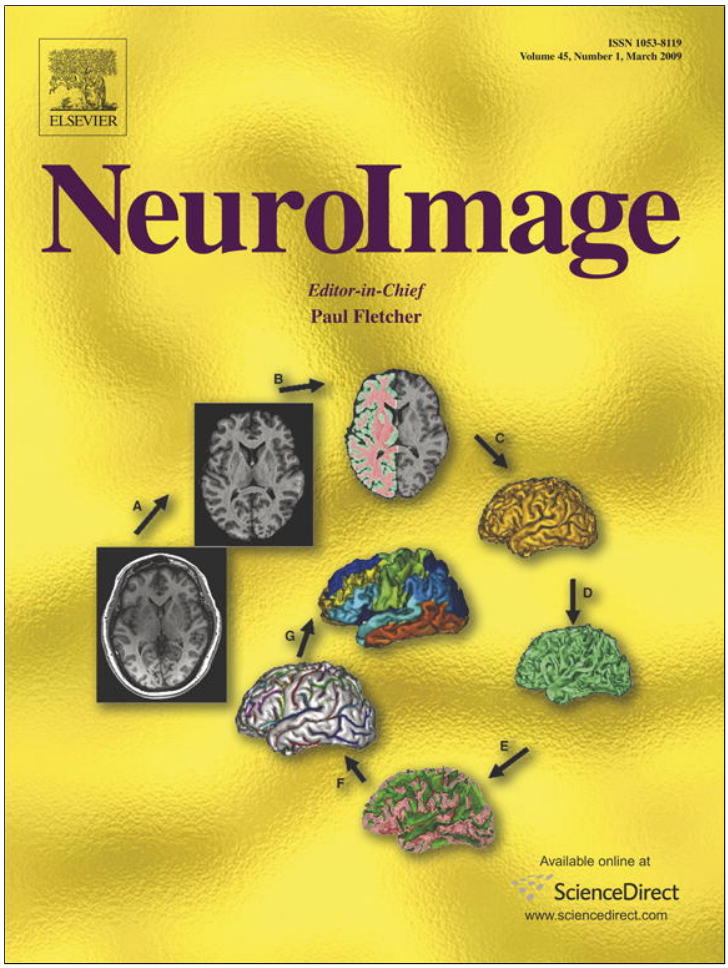

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Dissociable neural representations of future reward magnitude and delay during temporal discounting

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ABSTRACT

In temporal discounting, individuals often prefer smaller immediate rewards to larger delayed rewards, implying a trade off between the magnitude and delay of future rewards. While recent functional magnetic resonance imaging (fMRI) investigations of temporal discounting have generated conflicting findings, no studies have focused on whether distinct neural substrates respond to the magnitude and delay of future rewards. Combining a novel, temporally distributed discounting task with event-related fMRI, we found that while nucleus accumbens (NAcc), mesial prefrontal cortical (MPFC), and posterior cingulate cortical (PCC) activation positively correlated with future reward magnitude, dorsolateral prefrontal cortical (DLPFC) and posterior parietal cortical (PPC) activation negatively correlated with future reward delay. Further, more impulsive individuals showed diminished NAcc activation to the magnitude of future rewards and greater deactivations to delays of future rewards in the MPFC, DLPFC, and PPC. These findings suggest that while mesolimbic dopamine projection regions show greater sensitivity to the magnitude of future rewards, lateral cortical regions show greater (negative) sensitivity to the delay of future rewards, potentially reconciling different neural accounts of temporal discounting.

Introduction

Whether foraging for food or saving for retirement, organisms must often decide between immediate and future payoffs. Behavioral research indicates that beyond preferring larger rewards to smaller rewards, individuals also prefer immediate rewards to future rewards. As the delay until reward delivery increases, an individual's valuation of a future reward declines (Mazur, 1987), a phenomenon known as *temporal discounting* (Ainslie, 1975; Samuelson, 1937). Temporal discounting thus implies the potential for conflict, since individuals must sometimes trade off preferences for larger magnitudes against preferences for shorter delays. Individuals vary widely in the rate at which they discount future rewards, and these variations correlate with real-world behavior ranging from impatience to scholastic performance to substance abuse (Bickel and Marsch, 2001; Kirby et al., 2005; Reynolds, 2006). However, the neural processes underlying temporal discounting remain unclear.

Recent fMRI research has approached the neural correlates of temporal discounting from the perspective of different behavioral models, generating two distinct accounts. In an initial fMRI study, McClure et al. (2004) found that activation in mesolimbic dopamine projection regions (i.e., nucleus accumbens (NAcc) and medial prefrontal cortex (MPFC)) correlated with choices involving immediate rewards, while activation in lateral cortical regions (i.e., dorsolateral prefrontal cortex (DLPFC) and posterior parietal cortex (PPC)) correlated with choices involving all rewards, immediate or future (McClure et al., 2004; McClure et al., 2007). They interpreted these findings to support a two-component model of temporal discounting in which one system weights immediate rewards (called the "beta system") while another weights rewards at all delays (called the "delta system"; (Laibson, 1997)). In contrast to these initial findings, Kable and Glimcher (2007) found that activation in mesolimbic projection regions (including NAcc and MPFC) correlated with a combination of the magnitude and delay of future rewards. They interpreted these findings to support a one-component model of temporal discounting in which a single system responds to a combination of magnitude and delay information, discounting future rewards hyperbolically (Ainslie, 1975). While these studies have generated conflicting accounts of the neural basis of temporal discounting, neither focused on whether neural responses to the magnitude and delay of future rewards could be distinguished prior to choice.

One alternative to correlating brain activity with different behavioral models of temporal discounting is to examine the neural responses to independent decision components—in this case, the magnitude and delay of future rewards. Several fMRI studies have focused solely on the neural correlates of anticipated reward magnitude, spanning diverse reward modalities including monetarily, gustatorily, and socially rewarding stimuli. Together, these studies indicate that activation in mesolimbic projection regions, and the NAcc in particular, increase proportional to anticipated reward

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magnitude (Aharon et al., 2001; Knutson et al., 2001; O'Doherty et al., 2003b). Less fMRI research, however, has specifically focused on neural correlates of future reward delay.

Several brain regions may play a role in representing delays of future rewards. According to one account, delays of future rewards directly diminish the neural representation of future reward magnitude, and thus should decrease activation in regions implicated in reward processing including mesolimbic dopamine projection areas (e.g., NAcc and MPFC; (Kable and Glimcher, 2007)). According to another account, delays of future rewards evoke uncertainty about the time and likelihood of reward delivery (Read and Read, 2004) and thus might elicit increased activation in deep cortical regions implicated processing in uncertainty such as the anterior insula (Paulus, 2003; Preuschoff et al., 2008) and anterior cingulate cortices (Critchley et al., 2001). According to a third account, representation of future reward delay requires cognitive control (e.g., imagining one's self in the future or inhibiting automatic responses for immediate outcomes), and thus longer delays should elicit activation in cortical regions involved in cognitive control including the DLPFC, inferior frontal gyrus (IFG), and posterior parietal cortex (PPC) (Ainslie, 2001; McClure et al., 2004, 2007). Currently, however, no fMRI studies have directly demonstrated brain activation that correlates with future reward delay independent of magnitude.

The aim of this study was to examine whether dissociable neural substrates would respond to the magnitude and delay of a future reward, using an adaptation of traditional temporal discounting tasks (Kirby and Maraković, 1995; Richards et al., 1999). To independently examine the neural responses to the magnitude and delay of future rewards, we used an orthogonalized, parametric task with event-related fMRI. While we predicted that activation in mesolimbic projection regions (NAcc and MPFC) would correlate with the magnitude of future rewards, we also examined whether activation in other regions (i.e., either NAcc and MPFC, anterior insula and cingulate cortex, or lateral cortical regions) would correlate with the delay of future rewards. Finally, we explored whether individual differences in the sensitivity of these regions to future reward magnitude and delay correlated with individuals' temporal discounting rates.

Methods

Participants

Sixteen healthy right-handed native English-speaking adults (8 females; mean age 21.6 (±2.13)) participated in the study. Participants had no history of neurological or psychiatric disorders and gave informed consent for a protocol approved by the Institutional Review Board of the Stanford University School of Medicine.

Temporal discounting task

Each task trial included four periods that separately presented information related to reward magnitude, delay, and choice solicitation (see Fig. 1). Because we aimed to distinguish activity related to magnitude or delay information while maintaining consistency with previous studies, information was revealed in the order a subject would encounter in a typical discounting questionnaire (Kirby and Maraković, 1995; Richards et al., 1999). The first screen (2000 ms) presented the immediate option, which always offered a reward magnitude of $10.00 at a delay of 0 days. Presentation of this constant immediate reward provided a comparison standard for subsequently presented variable future rewards, and eliminated potential confounds due to individual differences in memory for the immediate option. Next, the magnitude of the future option was presented (mag period, 2000 ms), which varied over seven amounts ($10.00, $10.50, $11.00, $13.00, $15.00, $20.00, $25.00). Next, the delay of the future option was presented (del period, 2000 ms), which varied over six

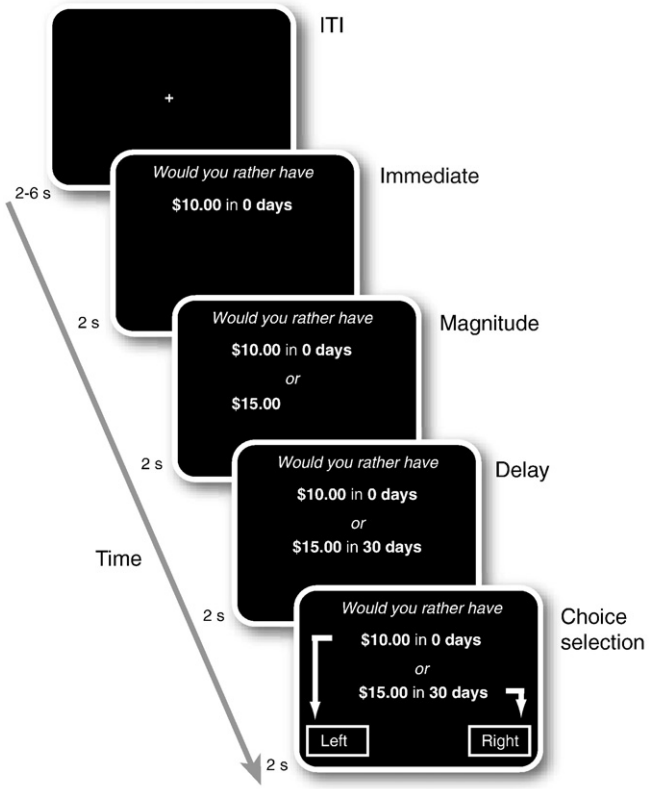

Fig. 1. Task design. The temporal discounting task staggered presentation of information for future reward magnitude, future reward delay, and choice selection, providing an opportunity to isolate brain activity related to each. The first screen (2 s) presented the immediate option, which always offered a reward magnitude of $10.00 at a delay of 0 days. Next, the reward magnitude of the future option was presented (2 s), which varied between seven different amounts (ranging from $10.00 to $25.00). Next, the delay of the future option was presented (2 s), which varied between 6 delays (ranging from 0 to 180 days). The last screen solicited subjects' choice for either the immediate or future option (2 s). Each trial ended with a 2–6 s variable inter-trial interval (ITI). Trial blocks included 42 pseudorandomized trial types such that every combination of magnitude and delay was presented once, and subjects played two blocks, yielding a total of 84 trials.

durations (0, 7, 30, 60, 90, 180 days). A fully crossed factorial design with orthogonal, parametric variation of magnitude and delay variables ensured the potential for separate visualization of neural responses to each variable, even in the case of temporal overlap (Buckner, 1998). Finally, the last screen solicited subjects' choice for either the immediate or future option with the appearance of left and right arrows (choice period, 2000 ms), which randomly linked each option to either the right or left button. Left and right spatial counterbalancing of choice options limited lateralized motor preparation to the choice period. Subjects responded within 2000 ms, and feedback indicated which of the options they had chosen (by changing color). Consistent timing of each phase (i.e., 2000 ms each for immediate, mag, del, and choice periods) allowed reliable and temporally targeted measurement of peak activation during each phase, which was necessary for subsequent analyses involving averaging by trial type and correlation with individual difference measures of temporal discounting. Each trial ended with a 2–6 s variable inter-trial interval (ITI). Trial blocks included 42 pseudorandomized trial types such that every combination of magnitude and delay was presented once within a block. Subjects played two blocks, yielding a total of 84 trials during both initial behavioral and subsequent fMRI sessions.

To verify that discounting measures were reliable within subjects, individuals participated in an initial behavioral practice session during which they played the task on a computer. Subjects were informed

that they would receive payment (between $10.00 and $25.00) for one randomly drawn trial to ensure incentive-compatibility. During scanning, subjects again played the task and again received payment for one randomly drawn trial, in addition to a payment of $20.00 per hour for undergoing scanning. If the outcome of the selected trial was an immediate gain, subjects received $10.00 at the end of the session; otherwise, payment was mailed to subjects at the specified delay.

Behavioral analysis

Individuals' choice behavior for behavioral and fMRI sessions was analyzed with Matlab (MATLAB, Mathworks Inc, Natick, MA). Subjects' indifference points were calculated at each delay to fit individualized discounting curves. This was accomplished by extracting subjects' choices for a given delay, assigning binary values for choosing the immediate (0) or future option (1), and then fitting a logistic function to determine the dollar amount at which there was a 0.5 probability of choosing the immediate versus the future option (and hence, subjects were "indifferent" to receiving either the immediate or the future option). Indifference points were averaged between blocks, and discounted value (DV) of the future option relative to the immediate option ($10.00) was calculated for each delay (DV = $10.00/indifference point).

To index individual differences in temporal discounting behavior, several models of discounting were considered; however, quantitative characterization of behavior rather than model comparison was the primary goal of the study. Exponential, hyperbolic, and beta–delta models of temporal discounting were fit to each subject's discounting behavior (see Supplementary Fig. 1). The hyperbolic discounting model fit individuals' behavior equally well as other models, and since this model has been widely adopted in both human and animal studies of discounting (see Green and Myerson, 2004 for review) and offers the most parsimonious summary of discounting behavior by fitting a single individualized parameter (k), we used the hyperbolic model to explore individual differences. Discounted value (DV) was fit to the hyperbolic model of temporal discounting according to the equation:

$$DV = 1/(1 + k*D)$$

(Mazur, 1987; Rodriguez and Logue, 1988), where D is the length of the delay in days and k is an individual discounting parameter. Larger values of k indicated more impulsivity, while smaller values of k indicated more patience.

FMRI acquisition and analysis

Images were acquired with a 1.5-T General Electric magnetic resonance scanner using a standard birdcage quadrature head coil. Twenty-four 4-mm-thick slices (in-plane resolution 3.75 × 3.75 mm, no gap) extended axially from the mid-pons to the top of the skull, providing whole-brain coverage and adequate spatial resolution of subcortical regions of interest (e.g. midbrain, NAcc, orbitofrontal cortex). Whole-brain functional scans were acquired with a T2*-sensitive spiral-in/-out pulse sequence (TR = 2 s, TE = 40 ms, flip = 90°) optimized to minimize signal dropout at the base of the brain (Glover and Law, 2001). High-resolution structural scans were also acquired to facilitate localization and coregistration of functional data using a T1-weighted spoiled grass sequence (TR = 100 ms, TE = 7 ms, flip = 90°).

Analyses were conducted using Analysis of Functional Neural Images (AFNI) software (Cox, 1996). For preprocessing, voxel time series were sinc-interpolated to correct for nonsimultaneous slice acquisition, bandpass filtered (admitting frequencies from 8 to 90 s), and normalized to percent signal change with respect to the voxel mean for the entire task. Visual inspection of motion correction estimates confirmed that no subject's head moved more than 2.0 mm in any dimension from one volume acquisition to the next.

Analyses proceeded through three stages: whole-brain localization, VOI time course verification, and correlation with individual differences. Localization analyses employed a multiple regression model using independent and parametric regressors representing future reward magnitude (modeled during the magnitude period), future reward delay (modeled during the delay period), and the interaction of magnitude and delay (modeled during the delay period). The model also included regressors of noninterest indexing residual motion (6), baseline, linear, and quadratic trends for each of the two blocks (6), and general period effects (i.e., immediate, magnitude, delay, and choice periods, as well the entire trial period (5)).

Maps of contrast coefficients for regressors of interest were coregistered with structural maps, spatially normalized by manually warping to Talairach space, spatially smoothed to minimize effects of anatomic variability (FWHM = 4 mm), and collectively submitted to a one-sample t-test against the null hypothesis of no activation to test for a group difference while controlling for random effects. Volumes of interest (VOIs) were defined in regions whose activation correlated with magnitude, delay, or interaction regressors at a $p < 0.001$ voxelwise threshold in group maps with a minimum cluster of 20 contiguous 2.0 mm cubic voxels (the minimum cluster criterion for a $p < 0.05$ whole-brain gray matter corrected threshold as specified by AFNI's AlphaSim; (Cox, 1996)).

For activation time course verification analyses, VOIs were specified based on regional foci identified in the localization analyses (i.e., right NAcc, MPFC, left DLPFC, PCC, posterior parietal cortex, temporal parietal junction, and right inferior frontal gyrus). Spatially averaged activation time courses were extracted from each VOI and then divided by the average activation for each VOI over the course of the entire experiment to derive measures of percent signal change. To separately examine the influence of magnitude and delay information on activation in these regions, VOI time courses were extracted and binned into nine conditions according to a 3 × 3 factorial design: low ($10.00, $10.50), medium ($11.00, $13.00, $15.00), and high ($20.00, $25.00) magnitude × low (0, 7 days), medium (30, 60 days), and high delays (90, 180 days). Since subjects' choice behavior was approximately linearly related to increasing parametric levels of magnitude and delay (see Supplementary Fig. 2), grouping of magnitude and delay into high, medium, and low levels simplified subsequent factorial analyses. VOI peak activation during magnitude and delay periods (lagged by 6 s to account for the hemodynamic response) was submitted to 2-way repeated-measures ANOVAs with magnitude and delay as the within-subjects factors and subjects as random effects. VOI peak activation from regions showing significant main effects of magnitude or delay, or their interaction was then submitted to post-hoc pair-wise t-tests to verify significant differences between low, medium and high levels of magnitude and delay.

For individual difference analyses, parameter estimates (in the form of beta coefficients) for the parametric magnitude and delay whole-brain regressors were extracted from individuals' regional VOIs identified in the group localization analyses. These coefficients indexed an individuals' neural sensitivity to magnitude or delay information. Averaged coefficients for each VOI were then correlated with individuals' tendency to discount the future option (as indexed by individuals' hyperbolic discounting rate, or k, normalized by a square root transform).

Results

Behavior

All subjects selected both immediate and future reward options during the task (i.e., no subject unconditionally chose all immediate or all future options), but individuals varied widely in their preferences for immediate versus future rewards. The percentage of choices for the immediate $10.00 option ranged from 24% to 81% of the trials. As

Table 1
Activation foci for magnitude, delay and the magnitude×delay interaction

Region	Volume	Max *Z* score	*R*	*A*	*S*
Magnitude					
R NAcc	232	4.228	9	5	−4
L MPFC	416	3.950	−11	41	−8
PCC	160	3.785	−1	−51	14
Delay					
L DLPFC	232	−4.264	−19	55	8
L TPJ	168	−4.013	−47	−57	26
R posterior parietal	216	−4.433	31	−73	30
Magnitude×delay interaction					
R IFG	168	−4.298	55	−1	20

All regions surpassed threshold of 20 contiguous 2.0 mm^3 voxels at $p<0.001$, uncorrected; $p<0.05$, corrected.

mentioned above, while individuals' behavior was fit to several models of discounting, in the present study we utilized *k* (the individual discounting parameter for the hyperbolic model) to index individual differences in temporal discounting.

Individuals' rates of temporal discounting (*k*) ranged from 0.0008 to 0.0814 (average 0.0207), similar to individual differences reported in other studies (Kable and Glimcher, 2007; Kirby and Maraković, 1995). Discounting rates were reliable within subjects between behavioral and fMRI sessions (test–retest $r=0.869$, $p<0.001$), suggestive of trait-like stability (Supplementary Fig. 3). Discounting rates did not differ according to gender ($t=-0.563$, $df=14$, $p=0.583$). Reaction time significantly decreased from the behavioral to the fMRI session ($t=-4.092$, $df=15$, sd=95.05; $p<0.001$), but did not significantly differ for choice of the immediate versus the future option ($t=-0.006$, $df=15$, sd=49.847; $p=0.995$), and did not significantly correlate with discounting rates, *k* ($r^2=0.179$) (Supplementary Fig. 4).

Brain activation

Localization

Whole-brain localization analyses revealed that predicted regions differed in sensitivity to magnitude versus delay information. Increasing future reward magnitudes positively correlated with activation in the right NAcc, MPFC, and posterior cingulate cortex (PCC). Increasing future reward delay, however, negatively correlated with activation in the left dorsolateral prefrontal cortex (DLPFC), right posterior parietal cortex (PPC), and left temporal–parietal junction (TPJ). The interaction of magnitude and delay negatively correlated with activation in the right inferior frontal gyrus (IFG) (See Table 1, and Fig. 2).

VOI time courses

Time courses of activation were extracted from each VOI to verify the timing of neural responses to magnitude or delay indicated by the statistical maps. As expected, activation in VOIs correlating with magnitude in group maps (NAcc, MPFC, PCC) significantly diverged according to the magnitude of the future reward specifically during the presentation of magnitude information, but did not diverge according to delay (Fig. 3). Similarly, activation in VOIs correlating with delay in group maps (DLPFC, TPJ, PPC) significantly diverged according to the delay of the future reward specifically during presentation of delay information, but did not diverge according to magnitude.

Two-way repeated-measures ANOVAs confirmed a significant double dissociation of magnitude and delay effects in these VOIs. During presentation of magnitude information, activation in mesolimbic projection regions including the NAcc ($F=13.9$, $df=2,135$ $p<0.001$), MPFC ($F=11.2$, $df=2,135$ $p<0.001$), and PCC ($F=12.2$, $df=2,135$ $p<.001$) showed significant main effects of magnitude but not delay. Activation in lateral cortical regions (DLPFC, TPJ, parietal cortex, IFG), however, did not show significant magnitude effects. Post-hoc *t*-tests confirmed significant differences ($p<0.05$) between low and medium and low and high magnitudes in the NAcc and PCC, and between all three levels of magnitude in the MPFC. These findings suggest that mesolimbic projection regions (as well as PCC) but not lateral cortical regions were sensitive to the magnitude of the future option.

During presentation of delay information, activation in lateral cortical regions including the DLPFC ($F=7.9$, $df=2,135$ $p=0.001$), TPJ ($F=6.3$, $df=2,135$ $p=0.002$), and posterior parietal cortex ($F=5.9$, $df=2,135$ $p=0.003$) showed main effects of delay but not magnitude. Activation in mesolimbic projection regions, however, did not show significant delay effects (Fig. 3). Post-hoc *t*-tests confirmed significant differences between low and high delays and medium and high delays in the DLPFC, significant differences between low and high delays in the left TPJ, and between low and high delays and low and medium delays in the right posterior parietal cortex.

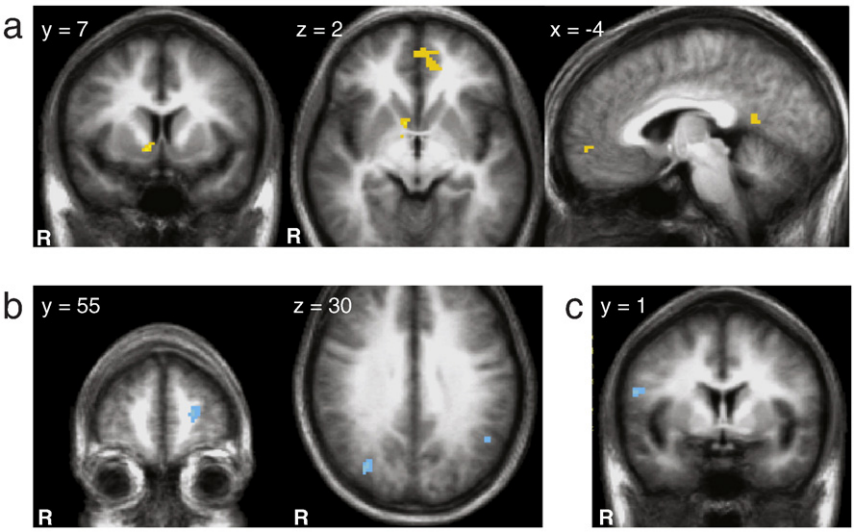

Fig. 2. Brain activation correlating with magnitude or delay. (a) Brain regions significantly correlating with the magnitude of the future option (right NAcc, MPFC, PCC). (b) Brain regions significantly correlating with the delay of the future option (left DLPFC, left TPJ, right posterior parietal cortex). (c) Brain regions significantly correlating with the interaction of magnitude and delay (right IFG). For all images warm colors indicate positive correlations, cool colors indicate negative correlations; $p<0.001$, uncorrected; $p<0.05$ corrected.

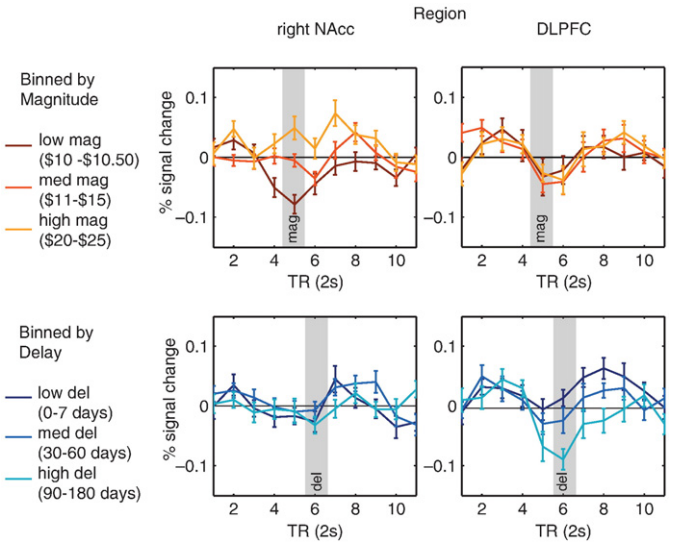

Fig. 3. Time courses of activation from representative magnitude-sensitive (right NAcc) and delay-sensitive (DLPFC) regions (columns). Row 1 shows time courses of % signal change binned by high, medium, and low magnitudes, where magnitude-sensitive regions like the NAcc clearly respond to different levels of magnitude during the magnitude period, while delay-sensitive regions like the DLPFC do not. Row 2 shows time courses of % signal change binned by high, medium, and low delays, where delay-sensitive regions like the DLPFC clearly respond to different levels of delay during the delay period, while magnitude-sensitive regions like the NAcc do not. Time courses from all VOIs are reported in supplementary materials (Supplementary Fig. 5).

Together, these findings suggest that lateral cortical regions, but not mesolimbic projection regions were sensitive to the delay of the future option. Finally, activation in the right IFG showed a significant magnitude × delay interaction when submitted to ANOVA ($F=3.25$, $df=4,135$ $p=0.014$).

Individual difference analyses

While localization and VOI analyses tested for group effects and controlled for individual differences, individual difference analyses probed variations between subjects. Specifically, we examined whether individuals' neural responsiveness to magnitude and delay information correlated with their rates of temporal discounting.

Individual differences in neural sensitivity to future reward magnitude negatively correlated with subjects' temporal discounting rates. Specifically, magnitude-related activation in the NAcc negatively correlated with discounting rates ($r=-0.509$, $p=0.044$), such that more impulsive subjects showed less neural activation to future rewards with large magnitudes (Fig. 4a). The NAcc was the only VOI to show magnitude sensitivity that significantly correlated with individuals' discount rates (see Supplementary Table 1 for all VOI correlation coefficients).

Additionally, subjects' temporal discounting rates correlated with individual differences in (negative) neural sensitivity to future reward delay. Specifically, delay-related deactivation in the DLPFC and posterior parietal cortex correlated with temporal discounting rates (DLPFC $r=-0.520$, $p=0.039$; PPC $r=-0.528$, $p=0.036$), such that more impulsive subjects showed greater deactivations to future rewards with long delays (Fig. 4b). Notably, delay-related activation in the magnitude-sensitive regions of the MPFC and PCC also negatively correlated with temporal discounting rates (MPFC $r=-0.624$, $p=0.010$; PCC $r=-0.728$, $p=0.001$), even though these regions did not show group-wide main effects of delay (Fig. 4c). Together, these findings suggest that more impulsive subjects show less neural sensitivity to the larger magnitudes of future rewards but greater (negative) neural sensitivity to the longer delays of future rewards.

Discussion

Using event-related fMRI and a novel parametric task, we observed distinct neural responses to the magnitude and delay of future rewards. Across subjects, activation in mesolimbic projection regions (including the NAcc, MPFC, and PCC) correlated with increasing magnitudes of future rewards, while activation in lateral cortical regions (including the DLPFC, TPJ, and posterior parietal cortex) negatively correlated with increasing delays of future rewards. Between subjects, more impulsive individuals showed diminished neural activation to the magnitude of future rewards as well as greater deactivations to the delay of future rewards.

These findings indicate that activity in the NAcc, MPFC, and PCC increases with larger magnitudes of a future reward, and so align with a substantial body of research implicating mesolimbic circuits in representing the magnitude of anticipated rewards (Knutson et al., 2001; Knutson and Cooper, 2005). Further, in the present study, NAcc activation responded specifically to future reward magnitude but not delay in both groupwise and individual difference analyses. These findings also provide initial evidence of dissociable delay-related brain activation, since activity in lateral cortical regions (i.e., DLPFC, TPJ, and posterior parietal cortex) decreased in response to longer delays of

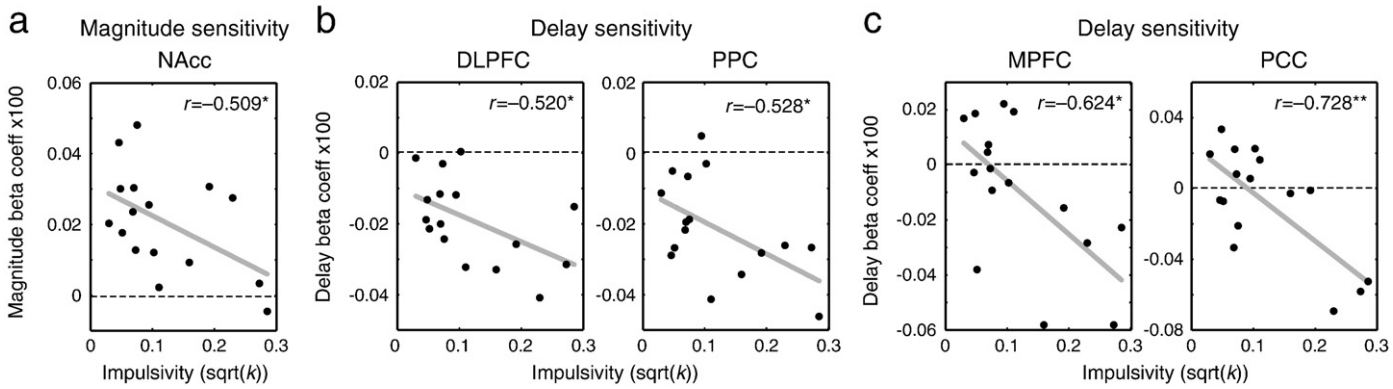

Fig. 4. Individual differences in neural sensitivity to future reward magnitudes and delays predict individuals' temporal discounting rates. (a) Neural response to magnitudes in the magnitude-sensitive NAcc negatively correlates with discounting rates (k, normalized by square-root transform). More "impulsive" individuals show less NAcc activation to large magnitudes of future rewards. (b) Neural response to delays in delay-sensitive regions (DLPFC, posterior parietal cortex) correlates with discounting rates (k, normalized by square-root transform). More "impulsive" individuals show more DLPFC and PPC deactivations to long delays of future rewards. (c) Neural response to delays in magnitude-sensitive regions (MPFC, PCC) also correlates with discounting rates (k, normalized by square-root transform). More "impulsive" individuals show MPFC and PCC deactivations to long delays, while more "patient" subjects do not show MPFC or PCC deactivations with delays.

future rewards. At the individual difference level, more impulsive individuals showed greater deactivations in these regions in response to longer delays. These findings are consistent with other fMRI evidence that decreased activation in lateral cortical regions correlates with choosing an immediate reward over a future reward (Boettiger et al., 2007; McClure et al., 2004, 2007), which is likely to occur when the delay of the future reward is unattractively long. Together, these results demonstrate for the first time a double dissociation of regions responsive to the magnitude (i.e., NAcc) versus delay (i.e., DLPFC) of future rewards in the context of temporal discounting.

The present findings further suggest that some regions (i.e., the MPFC and PCC) might respond to both the magnitude and delay of future rewards. Although these regions only demonstrated significant group effects of magnitude, in the most impulsive individuals, they also showed decreased activation in response to future rewards with long delays. Given the role of the MPFC in integrating different kinds of value information (e.g., preference, likelihood, cost; (Knutson et al., 2003, 2005, 2007; O'Doherty et al., 2003a; Plassmann et al., 2007), these regions may integrate perceived benefits and costs to potentially inform upcoming choice.

Finally, activation in a cortical region in the right IFG correlated with an interaction of future reward magnitude and delay. Specifically, IFG activation correlated negatively with longer delays, but only during trials offering high magnitudes of future rewards. While this finding was not initially predicted, it aligns well with previous fMRI research implicating the IFG in response inhibition and cognitive control of pre-potent responses (Aron et al., 2004b; Garavan et al., 2002; Menon et al., 2001). In the present task, IFG may be recruited when subjects must withhold fast, automatic responses, particularly when the stakes are high, in order to thoroughly evaluate the reward alternatives. However, further research is required to specifically test this hypothesis.

Implications for different neural accounts of temporal discounting

The present findings share both consistencies and inconsistencies with two distinct accounts of temporal discounting in the fMRI literature. A "two-system" account posits that mesolimbic dopamine projection regions evaluate immediate rewards while dorsolateral cortical regions evaluate all rewards (immediate or future) (McClure et al., 2004, 2007). Consistent with this account, our findings revealed a functional dissociation between a mesolimbic region (i.e., the NAcc) and a dorsal cortical region (i.e., the DLPFC). Inconsistent with this account, however, activation in both regions responded to different attributes of the future reward after controlling for response to the (constant) immediate reward, indicating that mesolimbic regions respond to attributes of delayed as well as immediate rewards.

An alternative "one system" account posits that mesolimbic projection regions (and PCC) respond to the combined magnitude and delay of all potential rewards, whether immediate or delayed (Kable and Glimcher, 2007). Consistent with this account, the current findings revealed that some mesolimbic regions (i.e., MPFC, PCC) responded to both the magnitude and delay of future rewards (but only in the most impulsive subjects). Inconsistent with this account, however, the functional dissociation revealed specialization within mesolimbic regions, such that the NAcc primarily responded to future reward magnitude, while lateral cortical regions (e.g., DLPFC) primarily responded to future reward delay. Thus, by independently manipulating both attributes of the future option, the present design yielded findings that might reconcile different accounts by indicating that both mesolimbic and lateral cortical regions respond to future rewards, but differentially according to magnitude versus delay attributes.

A body of human and monkey research now demonstrates that NAcc activation increases proportional to the magnitude of anticipated rewards (Cromwell and Schultz, 2003; Knutson et al., 2001; Knutson and Greer, 2008). The current findings, however, provide the first evidence that independent activation in lateral cortical regions decreases proportional to the delay until a future reward can be obtained. These findings inform at least three accounts of which neural substrates might represent the delay of future rewards. According to one account (similar to the one-system account), the delay of a future reward might reduce activation in regions whose activation correlates with reward magnitude (e.g., mesolimbic regions; (Kable and Glimcher, 2007)). Although there was some evidence that long delays could decrease activation in the MPFC and posterior cingulate of impulsive subjects, the main effect of delay in these regions was not significant across the entire group, and NAcc activation did not significantly change in response to delay information. A second account might posit that long delays elicit uncertainty (and/or fear of loss) and so should elicit activation in regions implicated in uncertainty (e.g., the anterior cingulate and insula; (Critchley et al., 2001; Kuhnen and Knutson, 2005; Paulus, 2003; Preuschoff et al., 2006, 2008)). Activation in these regions, however, did not increase proportional to the delay of the future reward. A third account (similar to the two system account) proposes that choosing to forego immediate gratification and wait for a larger future reward requires cognitive control and inhibition of prepotent responses, which recruits lateral cortical regions like the DLPFC, IFG, and posterior parietal cortex (Ainslie, 2001; Aron et al., 2003; Braver et al., 1997; McClure et al., 2004). Furthermore, executive control might represent a limited resource (as in the case of "willpower"; (Gailliot et al., 2007)) and thus might be depleted by longer delays. These notions are consistent with the present findings that activation in lateral cortical regions decreases proportional to the delay of the future reward, and does so more steeply for more impulsive individuals. Thus, the executive control account is most consistent with the findings of the present study with respect to neural correlates of future reward delay.

The present findings also parallel findings from animal research. Lesion studies of rats implicate both prefrontal and striatal regions in temporal discounting (Cardinal, 2006; Cardinal et al., 2004). Recent electrophysiological studies of monkeys indicate that the firing of DLPFC neurons (Kim et al., 2008) as well as dopamine neurons themselves (Kobayashi and Schultz, 2008) correlates with the magnitude and delay of future rewards. While these findings suggest apparent similarities with the present results, one cannot necessarily infer that increased neural firing translates to an increase in the signal measured by FMRI (Logothetis and Wandell, 2004), and so mechanistic links will require additional modeling and experimental triangulation across species (e.g., Knutson and Gibbs, 2007).

Strengths, limitations, and implications for future research

The present study features a number of novel strengths. This study is the first to examine parametric variations in magnitude and delay evaluation over the same choice option, occurring prior to choice. Magnitude and delay information was independently varied and staggered in time, facilitating disambiguation of neural responses to each type of information. Motor demands were counterbalanced and sequestered to the choice period, ruling out the potential influence of motor preparation on the observed patterns of activation. This temporally distributed design also allowed examination not only of group effects but also of the relationship between individual differences in neural responsiveness to magnitude and delay information and subsequent choice.

The benefits conferred by the present design also necessitated a few tradeoffs. Neural responses to the immediate option could not be examined separately (as in McClure et al., 2004), since the immediate option was intentionally held constant across all trials. This design sacrifice was necessary to allow parametric variation of both magnitude and delay information over the same choice option. Additionally, since the magnitude of the future option always

followed the constant immediate option, our findings are partially consistent with the interpretation that NAcc, MPFC, and PPC activation represent a reward prediction error (Knutson et al., 2003; McClure et al., 2003; O'Doherty et al., 2003c). One might also expect these regions to show reward prediction error-related activity in response to presented delay information; however, this was not observed in group analyses. Such an account may still apply to MPFC activation, since effects of delay were evident there, but only in individual difference analyses.

Finally, to approximate the structure of behavioral delay discounting tasks (Kirby and Maraković, 1995; Richards et al., 1999) while limiting the already large number of conditions (i.e., a 6×7 factorial design), magnitude information preceded delay information in each trial. While the proximity of these events might raise the concern that neural responses to the magnitude of the future option could carry over and "pollute" neural responses to the delay of the future option, the fully crossed factorial design and time course analyses suggested that this was not the case. Specifically, group analyses revealed no interaction of future reward magnitude and delay in any of the volumes of interest. Further, time course analyses of the actual signal demonstrated clearly dissociable effects of magnitude in NAcc and delay in DLPFC (see Fig. 3). Reversing the order of presentation of magnitude and delay information represents an interesting target for further research, but would require an additional study, since it would double the length of the present experimental design. Additionally, investigators would need to first establish that subjects show similar behavior when this magnitude and delay information delivery is reversed prior to scanning (Weber et al., 2007).

The finding that activation in dissociable regions correlates with the magnitude versus delay of future rewards holds several implications for future research. Modulation of NAcc activity or dopamine function (either transiently or permanently) might modify individuals' responsiveness to the magnitude of future rewards. On the other hand, damage to lateral prefrontal regions (e.g., either due to developmental influences, transient inactivation, or permanent lesion) might impair peoples' ability to extend reward value into the indefinite future. Because fMRI research provides correlational evidence, investigators will need to triangulate with findings generated by other more causally informative methods (e.g., drugs, stimulation, lesions) to support causal inferences (Aron et al., 2004a; Cools et al., 2003; Fregni et al., 2008; Knoch and Fehr, 2007).

Conclusion

These findings provide initial human evidence for dissociable neural representations of the magnitude and delay of future rewards in the context of temporal discounting. The sensitivity of the nucleus accumbens to magnitude information and of lateral cortical regions to delay information also correlates with individual differences in discounting behavior. These findings help to integrate currently disparate neural accounts of temporal discounting, and generate novel predictions about how neural development or damage might influence individuals' ability to balance future reward magnitude against delay.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2008.11.004.

References

Aharon, I., Etcoff, N., Ariely, D., Chabris, C.F., O'Connor, E., Breiter, H.C., 2001. Beautiful faces have variable reward value: fMRI and behavioral evidence. Neuron 32, 537–551.
Ainslie, G., 1975. Specious reward: a behavioral theory of impulsiveness and impulse control. Psychol. Bull. 82, 463–496.
Ainslie, G., 2001. Breakdown of Will. Cambridge University Press, Cambridge, UK.
Aron, A., Fletcher, P.C., Bullmore, E., Sahakian, B., Robbins, T.W., 2003. Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. Nat. Neurosci. 6, 115–116.
Aron, A.R., Monsell, S., Sahakian, B.J., Robbins, T.W., 2004a. A componential analysis of task-switching deficits associated with lesions of left and right frontal cortex. Brain 127, 1561–1573.
Aron, A.R., Robbins, T.W., Poldrack, R.A., 2004b. Inhibition and the right inferior frontal cortex. Trends Cogn. Sci. 8, 170–177.
Bickel, W.K., Marsch, L.A., 2001. Toward a behavioral economic understanding of drug dependence: delay discounting processes. Addiction 96, 73–86.
Boettiger, C.A., Mitchell, J.M., Tavares, V.C., Robertson, M., Joslyn, G., D'Esposito, M., Fields, H.L., 2007. Immediate reward bias in humans: fronto-parietal networks and a role for the catechol-O-methyltransferase 158(Val/Val) genotype. J. Neurosci. 27, 14383–14391.
Braver, T.S., Cohen, J.D., Nystrom, L.E., Jonides, J., Smith, E.E., Noll, D.C., 1997. A parametric study of prefrontal cortex involvement in human working memory. NeuroImage 5, 49–62.
Buckner, R.L., 1998. Event-related fMRI and the hemodynamic response. Hum. Brain Mapp. 6, 373–377.
Cardinal, R., 2006. Neural systems implicated in delayed and probabilistic reinforcement. Neural Netw. 19, 1277–1301.
Cardinal, R.N., Winstanley, C.A., Robbins, T.W., Everitt, B.J., 2004. Limbic corticostriatal systems and delayed reinforcement. Ann. N. Y. Acad. Sci. 1021, 33–50.
Cools, R., Barker, R.A., Sahakian, B.J., Robbins, T.W., 2003. L-Dopa medication remediates cognitive inflexibility, but increases impulsivity in patients with Parkinson's disease. Neuropsychologia 41, 1431–1441.
Cox, R.W., 1996. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput. Biomed. Res. 29, 162–173.
Critchley, H.D., Mathias, C.J., Dolan, R.J., 2001. Neural activity in the human brain relating to uncertainty and arousal during anticipation. Neuron 29, 537–545.
Cromwell, H., Schultz, W., 2003. Effects of expectations for different reward magnitudes on neuronal activity in primate striatum. J. Neurophysiol. 89, 2823–2838.
Fregni, F., Orsati, F., Pedrosa, W., Fecteau, S., Tome, F., Nitsche, M., Mecca, T., Macedo, E., Pascualleone, A., Boggio, P., 2008. Transcranial direct current stimulation of the prefrontal cortex modulates the desire for specific foods. Appetite 51, 34–41.
Gailliot, M., Baumeister, R., Dewall, C., Maner, J., Plant, E., Tice, D., Brewer, L., Schmeichel, B., 2007. Self-control relies on glucose as a limited energy source: willpower is more than a metaphor. J. Pers. Soc. Psychol. 92, 325–336.
Garavan, H., Ross, T.J., Murphy, K., Roche, R.A., Stein, E.A., 2002. Dissociable executive functions in the dynamic control of behavior: inhibition, error detection, and correction. NeuroImage 17, 1820–1829.
Glover, G.H., Law, C.S., 2001. Spiral-in/out BOLD fMRI for increased SNR and reduced susceptibility artifacts. Magn. Reson. Med. 46, 515–522.
Green, L., Myerson, J., 2004. A discounting framework for choice with delayed and probabilistic rewards. Psychol. Bull. 130, 769–792.
Kable, J.W., Glimcher, P.W., 2007. The neural correlates of subjective value during intertemporal choice. Nat. Neurosci. 10, 1625–1633.
Kim, S., Hwang, J., Lee, D., 2008. Prefrontal coding of temporally discounted values during inter-temporal choice. Neuron 59, 161–172.
Kirby, K.N., Maraković, N.N., 1995. Modeling myopic decisions: evidence for hyperbolic delay-discounting within subjects and amounts. Org. Behav. Human Decis. Process 64, 22–30.
Kirby, K.N., Winston, G.C., Santiesteban, M., 2005. Impatience and grades: delay-discount rates correlate negatively with college GPA. Learn. Individ. Differ. 15, 213–222.
Knoch, D., Fehr, E., 2007. Resisting the power of temptations: the right prefrontal cortex and self-control. Ann. N. Y. Acad. Sci. 1104, 123–134.
Knutson, B., Cooper, J.C., 2005. Functional magnetic resonance imaging of reward prediction. Curr. Opin. Neurol. 18, 411–417.
Knutson, B., Gibbs, S.E., 2007. Linking nucleus accumbens dopamine and blood oxygenation. Psychopharmacology 191, 813–822 (Berl).
Knutson, B., Greer, S.M., 2008. Anticipatory affect: neural correlates and consequences for choice. Philos. Trans. R. Soc. B 363, 3771–3786.
Knutson, B., Adams, C.M., Fong, G.W., Hommer, D., 2001. Anticipation of increasing monetary reward selectively recruits nucleus accumbens. J. Neurosci. 21, RC159.
Knutson, B., Fong, G.W., Bennett, S.M., Adams, C.M., Hommer, D., 2003. A region of mesial prefrontal cortex tracks monetarily rewarding outcomes: characterization with rapid event-related fMRI. NeuroImage 18, 263–272.
Knutson, B., Taylor, J., Kaufman, M., Peterson, R., Glover, G., 2005. Distributed neural representation of expected value. J. Neurosci. 25, 4806–4812.
Knutson, B., Rick, S., Wimmer, G.E., Prelec, D., Loewenstein, G., 2007. Neural predictors of purchases. Neuron 53, 147–156.
Kobayashi, S., Schultz, W., 2008. Influence of reward delays on responses of dopamine neurons. J. Neurosci. 28, 7837–7846.
Kuhnen, C.M., Knutson, B., 2005. The neural basis of financial risk taking. Neuron 47, 763–770.
Laibson, D., 1997. Golden eggs and hyperbolic discounting. Q. J. Econ. 112, 443–477.
Logothetis, N.K., Wandell, B.A., 2004. Interpreting the BOLD signal. Annu. Rev. Physiol. 66, 735–769.

Mazur, J., 1987. An Adjusting Procedure for Studying Delayed Reinforcement. Erlbaum, Hillsdale, NJ.
McClure, S.M., Berns, G.S., Montague, P.R., 2003. Temporal prediction errors in a passive learning task activate human striatum. Neuron 38, 339–346.
McClure, S.M., Laibson, D.I., Loewenstein, G., Cohen, J.D., 2004. Separate neural systems value immediate and delayed monetary rewards. Science 306, 503–507.
McClure, S.M., Ericson, K.M., Laibson, D.I., Loewenstein, G., Cohen, J.D., 2007. Time discounting for primary rewards. J. Neurosci. 27, 5796–5804.
Menon, V., Adleman, N.E., White, C.D., Glover, G.H., Reiss, A.L., 2001. Error-related brain activation during a Go/NoGo response inhibition task. Hum. Brain Mapp. 12, 131–143.
O'Doherty, J., Critchley, H., Deichmann, R., Dolan, R.J., 2003a. Dissociating valence of outcome from behavioral control in human orbital and ventral prefrontal cortices. J. Neurosci. 23, 7931–7939.
O'Doherty, J., Winston, J., Critchley, H., Perrett, D., Burt, D.M., Dolan, R.J., 2003b. Beauty in a smile: the role of medial orbitofrontal cortex in facial attractiveness. Neuropsychologia 41, 147–155.
O'Doherty, J.P., Dayan, P., Friston, K., Critchley, H., Dolan, R.J., 2003c. Temporal difference models and reward-related learning in the human brain. Neuron 38, 329–337.
Paulus, M., 2003. Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. NeuroImage 19, 1439–1448.
Plassmann, H., O'Doherty, J., Rangel, A., 2007. Orbitofrontal cortex encodes willingness to pay in everyday economic transactions. J. Neurosci. 27, 9984–9988.
Preuschoff, K., Bossaerts, P., Quartz, S.R., 2006. Neural differentiation of expected reward and risk in human subcortical structures. Neuron 51, 381–390.
Preuschoff, K., Quartz, S.R., Bossaerts, P., 2008. Human insula activation reflects risk prediction errors as well as risk. J. Neurosci. 28, 2745–2752.
Rachlin, H., 1989. Judgment, Decision, and Choice: a Cognitive/Behavioral Synthesis. Freeman, New York, NY.
Read, D., Read, N.L., 2004. Time discounting over the lifespan. Org. Behav. Human Decis. Process 94, 22–32.
Reynolds, B., 2006. A review of delay-discounting research with humans: relations to drug use and gambling. Behav. Pharmacol. 17, 651–667.
Richards, J.B., Zhang, L., Mitchell, S.H., de Wit, H., 1999. Delay or probability discounting in a model of impulsive behavior: effect of alcohol. J. Exp. Anal. Behav. 71, 121–143.
Rodriguez, M.L., Logue, A.W., 1988. Adjusting delay to reinforcement: comparing choice in pigeons and humans. J. Exp. Psychol. 14, 106–117.
Samuelson, P.A., 1937. A note on measurement of utility. Rev. Econ. Stud. 4, 155–161.
Weber, E.U., Johnson, E.J., Milch, K.F., Chang, H., Brodscholl, J.C., Goldstein, D.G., 2007. Asymmetric discounting in intertemporal choice: a query-theory account. Psychol. Sci. 18, 516–523.