

Opposing BOLD responses to reciprocated and unreciprocated altruism in putative reward pathways

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Mesencephalic dopamine neurons are believed to facilitate reward-dependent learning by computing errors in reward predictions. We used fMRI to test whether this system was activated as expected in response to errors in predictions about whether a social partner would reciprocate an act of altruism. Nineteen subjects received fMRI scans as they played a series of single-shot Prisoner's Dilemma games with partners who were outside the scanner. In both ventromedial prefrontal cortex and ventral striatum,

reciprocated and unreciprocated cooperation were associated with positive and negative BOLD responses, respectively. Our results are consistent with the hypothesis that mesencephalic dopamine projection sites carry information about errors in reward prediction that allow us to learn who can and cannot be trusted to reciprocate favors. *NeuroReport* 15:2539–2543 © 2004 Lippincott Williams & Wilkins.

Key words: Altruism; Cooperation; Dopamine; fMRI; Prisoner's Dilemma; Reciprocity; Reward

INTRODUCTION

Many social relationships are based on the reciprocal exchange of favors, otherwise known as reciprocal altruism [1]. In general, we benefit from relationships in which we help others in their time of need and vice-versa. However, we suffer when we help someone who fails to reciprocate in our time of need. Thus, it is important that we be endowed with neural mechanisms that allow us to learn who is a good social partner and who is a cheater, so that the former can be sought out and the latter avoided [2].

An earlier study used fMRI to measure brain activity in subjects playing an iterated Prisoner's Dilemma game with other subjects who were outside the MRI scanner [3] (see Materials and Methods for a description of the game). The outcome of mutual cooperation (CC) in the game was uniquely associated with activation in the anteroventral striatum and ventromedial prefrontal cortex (VMPFC), regions that receive mesencephalic dopamine projections, and have been consistently activated by a diverse array of rewarding stimuli in human fMRI studies [4–11]. This result suggested that mutual cooperation was rewarding, and that this reward might enable players to overcome the temptation to act in their immediate self-interest and defect, rather than cooperate.

Based on single cell recordings of dopamine neurons in awake monkeys [12], it has been suggested that midbrain dopamine cells compute errors in reward predictions [13], defined as the discrepancy between the probability with

which a reward is predicted and an actual outcome [14]. For example, when monkeys view visual stimuli that have perfectly predicted reward ($p=1.0$), there is no change in the cell's firing rate upon receiving the reward, but a pronounced decrease if the reward is omitted. On the other hand, upon viewing stimuli that have always predicted the absence of reward ($p=0.0$), there is no change in firing rate upon not receiving a reward, but a marked increase in firing rate upon receiving a completely unexpected reward. Finally, when viewing stimuli that predict reward on 50% of trials, the firing rate of midbrain dopamine cells both increases in response to reward and decreases in response to its absence, though in both cases to a lesser magnitude than for more severe violations of predictions (i.e. $p=0.0, 1.0$). The Prisoner's Dilemma game is similar to this last situation in which the reward is uncertain, the uncertainty stemming from the unpredictability of a human partner's decision. This leads to the hypothesis that reciprocated cooperation will increase the firing frequency of midbrain dopamine neurons, whereas unreciprocated cooperation will decrease the firing frequency. We attempted to evaluate this hypothesis in the following fMRI experiment.

MATERIALS AND METHODS

This study was approved by the Princeton University Institutional Review Panel and conducted with the understanding and written consent of each participant.

Subjects: Participants were 11 females and eight males recruited from the Princeton University campus, with a mean (\pm s.d.) age of 21.8 ± 7.8 years.

The Prisoner's Dilemma game: We used the single-shot Prisoner's Dilemma game to observe reciprocated and unreciprocated altruism. In this game, two players choose to either cooperate with each other or not, and each is awarded a sum of money that depends upon the interaction of both players' choices. There are four possible outcomes: player A and player B cooperate (CC), player A cooperates and player B defects (CD), player A defects and player B cooperates (DC), or player A and player B defect (DD). The payoffs for the outcomes are arranged such that $DC > CC > DD > CD$, and $CC > (CD + DC)/2$. Each cell of the payoff matrix (Fig. 1a) corresponds to a different outcome of a social interaction. DC represents the situation where player A opts for non-cooperation and player B cooperates so that player A benefits at player B's expense. CD is the converse. CC involves mutual cooperation and DD involves mutual non-cooperation. In the version of the game we use here (i.e. the single-shot version), the game is played a single time with each partner.

Behavioral procedures: This was the second part of a two-part study in which subjects first played a single-shot Ultimatum game with each partner. After all Ultimatum game trials were complete, subjects played a single-shot Prisoner's Dilemma game with each partner. All subjects saw the same set of offers in the Ultimatum game, half fair and half unfair, before beginning the Prisoner's Dilemma game. Methods and findings for the Ultimatum game have been published previously [15]. Prior to being scanned, each subject completed a tutorial that explained the rules of the

two games. For the Prisoner's Dilemma, subjects were informed that they would choose first in each game and that their partner would witness that choice before making a decision of their own. After the tutorial, each subject was introduced to a group of 10 human confederates. Investigators first introduced the subject to the confederates by stating his/her name and indicating that confederates would each play one round of each game with the subject. Each confederate then stated his/her name for the subject. Afterwards, the subject was escorted to the scanner room and digital photographs were taken of the confederates for use in the experiment. Following acquisition of anatomical scans, functional images were acquired as subjects played the games with the confederates. A time-line for a single Prisoner's Dilemma trial is shown in Fig. 1b. Each trial began with a 12 s preparation interval. Subjects were then shown a photograph of the partner for that trial for 6 s. During the next 6 s epoch, subjects chose to cooperate or defect by pressing one of two buttons on a button box. During the subsequent 6 s epoch, subjects were told that their partner would be able to view their choice and then would respond in turn by cooperating or defecting. The partner's choice and the trial outcome were then displayed for 12 s.

In reality, partner choices were determined in advance and administered by a computer algorithm, so that half of all partners reciprocated cooperation and the other half did not. Each subject completed 28 Prisoner's Dilemma trials while in the scanner. Ten were with putative human partners, as described above. For simplicity, we will henceforth refer to those trials in which subjects believed they were playing the game with another person as trials involving human partners. Another 10 trials were with computer partners. For these trials, subjects saw a picture of a computer rather than a confederate photograph. They

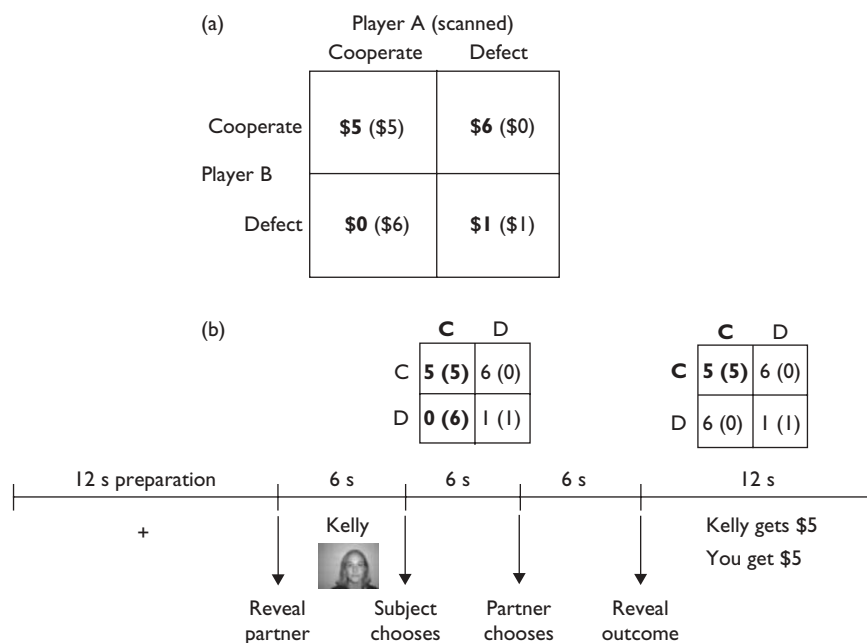


Fig. 1. Illustration of Prisoner's Dilemma task. (a) Payoff matrix for Prisoner's Dilemma game. Scanned subject's choices (player A) are listed atop columns and non-scanned subject's choices (player B) are listed aside rows. Dollar amounts in bold are awarded to player A. Amounts in parentheses are awarded to player B. (b) Time-line for a single Prisoner's Dilemma trial. Each trial lasted 42 s.

were told only that the computer would make choices according to programmed probabilities. In actuality, the same computer algorithm was used to make decisions for both human and computer trials, except that for computer trials, the algorithm reciprocated defection only half the time as opposed to human trials where it always reciprocated defection. The latter modification was implemented to make the algorithm consistent with plausible human decision-making (i.e., not willingly choosing to accept less so that one's partner can earn dramatically more). The final eight trials were designed to control for the BOLD response to monetary reinforcement, independent of the social interaction. In these trials, subjects saw a picture of a roulette wheel rather than a confederate photograph or a picture of the computer. They were then presented with one of two payoff matrices. The first had \$0 in all four squares. The second had \$5 in both squares of one column and \$0 in both squares of the other. Subjects were simply asked to select either column whereby they would receive the payoff for that column. The selection was included to control for choice and motor processing. Subjects chose one of the two \$0 columns in the first matrix and overwhelmingly chose the \$5 column in the second (i.e., on 99% of trials). The final 12s of the control trial indicated how much money the subject had earned (either \$5 or \$0). These payoffs were matched to those for CC (\$5) and CD (\$0) outcomes. Subjects were compensated at a rate of one-third their cumulative earnings in the task.

Image acquisition: Anatomical scans were collected using a T1-weighted MP-RAGE protocol (256 × 256 matrix, FOV=256 mm, 128 1.33 mm sagittal slices). Functional images with blood oxygen level-dependent (BOLD) contrast [16,17] were acquired with a Siemens 3.0T head-dedicated MRI scanner using T2*-weighted EPI (TR=3000 ms, TE=22 ms, 64 × 64 matrix, FOV=192 mm, 30 2.5 mm axial slices with 1.5 mm gap). Following two functional runs during which subjects played the Ultimatum game, two functional runs (200 scans each) were collected as subjects played the Prisoner's Dilemma game.

Image analysis: Data were preprocessed and analyzed using BrainVoyager software (Maastricht, The Netherlands). Image preprocessing included: 6-parameter, 3D motion correction, slice scan time correction using linear interpolation, spatial smoothing with a 6 mm FWHM Gaussian kernel, voxel-wise linear detrending, and high pass filter of frequencies <3 cycles/time course. Spatial normalization was performed using the standard 9-parameter landmark method of Talairach and Tournoux [18]. A separate general linear model was defined for each subject [19] that included six regressors which modeled the BOLD response to the 6s epoch following the revelation of the trial outcome: reciprocated cooperation (CC) from a human partner, unreciprocated cooperation (CD) from a human partner, reciprocated cooperation (CC) from a computer partner, unreciprocated cooperation (CD) from a computer partner, a \$5 reward in a non-social control task, and a \$0 reward in a non-social control task. Each regressor was convolved with a standard gamma model of the hemodynamic impulse-response function. The resulting general linear model was corrected for temporal autocorrelation using a first-order autoregressive model. For each subject, contrasts were

Table 1. Areas activated for the contrast between CC and CD outcomes with human partners ($p < 0.005$, 8 voxel spatial extent threshold).

Brain region	Talairach coordinate	# voxels	Peak t statistic
CC > CD			
Right middle frontal gyrus (BA 10)	27 57 14	15	4.92*
Right middle frontal gyrus (BA 10)	28 56 0	13	4.12*
Right medial frontal gyrus (BA 10)	8 39 -5	9	4.1*
Ventral caudate	10 17 -4	25	4.21*
Left middle frontal gyrus (BA 6)	-27 7 43	38	4.22*
Left putamen/caudate	-27 -10 7	25	3.82
Left medial frontal gyrus (BA 6)	-10 -10 51	15	4.42*
Left central sulcus (BA 4)	-27 -27 52	29	4.51*
Left middle temporal gyrus (BA 21)	-52 -31 -7	10	3.85
Right superior temporal sulcus (BA 22)	42 -52 16	22	4.6*
Left calcarine sulcus (BA 17)	-19 -69 11	40	4.25*
CD > CC			
No significant activations at this threshold			

calculated at every voxel in the brain between regression coefficients for reciprocated (CC) and unreciprocated cooperation (CD) from a human partner. A one-sample t -test was then used to determine where the average contrast value for the group as a whole ($n=19$ subjects) differed significantly from zero (a random-effects analysis). The resulting map of the t -statistic was thresholded to display only those voxels where the t -statistic reached $p < 0.005$. While this is a less stringent threshold than is typically reported in neuroimaging studies, we feel it is justified by the fact that activated areas were *a priori* regions of interest, given that they receive mesencephalic dopamine projections. In actuality, these regions survive at more stringent thresholds (see Table 1 for $p < 0.001$), but with a reduced spatial extent. We therefore consider it unlikely that these activations represent false positives.

RESULTS

Behavioral data: Subjects cooperated on 81% of trials with human partners and on 66% of computer trials, demonstrating that they distinguished behaviourally between human and computer playing partners ($\chi^2=11.3$, 1 df, $p < 0.001$).

fMRI data: The contrast between reciprocated (CC) and unreciprocated (CD) cooperation from human partners identified two regions of interest (ROIs) that are consistent with the known anatomical projection sites of the mesencephalic dopamine system (Fig. 2a, Table 1). One spans the ventral striatum and the subcallosal cortex (BA 25/11, centered at Talairach coordinate 10, 17, -4). The other is in the ventromedial frontal cortex, (VMPFC) including BA 10, 11 and 32 (centered at 8, 39, -5). The contrast map indicates that these areas show a larger BOLD response to reciprocated *vs* unreciprocated cooperation from human partners. However, it does not reveal whether this represents a positive BOLD response to CC, a negative BOLD response to CD, or, as theory predicts, both. To answer this question, a general linear model was run on these two ROIs to determine the sign and magnitude of the coefficients for the two regressors (CC human and CD human), using the remainder of the trial as the baseline against which the response is measured. We also used data from computer and control trials to estimate the BOLD response of the four

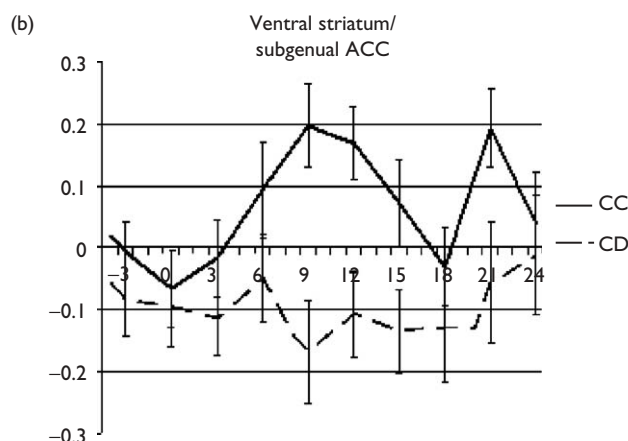
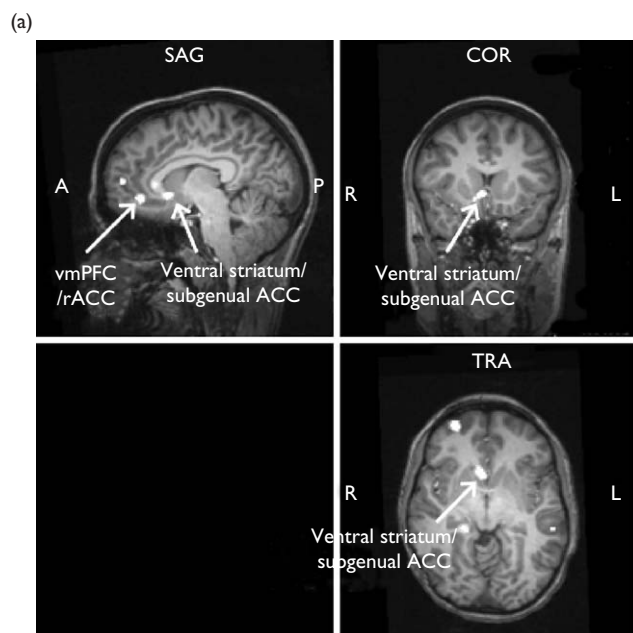


Fig. 2. Activation related to reciprocated and unreciprocated altruism. (a) Map of the *t*-statistic for the contrast CC human minus CD human. Areas in white showed greater activation following CC compared with CD outcomes ($p < 0.005$). rACC=rostral anterior cingulate cortex, subgenual ACC=subgenual anterior cingulate cortex. (b) Event-related plot for CC and CD outcomes in the striatal ROI. The game outcome was revealed at $t=0$ on the x-axis. Error bars are ± 1 s.e.

outcomes (CC computer, CD computer, \$5 control, \$0 control) in these ROIs. The results, shown in Table 2, indicate that in both ROIs, there is both a significant positive BOLD response to CC and a significant negative BOLD response to CD outcomes with human partners (Fig. 2b). CD outcomes with computer partners and \$0 control outcomes are also associated with negative BOLD responses in the striatum, but not in VMPFC. In contrast to CC outcomes with human partners, in neither ROI were CC outcomes with computer partners or \$5 control outcomes associated with significant positive BOLD responses.

DISCUSSION

In the Prisoner’s Dilemma game, each subject probably has his/her own idiosyncratic estimate of the probability that

Table 2. Regression coefficients for GLM of striatal and ventromedial frontal ROIs from Figure 2. $n=19$, $p < 0.005$.

Striatum				
Regressor	Value	Se	t	<i>p</i>
CC human	0.30	0.10	2.96	0.003
CD human	-0.21	0.10	-2.03	0.04
\$0 control	-0.22	0.10	-2.15	0.03
\$5 control	-0.02	0.10	-0.17	0.87
CC computer	-0.01	0.10	-0.11	0.92
CD computer	-0.29	0.13	-2.16	0.03
VMPFC				
Regressor	Value	Se	t	<i>p</i>
CC human	0.34	0.10	3.37	0.0008
CD human	-0.36	0.10	-3.47	0.0005
\$0 control	-0.11	0.10	-1.07	0.28
\$5 control	-0	0.10	-0.02	0.98
CC compute	0.03	0.10	0.32	0.75
CD computer	-0.14	0.13	-1.08	0.27

Betas for regressors in bold type differed significantly from zero at $p < 0.05$.

cooperation will be reciprocated, but that estimate is unlikely to be 0 or 1.0, given that human behavior is rarely 100% predictable. Therefore, when reward prediction errors are defined as a discrepancy between the probability with which a reward is predicted and an actual outcome [14], PD outcomes will always involve an error in reward prediction. Reciprocated cooperation involves a positive reward prediction error, and unreciprocated cooperation involves a negative reward prediction error. According to the model of Montague *et al.* [13], these positive and negative reward prediction errors should result in increased and decreased firing of mesencephalic dopamine neurons, respectively. But how should these changes in neuronal firing frequency be manifest in the BOLD fMRI signal? BOLD fMRI responses reflect neuronal input to an area rather than neuronal output in terms of spike frequency [20]. Thus, mesolimbic dopamine projection sites should exhibit an increased BOLD response to reciprocated cooperation due to increased input and a decreased BOLD response to unreciprocated cooperation due to decreased input. This prediction is supported by two sources of evidence: (1) positive and negative BOLD responses following positive and negative errors in reward predictions have also been observed for the delivery of juice and monetary rewards [5,9,21,22] (but see [10] for an exception), and (2) dopamine agonists have been shown to increase BOLD responses in the striatum of monkeys [23], suggesting that dopamine release in the striatum should lead to an increased BOLD response. We observed the predicted pattern of response in two target regions that receive mesencephalic dopamine projections, the ventral striatum and VMPFC.

Alterations in neural activity in response to errors in reward predictions are thought to be important for reward-dependent learning [12]. Presumably, they motivate adaptive changes in behavior such that, over time, behaviors that are more rewarding than predicted are adopted more frequently and those that are less rewarding than predicted are adopted less frequently. Thus, activity in the mesolimbic dopamine system may help us to learn whom we can and cannot trust to reciprocate favors, motivating us to seek out future interactions with the former and avoid future interactions with the latter.

In the striatum, the magnitude of the activation exceeded that of the deactivation (Table 1, Fig. 2b). This may relate to subject's estimates of the likelihood that cooperation would be reciprocated. In their single-cell recording study with awake monkeys, Fiorillo *et al.* [14] found that visual stimuli that predicted rewards with a probability between 0 and 1 resulted in both an increased response to reward and a decreased response to its absence, however the magnitude of the increase exceeded that of the decrease when the probability of reward dropped below 0.5. These data suggest that our subjects' expectation that their partner would reciprocate cooperation may have been less than 50%, but that cooperation was worth the risk given the large payoff for occasional CC outcomes. Thus, subjects may have been intuitively aware that a rational partner would defect [24], and guessed that rational motives would prevail on their partner more often than not.

Negative BOLD responses in the striatum were also observed for CD outcomes with known computer partners, as well as \$0 control outcomes, indicating that this negative response is not dependent on the social interaction itself, but on the absence of an expected material reward that accompanies it. On the other hand, the positive BOLD response to CC depends on the nature of the interaction; it is only elicited when a human partner reciprocates altruism; not by a computer that reciprocates altruism or by a \$5 reward in a control trial. The absence of positive BOLD responses to these two outcomes may indicate that they are not sufficiently rewarding to provoke a robust response in midbrain dopamine neurons; and that there is something particularly rewarding about positive social interactions with other people. This is consistent with our observation that subjects behaviorally distinguish between human and computer playing partners. In VMPFC, both activations and deactivations were specific to trials with alleged human partners and were not observed for computer or control trials.

CONCLUSION

Brain regions that receive mesencephalic dopamine projections, the ventral striatum and VMPFC, showed an increased BOLD response to reciprocated altruism and a decreased BOLD response to unreciprocated altruism. Our results are therefore consistent with the hypothesis that the mesolimbic dopamine system computes errors in predictions about whether a social partner will reciprocate an act of altruism. This error signal may teach us to seek out reciprocators and avoid nonreciprocators as social partners.

REFERENCES

1. Trivers RL. The evolution of reciprocal altruism. *Q Rev Biol* 1971; **46**: 35–57.

2. Cosmides L and Tooby J. The cognitive neuroscience of social reasoning. In: Gazzaniga MS (ed.). *The New Cognitive Neurosciences*. Champaign, IL: Massachusetts Institute of Technology; 2000, pp. 1259–1270.
3. Rilling JK, Gutman DA, Zeh TR, Pagnoni G, Berns GS and Kilts CD. A neural basis for social cooperation. *Neuron* 2002; **35**:395–405.
4. Aharon I, Etcoff N, Ariely D, Chabris CF, O'Connor E and Breiter H. Beautiful faces have variable reward value: fMRI and behavioral evidence. *Neuron* 2001; **32**:537–551.
5. Berns GS, McClure SM, Pagnoni G and Montague PR. Predictability modulates human brain response to reward. *J Neurosci* 2001; **21**:2793–2798.
6. Delgado MR, Nystrom LE, Fissell C, Noll DC and Fiez JA. Tracking the hemodynamic responses to reward and punishment in the striatum. *J Neurophysiol* 2000; **84**:3072–3077.
7. Elliott R, Friston KJ and Dolan RJ. Dissociable neural responses in human reward systems. *J Neurosci* 2000; **20**:6159–6165.
8. Francis S, Rolls ET, Bowtell R, McGlone F, O'Doherty J, Browning A *et al.* The representation of pleasant touch in the brain and its relationship with taste and olfactory areas. *Neuroreport* 1999; **10**:453–459.
9. Knutson B, Fong GW, Adams CM, Varner JL and Hommer D. Dissociation of reward anticipation and outcome with event-related fMRI. *Neuroreport* 2001; **12**:3683–3687.
10. Pagnoni G, Zink CF, Mantague PR and Berns GS. Activity in human ventral striatum locked to errors of reward prediction. *Nature Neurosci* 2002; **5**:97–98.
11. Breiter HC, Aharon I, Kahneman D, Dale A and Shizgal P. Functional imaging of neural responses to expectancy and experience of monetary gains and losses. *Neuron* 2001; **30**:619–639.
12. Schultz W. Dopamine neurons and their role in reward mechanisms. *Curr Opin Neurobiol* 1997; **7**:191–197.
13. Montague PR, Dayan P and Sejnowski TJ. A framework for mesencephalic dopamine systems based on predictive Hebbian learning. *J Neurosci* 1996; **16**:1936–1947.
14. Fiorillo CD, Tobler PN and Schultz W. Discrete coding of reward probability and uncertainty by dopamine neurons. *Science* 2003; **299**:1898–1902.
15. Sanfey AG, Rilling JK, Aronson JA, Nystrom LE and Cohen JD. The neural basis of economic decision-making in the ultimatum game. *Science* 2003; **300**:1755–1758.
16. Ogawa S, Tank DW, Menon R, Ellermann JM, Kim SG, Merkle H and Ugurbil K. Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. *Proc Natl Acad Sci USA* 1992; **89**:5951–5955.
17. Kwong K, Belliveau J, Chesler D, Goldberg J, Weisskoff R, Poncelet B *et al.* Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc Natl Acad Sci USA* 1992; **89**:5675–5679.
18. Talairach J and Tournoux P. *Co-Planar Stereotaxic Atlas of the Human Brain*. New York: Thieme Medical Publishers; 1988.
19. Friston KJ, Frith CD, Frackowiak RSJ and Turner R. Characterizing dynamic brain responses with fMRI: a multivariate approach. *Neuroimage* 1995; **2**:166–172.
20. Logothetis NK. The neural basis of the blood-oxygen-level-dependent functional magnetic resonance imaging signal. *Phil Trans R Soc Lond B Biol Sci* 2002; **357**:1003–1037.
21. O'Doherty JP, Dayan P, Friston K, Critchley H and Dolan RJ. Temporal difference models and reward-related learning in the human brain. *Neuron* 2003; **38**:329–337.
22. McClure SM, Berns GS and Montague PR. Temporal prediction errors in a passive learning task activate human striatum. *Neuron* 2003; **38**:339–346.
23. Zhang Z, Andersen AH, Avison MJ, Gerhardt GA and Gash DM. Functional MRI of apomorphine activation of the basal ganglia in awake rhesus monkeys. *Brain Res* 2000; **852**:290–296.
24. Nash JF. Equilibrium points in n-person games. *Proc Natl Acad Sci USA* 1950; **36**:48–49.

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