thalamic nucleus, a replication of our previous experiment, where reward significantly differed from punishment (Delgado, Nystrom, et al., 2000). Other brain regions activated by this contrast that showed an increase in activity at the onset of the trial included the right inferior parietal cortex (BA 40) and the ventromedial frontal gyrus (BA 10). The inferior parietal ROI showed a higher response for punishment trials at later time points, a pattern opposite to the one observed in the ventromedial frontal ROI, where reward trials had a higher response, although a noisier time series was recorded in this ROI because of its proximity to the edge of the brain.

A set of other ROIs showed patterns of decreasing activation relative to baseline at the onset of the trial. In the middle frontal gyri (bilateral BA 6) and the right superior frontal gyrus (BA 9) ROIs, activity decreased sharply

Table 2
Interactions of Magnitude and Time

Region of Activation	Brodmann Areas	Talairach Coordinates *x*	*y*	*z*	Average *F* Ratio
Right middle frontal gyrus	8	35	35	45	5.33
Right precuneus	7	10	−67	38	5.79
Right posterior cingulate gyrus	31	7	−44	38	5.68
Right inferior parietal gyrus	40	42	−37	37	5.45
Right middle frontal gyrus	9	26	19	36	5.50
Left cuneus	18	−2	−76	16	6.47
Right occipital gyrus	19	29	−85	15	5.97
Right putamen/globus pallidus		27	−7	7	5.16
Left putamen/globus pallidus		−23	1	2	5.29
Left parahippocampal gyrus	30	−11	−40	−2	6.54
Right parahippocampal gyrus	30/19	16	−41	−4	6.76
Right lingual gyrus	19	−16	−52	−4	6.53

Note—$p < .005$.

Table 3
Interactions of Valence and Time

Region of Activation	Brodmann Areas	Talairach Coordinates			Average *F* Ratio
		x	*y*	*z*	
Right middle frontal gyrus	6	34	−18	40	6.27
Right superior frontal gyrus	9	32	39	38	6.16
Left middle frontal gyrus	6	31	−13	38	5.73
Right inferior parietal gyrus	40	57	−34	33	6.44
Right cingulate gyrus	24	20	−1	27	6.68
Left cingulate gyrus	24	−12	−3	27	6.06
Right middle frontal gyrus	9/46	51	38	26	5.45
Left middle frontal gyrus	9/46	−38	38	24	6.82
Left cuneus	18	−1	−95	19	6.10
Right thalamus		5	−24	12	10.33
Left caudate nucleus		−8	11	7	11.55
Right caudate nucleus		15	18	7	6.79
Right ventromedial frontal gyrus	10	4	60	−2	6.46
Left ventral striatum		−4	12	−5	6.60
Right ventral striatum		15	11	−5	5.55

Note—$p < .005$.

at the onset of the trial, showing a larger decrease for reward events than for punishment events at later time points. A similar pattern was observed in both right and left cingulate gyrus ROIs, where the reward events decreased more than the punishment events at later time points, before returning to baseline at the end of the trial.

Other regions showed an initial decrease in activation, followed by a rise above baseline at Time Point T2. In the left and right middle frontal gyrus ROIs (BA 9/46), the rise above baseline was highest for punishment trials, whereas in the cuneus the rise was highest for reward trials.

In summary, this contrast identified regions that exhibited both increasing and decreasing patterns of activation across time. On the basis of our prior work, we were most interested in ROIs that showed an initial increase of activity. These ROIs included a cortico-striatal loop comprising the bilateral striatum, the thalamus, and the right ventromedial frontal gyrus, all of which showed a higher response for reward than for punishment trials. The right inferior parietal was also activated showing the opposite pattern (punishment higher than reward).

The left-striatum ROI included two peaks of activity: one in the dorsal and one in the ventral portions of the striatum (at or near the nucleus accumbens). Further analyses were performed to investigate hemodynamic responses in the ventral striatum. Although a significant three-way interaction between time, valence, and magnitude was not observed in the ventral striatum, this region did show an interaction between time and valence. The locus of activity in the left ventral striatum showed a pattern of response similar to that observed in the left dorsal striatum, where reward was significantly higher than punishment at T3 [$t(17) = 3.73, p < .01$] and a trend was observed at T4 [$t(17) = 1.50, p < .08$]. Interestingly, no significant differences between conditions were observed at T2 in this ventral striatum focus [$t(17) = 0.16$, $p = .44$], similar to the null effect observed in our previous study (Delgado, Nystrom, et al., 2000).

Thus, although dorsal and ventral striatum responses appear to be similar during the 6- to 9-sec time window after reward delivery, the largest effects are observed in the dorsal striatum. Furthermore, an early response seems to be observed only in the dorsal striatum. To further understand the validity of the differential responses observed during the initial 3 sec after feedback presentation, we conducted Experiment 2, which was a replication of the present experiment with increased temporal resolution.

EXPERIMENT 2

Method

Twelve different paid volunteers participated in Experiment 2 (6 males, 6 females; average age = 24.58 years, *SD* = 3.8). Two participants were removed from final analysis due to excessive motion and artifact-induced noise in their data sets. The cognitive task was identical to the first experiment. The only difference was in the imaging parameters, where functional images were acquired using a one-shot spiral pulse sequence (TR = 1,500 msec, TE = 34 msec, FOV = 24 cm, flip angle = 70°; Noll et al., 1995). This allowed for greater temporal resolution (1.5- vs. 3-sec scans) and the acquisition of 10, rather than 5, time points. Because of a smaller sample size and a more restricted focus of the investigation, we looked at ROIs defined by the interaction of condition and time, where valence was collapsed across magnitude to increase the number of trials for each condition (Table 4).

Results

A repeated measures two-way ANOVA was performed [$F(7,63) = 4.39, p < .0005$], and the left caudate,

Table 4
Experiment 2: Interaction of Valence and Time

Region of Activation	Brodmann Areas	Talairach Coordinates			Average *F* Ratio
		x	*y*	*z*	
Right cuneus	18	2	−76	18	5.61
Right thalamus		6	−24	11	5.32
Left caudate nucleus		−11	11	5	5.42

Note—$p < .0005$.

the thalamus, and the cuneus showed an interaction of valence (reward vs. punishment) and time (T3–T10, each time point reflecting 1.5 sec). Focusing on the striatal activation, one can see a result similar to that shown in the valence × time interaction of Experiment 1, where reward trials were significantly higher than punishment events (Figure 4). Two-tailed, paired *t* tests of all striatal time points confirmed a difference for reward versus punishment trials during the 6- to 9-sec time window after delivery of a feedback: Time Points T7 [$t(9) = 4.72$, $p < .01$] and T8 [$t(9) = 2.53$, $p < .05$; corresponding to T4 in Experiment 1]. In previous work (Delgado, Nystrom, et al., 2000) and in Experiment 1, punishment events had a higher signal than did reward outcomes during the initial 3 sec when the reward was presented (Time Point T2, corresponding to T3 and T4 in Experiment 2). The faster temporal acquisition allowed us to observe that in Experiment 2, the higher punishment response was not significant at T3 [0–1.5 sec after the feedback; $t(9) = 1.93$, $p = .09$], but was significant at T4 [1.5–3 sec after feedback; $t(9) = 2.83$, $p < .05$]. This response was exclusive to the caudate nucleus, since thalamic activation did not show significant differences between reward and punishment trials during Time Points T3 [$t(9) = 0.15$, $p = .89$] and T4 [$t(9) = 0.32$, $p = .76$], although there was an effect of valence in the thalamus during the 6- to 9-sec time window after delivery of feedback [T7, $t(9) = 2.94$, $p < .05$; T8, $t(9) = 5.23$, $p < .05$]. Exploratory analysis revealed a small ventral striatum focus [$F(7,63) = 3.27$, $p < .005$; 4 voxels] that did not show a difference during the 3 sec after presentation of a feedback [T3, $t(9) = 1.53$, $p = .16$; T4, $t(9) = 1.33$, $p = .22$] but did show a higher response for reward trials at T7 [$t(9) = 3.5$, $p < .05$].

Thus, the results of Experiments 1 and 2 suggest that the dorsal striatum is activated after presentation of an affective stimulus and that such activation is sensitive to the valence and magnitude of a stimulus. The reward response is more sustained and significantly higher than punishment during the 6- to 9-sec time window after the presentation of a reward. The punishment response shows an early peak, roughly 1.5–3 sec after the presentation of a punishment feedback, which decreases below baseline until the onset of the next trial. The early response appears to be limited to the dorsal striatum. Significant differences in the 1.5- to 3-sec time window were not found in the thalamus or ventral striatum in either Experiment 1 or Experiment 2, although in both experiments these regions were sensitive to valence in the later 6- to 9-sec time window.

GENERAL DISCUSSION

The goal of these experiments was to further our understanding of how the human striatum responds to the delivery of an affective feedback. Using a modified version of a gambling paradigm, in which the delivery of rewards and punishments varied according to magnitude, we found that the dorsal striatum differentiated between the valence of an event (reward and punishment) irrespective of the magnitude (large or small). Furthermore, during the 6- to 9-sec time window after the delivery of an outcome, the dorsal striatum activation was parametrically arranged according to magnitude, where large reward yielded the highest signal and large punishment the lowest signal. An early response to the presentation of a feedback was also observed and replicated in a second, follow-up experiment in which the temporal sampling was increased.

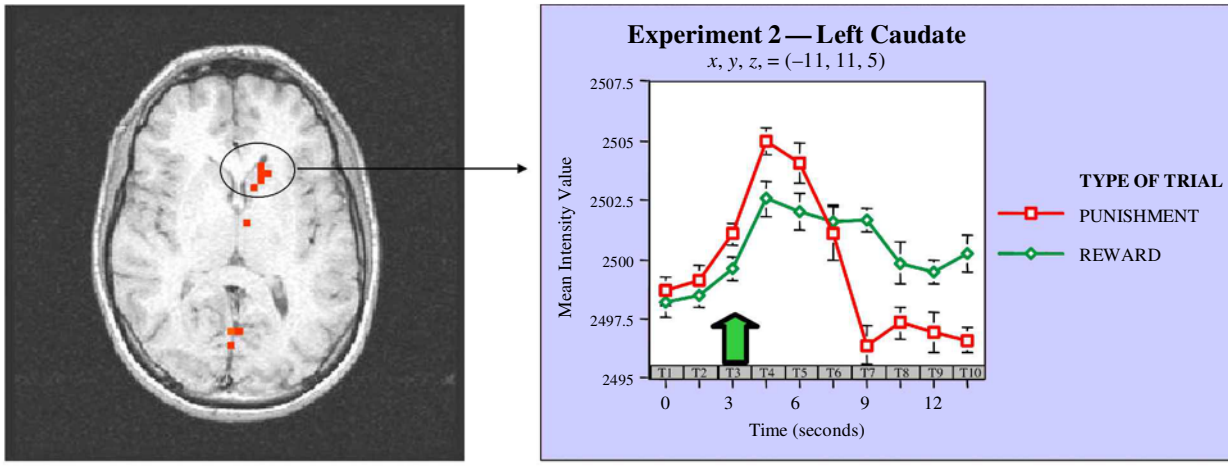

Figure 4. Activation of the left caudate nucleus in Experiment 2, where the paradigm from Experiment 1 was replicated with greater temporal resolution (1.5-sec scans). Identified by an interaction of valence and time, the left caudate nucleus showed differential responses to reward and punishment during the 6- to 9-sec time window after delivery of feedback (T7 and T8). A higher response to punishment was observed during the 1.5- to 3-sec time window after feedback presentation (T4), suggesting that an early response was evoked by the feedback presentation.

Converging support for our findings come from prior studies of reward processing in animals and humans. For example, single-cell studies have shown striatal responses to both the anticipation of a reward (Apicella, Scarnati, Ljungberg, & Schultz, 1992; Hikosaka et al., 1989; Schultz, Apicella, Scarnati, & Ljungberg, 1992) and the reception of a rewarding event, such as a drop of liquid (Aosaki et al., 1994; Apicella et al., 1991; Hikosaka et al., 1989; Shidara, Aigner, & Richmond, 1998). Specific recordings in the caudate nucleus have shown both that neurons in this area are modulated by the expectation of a reward (Hollerman, Tremblay, & Schultz, 1998; Kawagoe, Takikawa, & Hikosaka, 1998) and that they are sensitive to the reception of a stimulus of positive valence (Aosaki et al., 1994; Apicella et al., 1991; Hikosaka et al., 1989; Shidara et al., 1998). The striatum has also been implicated in reward processing in different types of imaging paradigms (Berns et al., 2001; Breiter et al., 2001; Breiter & Rosen, 1999; Delgado, Nystrom, et al., 2000; Elliott, Friston, & Dolan, 2000; Knutson, Adams et al., 2001; Knutson, Westdorp, Kaiser, & Hommer, 2000; Koepp et al., 1998; Pagnoni et al., 2002). Activation of the caudate nucleus, specifically, has been reported in paradigms in which anticipation of a monetary reward (Breiter et al., 2001; Knutson et al., 2000) and responses to the delivery of monetary rewards and punishments (Breiter et al., 2001; Delgado, Nystrom, et al., 2000; Elliott et al., 2000) have been measured, as well as in paradigms in which responses to positive and negative nonmonetary feedback have been measured (Elliott, Sahakian, Michael, Paykel, & Dolan, 1998).

Although there is an extensive literature on how the striatum responds to reward, paradigms in which the question of how these responses are modulated by magnitude has been examined have been less common. Changes in reward magnitude have been shown to influence neuronal activity in the prefrontal cortex (Leon & Shadlen, 1999; O'Doherty et al., 2001; Rogers et al., 1999) and the amygdala (Salinas & White, 1998). Within the striatum, recent recordings in the monkey have suggested that neurons in that region may encode more than just valence, since activity varies according to the type of liquid reinforcement expected during a spatial delayed-response task (Hassani et al., 2001). These findings have been supported by recent neuroimaging studies (Breiter et al., 2001; Delgado, Sypher, Stenger, & Fiez, 2000; Knutson, Adams, et al., 2001; O'Doherty et al., 2001; Rogers et al., 1999). For example, Breiter et al. (2001) showed ventral striatum activity after the spinning of a wheel, where of three possible outcomes, the largest ($10.00 reward) yielded the highest activity, whereas the lowest ($0.00 reward) was less active. Knutson, Adams, et al. (2001) used a delay task in which participants anticipated a reward or a punishment of different magnitudes. The study showed that during the anticipation phase of the task, the medial caudate responded to increases in both rewards and punishments.

The present study concentrated on the consummatory period and is unique in showing the effects of valence and magnitude in the dorsal striatum after delivery of a reward-related stimulus. Not only does the caudate nucleus differentiate between valence (rewards and punishments), but it also does so with respect to magnitude (large and small). The parametric ordering of the outcome is in accordance with how preferable or valuable a specific outcome is to an individual. Thus, a possible interpretation of the role of the caudate in the coding of rewards of different magnitudes is that, during the anticipation phase, it elicits approach behavior on the basis of magnitude (Knutson, Fong, Adams, Varner, & Hommer, 2001). During the outcome phase, a more consummatory and reinforcing role is performed (Robbins & Everitt, 1992, 1996), where the caudate detects and dissociates between not only the valences, but also the magnitudes of a stimulus (Delgado, Sypher, et al., 2000).

Similar to our previous design (Delgado, Nystrom, et al., 2000) and in accordance with classic decision-making theory (Kahneman & Tversky, 1979; Tversky & Kahneman, 1981), the ratio of gain to loss was 2:1, since the literature suggests that the impact of negative outcomes is larger than the impact of positive outcomes. It is unfair to say, however, that a reward outcome recruits the striatum more than does a punishment outcome. Our findings suggest, instead, that both the dorsal striatum and the ventral striatum respond to the presentation of monetary rewards and monetary punishments, showing differential responses to both events. This result has been supported by another neuroimaging study that also employed a disproportionate ratio of gains and losses and showed responses in the striatum to both monetary rewards and punishments (Breiter et al., 2001).

The differential responses to valence and magnitude in the striatum were observed during the 6- to 9-sec time window after the presentation of feedback. The BOLD hemodynamic response can be elicited by a brief period of neuronal activity (Aguirre, Zarahn, & D'Esposito, 1998; Buckner, 1998; Buckner & Logan, 2001). Early studies in the motor and sensory realms showed signal changes in response to finger movements that lasted as little as 0.5 sec (Bandettini, 1999). The BOLD hemodynamic response also has a typical shape (Aguirre et al., 1998; Buckner & Logan, 2001), characterized by a delay of 2–6 sec between neuronal activity and the onset of the hemodynamic response (Kwong et al., 1992), as well as a response that may last anywhere between 10–12 sec (Blamire et al., 1992). Thus, the point at which reward and punishment should differ, and furthermore, order parametrically, in this paradigm should be roughly 6–9 sec after the reward presentation.

Although we found differences at the expected period in both Experiments 1 and 2, we found significant differences during the initial 3 sec after the outcome was revealed. Even though higher temporal sampling in Experiment 2 allowed us to observe that the response was actually occurring 1.5–3 sec after feedback presentation, this is still early, relative to the typical hemodynamic response. An unexpected and interesting result, this response is puzzling nevertheless and merits further research.

This early response has now been replicated in three designs, however, and it is conceivable that it reflects a brief, almost immediate hemodynamic response in the dorsal striatum. Although further research will be necessary to fully understand such a response, three possible explanations can be provided. First, most investigations of the hemodynamic responses have focused primarily on motor and sensory regions. Although some cognitive paradigms have been used more recently, they focused mostly on cortical responses (Buckner et al., 1998; Cohen et al., 1997; Courtney, Ungerleider, Keil, & Haxby, 1997), and not much is known about the hemodynamic properties of subcortical structures. Perhaps the use of an ANOVA to analyze the data allowed us the sensitivity to pick up on these more rapid changes, since unlike a more traditionally used general linear model, an ANOVA does not assume a shape for the hemodynamic response. Second, it is possible that the observed early response reflects an autonomic response, rather than a cognitive process. The presentation of a conditioned stimulus (such as a tone that was paired with a shock) elicits autonomic (changes in heart rate) and behavioral (freezing) responses (LeDoux, 2000). The immediate defensive responses displayed by rats in fear-conditioning paradigms suggest that the early response to feedback might be related to attention-like mechanisms necessary for instantaneous fight-or-flight reactions. The participant might initially have an autonomic reaction to the large punishment arrow, for example, which might show a different coupling to blood flow than do responses to the more cognitive evaluation of the event. A third possibility is that the early response reflects modulation of an already ongoing response. At the onset of the trial, there is a rise in activity as participants are presented with a question mark and are prompted to make a fast guess. Since they find out the actual value of the card 2.5 sec into the trial, the knowledge of being incorrect, compounded by the almost immediate presentation of a large feedback arrow denoting a monetary loss of $2.00, may reflect a rapid modulation of an already rising hemodynamic response, leading to an early differentiation between conditions.

It is worth noting that many neuroimaging studies of reward processes have focused on ventral striatal activation (Aharon et al., 2001; Berns et al., 2001; Breiter et al., 2001; Elliott et al., 2000; Knutson, Adams, et al., 2001; Knutson, Fong, et al., 2001; Knutson et al., 2000; Koepp et al., 1998; Pagnoni et al., 2002), because work in animals indicates that the nucleus accumbens (part of the ventral striatum) is integral to the brain's reward system and that it is linked to addictive behavior (Di Chiara et al., 1999; Everitt et al., 1999; Koob, 1999; Koob & Nestler, 1997). A growing literature, however, also suggests that the dorsal striatum is involved in motivated behaviors, ranging from lesion and microdialysis studies in rats (Ito, Dalley, Robbins, & Everitt, 2002; Robbins & Everitt, 1992), to single-cell recordings in nonhuman primates (Kawagoe et al., 1998; Lauwereyns, Takikawa, et al., 2002; Lauwereyns, Watanabe, Coe, & Hikosaka, 2002), and even to dopamine measurements in humans (Volkow et al., 2002).

Regarding the ventral striatum, we found that activity in this region showed a main effect of time and an interaction of time and valence in both the present (Experiments 1 and 2) and previous studies (Delgado, Nystrom, et al., 2000), but a three-way interaction (magnitude, valence, and time) was found exclusively in the dorsal striatum. Another study has also not found magnitude influences in the ventral striatum (Brown & Bowman, 1995). In a cued task, where a light indicated how many pellets of food a rat was about to receive, decreases in reaction time were often observed. After ventral striatal lesions, performance in the task or reaction time was not affected. In contrast, a recent neuroimaging experiment has suggested that the ventral striatum responds to the anticipation of increasing rewards (Knutson, Adams, et al., 2001).

In our neuroimaging paradigm, activation may be more robust in the dorsal striatum because it may be more concerned with the consummatory period, where rat lesion studies suggest a larger role for the dorsal, rather than the ventral, striatum (Robbins & Everitt, 1992, 1996). Another potential difference between dorsal striatum and ventral striatum activation was the observed early response to the presentation of feedback, which was significant only in the dorsal striatum in the present and previous studies (Delgado, Nystrom, et al., 2000), perhaps due to differential circuitry that includes separate inputs into each region.

In summary, the activation of the striatum in a gambling paradigm in which valence and magnitude are manipulated is concurrent with animal and other neuroimaging experiments. This experiment further implicates the dorsal striatum as an integral component of a reward circuitry responsible for the control of motivated behavior, where the striatum decodes the valence of a feedback and ranks it on the basis of preference or magnitude.

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