



Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev



Review

Common and distinct networks underlying reward valence and processing stages: A meta-analysis of functional neuroimaging studies

Xun Liu^{a,b,*}, Jacqueline Hairston^b, Madeleine Schrier^b, Jin Fan^{b,c,d}

^a Key Laboratory of Behavioral Science, Institute of Psychology, Chinese Academy of Sciences, Beijing 100101, China

^b Department of Psychiatry, Mount Sinai School of Medicine, New York, NY 10029, United States

^c Department of Neuroscience, Mount Sinai School of Medicine, New York, NY 10029, United States

^d Department of Psychology, Queens College, The City University of New York, Flushing, NY 11367, United States

ARTICLE INFO

Article history:

Received 4 June 2010

Received in revised form 1 December 2010

Accepted 16 December 2010

Keywords:

Meta-analysis

Reward

Nucleus accumbens

Orbitofrontal cortex

Anterior cingulate cortex

Anterior insula

ABSTRACT

To better understand the reward circuitry in human brain, we conducted activation likelihood estimation (ALE) and parametric voxel-based meta-analyses (PVM) on 142 neuroimaging studies that examined brain activation in reward-related tasks in healthy adults. We observed several core brain areas that participated in reward-related decision making, including the nucleus accumbens (NAcc), caudate, putamen, thalamus, orbitofrontal cortex (OFC), bilateral anterior insula, anterior cingulate cortex (ACC) and posterior cingulate cortex (PCC), as well as cognitive control regions in the inferior parietal lobule and prefrontal cortex (PFC). The NAcc was commonly activated by both positive and negative rewards across various stages of reward processing (e.g., anticipation, outcome, and evaluation). In addition, the medial OFC and PCC preferentially responded to positive rewards, whereas the ACC, bilateral anterior insula, and lateral PFC selectively responded to negative rewards. Reward anticipation activated the ACC, bilateral anterior insula, and brain stem, whereas reward outcome more significantly activated the NAcc, medial OFC, and amygdala. Neurobiological theories of reward-related decision making should therefore take distributed and interrelated representations of reward valuation and valence assessment into account.

© 2010 Elsevier Ltd. All rights reserved.

Contents

1. Introduction	00
2. Methods	00
2.1. Literature search and organization	00
2.1.1. Study identification	00
2.1.2. Experiment categorization	00
2.2. Activation likelihood estimation (ALE)	00
2.2.1. Main analysis of all studies	00
2.2.2. Individual analyses of sub-lists	00
2.2.3. Subtraction analyses	00
2.3. Parametric voxel-based meta-analysis (PVM)	00
2.3.1. Main analysis of all studies	00
2.3.2. Individual analyses of sub-lists	00
2.3.3. Comparison analyses	00
3. Results	00
3.1. ALE results	00
3.2. PVM results	00
3.3. Comparison of ALE and PVM results	00
4. Discussion	00
4.1. Core reward areas: NAcc and OFC	00
4.2. Valence-related assessment	00

* Corresponding author at: Institute of Psychology, Chinese Academy of Sciences, 4A Datun Road, Chaoyang District, Beijing 100101, China. Tel.: +86 10 64847153; fax: +86 10 64847153.

E-mail address: liux@psych.ac.cn (X. Liu).

4.3. Anticipation versus outcome	00
4.4. A schematic illustration of reward processing	00
4.5. Caveats	00
Contributions	00
Acknowledgements	00
Appendix A	00
Appendix B. Supplementary data	00
References	00

1. Introduction

People face countless reward-related decision making opportunities everyday. Our physical, mental, and socio-economical well-being critically depends on the consequences of the choices we make. It is thus crucial to understand what underlies normal functioning of reward-related decision making. Studying the normal functioning of reward-related decision making also helps us to better understand the various behavioral and mental disorders which arise when such function is disrupted, such as depression (Drevets, 2001), substance abuse (Bechara, 2005; Garavan and Stout, 2005; Volkow et al., 2003), and eating disorders (Kringelbach et al., 2003; Volkow and Wise, 2005).

Functional neuroimaging research on reward has become a rapidly growing field. We have observed a huge surge of neuroimaging research in this domain, with dozens of relevant articles showing up in the PubMed database every month. On the one hand, this is exciting because the mounting results are paramount to formalizing behavioral and neural mechanisms of reward-related decision making (Fellows, 2004; Trepel et al., 2005). On the other hand, the heterogeneity of the results in conjunction with the occasional opposing patterns make it difficult to obtain a clear picture of the reward circuitry in human brain. The mixture of results is partly due to diverse experimental paradigms developed by various research groups that aimed to address different aspects of reward-related decision making, such as the distinction between reward anticipation and outcome (Breiter et al., 2001; Knutson et al., 2001b; McClure et al., 2003; Rogers et al., 2004), valuation of positive and negative rewards (Liu et al., 2007; Nieuwenhuis et al., 2005; O'Doherty et al., 2001, 2003a; Ullsperger and von Cramon, 2003), and assessment of risk (Bach et al., 2009; d'Acromont and Bossaerts, 2008; Hsu et al., 2009; Huettel, 2006).

Therefore, it is crucial to pool existing studies together and examine the core reward networks in human brain, from both data-driven and theory-driven approaches to test the commonality and distinction of different aspects of reward-related decision making. To achieve this goal, we employed and compared two coordinate-based meta-analysis (CBMA) methods (Salimi-Khorshidi et al., 2009), activation likelihood estimation (ALE) (Laird et al., 2005; Turkeltaub et al., 2002) and parametric voxel-based meta-analysis (PVM) (Costafreda et al., 2009), so as to reveal the concordance across a large number of neuroimaging studies on reward-related decision making. We anticipated that the ventral striatum and orbitofrontal cortex (OFC), two major dopaminergic projection areas that have been associated with reward processing, would be consistently activated.

In addition, from a theory-driven perspective, we aimed to elucidate whether there exist distinctions in the brain networks that are responsible for processing positive and negative reward information, and that are preferentially involved in different stages of reward processing such as reward anticipation, outcome monitoring, and decision evaluation. Decision making involves encoding and representation of the alternative options and comparing the values or utilities associated with these options. Across these processes, decision making is usually affiliated with positive or neg-

ative valence from either the outcomes or emotional responses toward the choices made. Positive reward valence refers to the positive subjective states we experience (e.g., happiness or satisfaction) when the outcome is positive (e.g., winning a lottery) or better than we anticipate (e.g., losing less value than projected). Negative reward valence refers to the negative feelings we go through (e.g., frustration or regret) when the outcome is negative (e.g., losing a gamble) or worse than what we expect (e.g., stock value increasing lower than projected). Although previous studies have attempted to distinguish reward networks that are sensitive to processing positive or negative information (Kringelbach, 2005; Liu et al., 2007), as well as those that are involved in reward anticipation or outcome (Knutson et al., 2003; Ramnani et al., 2004), empirical results have been mixed. We aimed to extract consistent patterns by pooling over a large number of studies examining these distinctions.

2. Methods

2.1. Literature search and organization

2.1.1. Study identification

Two independent researchers conducted a thorough search of the literature for fMRI studies examining reward-based decision making in humans. The terms used to search the online citation indexing service PUBMED (through June 2009) were “fMRI”, “reward”, and “decision” (by the first researcher), “reward decision making task”, “fMRI”, and “human” (by the second researcher). These initial search results were merged to yield a total of 182 articles. Another 90 articles were identified from a reference database of a third researcher accumulated through June 2009 using “reward” and “MRI” as filtering criteria. We also searched the BrainMap database using Sleuth, with “reward task” and “fMRI” as search terms, and found 59 articles. All of these articles were pooled into a database and redundant entries were eliminated. We then applied several exclusion criteria to further eliminate articles that are not directly relevant to the current study. These criteria are: (1) non-first hand empirical studies (e.g., review articles); (2) studies that did not report results in standard stereotactic coordinate space (either Talairach or Montreal Neurological Institute, MNI); (3) studies using tasks unrelated to reward or value-based decision making; (4) studies of structural brain analyses (e.g., voxel-based morphometry or diffusion tensor imaging); (5) studies purely based on region of interest (ROI) analysis (e.g., using anatomical masks or coordinates from other studies); (6) studies of special populations whose brain functions may be deviated from those of normal healthy adults (e.g., children, aging adults, or substance dependent individuals), although coordinates reported in these studies for the healthy adult group alone were included. Variability among methods with which subjects were instructed to report decisions during the tasks (i.e., verbal, nonverbal button-press) was accepted. This resulted in 142 articles in the final database (listed in Appendix A).

During the data extraction stage, studies were then grouped by different spatial normalization schemes according to coordinate transformations implemented in the GingerALE toolbox (<http://brainmap.org>, Research Imaging Center of the University

of Texas Health Science Center, San Antonio, Texas): using FSL (<http://www.fmrib.ox.ac.uk/fsl>) to report MNI coordinates, using SPM (<http://www.fil.ion.ucl.ac.uk/spm>) to report MNI coordinates, using other programs to report MNI coordinates, using Brett methods to convert MNI coordinates into Talairach space, using a Talairach native template. Lists of coordinates that were in Talairach space were converted into the MNI space according to their original normalization schemes. For the Brett-Talairach list, we converted the coordinates back into the MNI space using reverse transformation by Brett et al. (2002) (i.e., tal2mni). For the native Talairach list, we used BrainMap's Talairach-MNI transformation (i.e., tal2icbm_other). A master list of all studies was created by combining all coordinates in MNI space in preparation for the ALE meta-analyses in GingerALE.

2.1.2. Experiment categorization

To test hypotheses with regards to the common and distinct reward pathways that are recruited by different aspects of reward-related decision making, we categorized coordinates according to two types of classification: reward valence and decision stages. We adopted the term of “experiments” used by the BrainMap database to refer to individual regressors or contrasts typically reported in fMRI studies. For reward valence, we organized the experiments into positive and negative rewards. For decision stages, we separated the experiments into reward anticipation, outcome, and evaluation. Coordinates in the master list that fit into these categories were put into sub-lists; those that were difficult to interpret or not clearly defined were omitted. Below we list some examples that were put into each of these categories.

The following contrasts were classified as processing of positive rewards: those in which subjects won money or points (Elliott et al., 2000) (reward during run of success); avoided losing money or points (Kim et al., 2006) (direct comparison between avoidance of an aversive outcome and reward receipt); won the larger of two sums of money or points (Knutson et al., 2001a) (large vs. small reward anticipation); lost the smaller of two sums of money or points (Ernst et al., 2005) (no-win \$0.50 > no-win \$4); received encouraging words or graphics on the screen (Zalla et al., 2000) (increase for “win”); received sweet taste in their mouths (O'Doherty et al., 2002) (glucose > neutral taste); positively evaluated the choice (Liu et al., 2007) (right > wrong), or received any other type of positive rewards as a result of successful completion of the task.

Experiments classified for negative rewards included those in which subjects lost money or points (Elliott et al., 2000) (penalty during run of failure); did not win money or points (Ernst et al., 2005) (dissatisfaction of no-win); won the smaller of two sums of money or points (Knutson et al., 2001a) (\$1 vs. \$50 reward); lost the larger of two sums of money or points (Knutson et al., 2001a) (large vs. small punishment anticipation); negatively evaluated the choice (Liu et al., 2007) (wrong > right); or received any other negative rewards such as the administration of a bitter taste in their mouths (O'Doherty et al., 2002) (salt > neutral taste) or discouraging words or images (Zalla et al., 2000) (increase for “lose” and decrease for “win”).

Reward anticipation was defined as the time period when the subject was pondering potential options before making a decision. For example, placing a bet and expecting to win money on that bet would be classified as anticipation (Cohen and Ranganath, 2005) (high-risk vs. low-risk decision). Reward outcome/delivery was classified as the period when the subject received feedback on the chosen option, such as a screen with the words “win x\$” or “lose x\$” (Bjork et al., 2004) (gain vs. non-gain outcome). When the feedback influenced the subject's decision and behavior in a subsequent trial or was used as a learning signal, the contrast was classified as reward evaluation. For example, a risky decision that is rewarded in the initial trial may lead a subject to take another, perhaps big-

ger, risk in the next trial (Cohen and Ranganath, 2005) (low-risk rewards followed by high-risk vs. low-risk decisions). Loss aversion, the tendency for people to strongly prefer avoiding losses to acquiring gains, is another example of evaluation (Tom et al., 2007) (relation between lambda and neural loss aversion).

2.2. Activation likelihood estimation (ALE)

The algorithm of ALE is based on (Eickhoff et al., 2009). ALE models the activation foci as 3D Gaussian distributions centered at the reported coordinates, and then calculates the overlap of these distributions across different experiments (ALE treats each contrast in a study as a separate experiment). The spatial uncertainty associated with activation foci is estimated with respect to the number of subjects in each study (i.e., a larger sample produces more reliable activation patterns and localization; therefore the coordinates are convolved with a tighter Gaussian kernel). The convergence of activation patterns across experiments is calculated by taking the union of the above modeled activation maps. A null distribution that represents ALE scores generated by random spatial overlap across studies is estimated through permutation procedure. Finally the ALE map computed from the real activation coordinates is tested against the ALE scores from the null distribution, producing a statistical map representing the p values of the ALE scores. The nonparametric p values are then transformed into z scores and thresholded at a cluster-level corrected $p < 0.05$.

Six different ALE analyses were conducted using GingerALE 2.0 (Eickhoff et al., 2009), one for the main analysis of all studies, and one for each of the five sub-lists characterizing brain activation by positive or negative rewards as well as anticipation, outcome, and evaluation. Two subtraction ALE analyses were conducted using GingerALE 1.2 (Turkeltaub et al., 2002), one for the contrast between positive and negative rewards, and the other for the contrast between anticipation and outcome.

2.2.1. Main analysis of all studies

All 142 studies were included in the main analysis, which consisted of 5214 foci from 655 experiments (contrasts). We used the algorithm implemented in GingerALE 2.0, which models the ALE based on the spatial uncertainty of each focus using an estimation of the inter-subject and inter-experiment variability. The estimation was constrained by a gray matter mask and estimated the above-chance clustering with the experiments as a random-effects factor, rather than using a fixed-effects analysis on foci (Eickhoff et al., 2009). The resulting ALE map was thresholded using the false discover rate (FDR) method with $p < 0.05$ and a minimum cluster size of 60 voxels of $2 \text{ mm} \times 2 \text{ mm} \times 2 \text{ mm}$ (for a total of 480 mm^3) to protect against false positives of multiple comparisons.

2.2.2. Individual analyses of sub-lists

Five other ALE analyses were also conducted based on the sub-lists that categorize different experiments into positive and negative rewards, as well as reward anticipation, reward delivery (outcome), and choice evaluation. For the positive reward analysis, 2167 foci from 283 experiments were included. The negative reward analysis consisted of 935 foci from 140 experiments. The numbers of foci included in the analyses for anticipation, outcome, and choice evaluation were 1553 foci (185 experiments), 1977 (253), and 520 (97), respectively. We applied the same analysis and threshold approaches as we did for the main analysis above.

2.2.3. Subtraction analyses

We were also interested in contrasting the brain areas that were selectively or preferentially activated by positive versus negative rewards, and by reward anticipation versus reward delivery. GingerALE 1.2 was used to conduct these two analyses. ALE maps were

smoothed with a kernel with a FWHM of 10 mm. A permutation test of randomly distributed foci with 10,000 simulations was run to determine statistical significance of the ALE maps. To correct for multiple comparisons, the resulting ALE maps were thresholded using the FDR method with $p < 0.05$ and a minimum cluster size of 60 voxels.

2.3. Parametric voxel-based meta-analysis (PVM)

We also analyzed the same coordinate lists using another meta-analysis approach, PVM. In contrast to the ALE analysis, which treats different contrasts within a study as distinct experiments, PVM analysis pools peaks from all different contrasts within a study and creates a single coordinate map for the specific study (Costafreda et al., 2009). Therefore, the random-effects factor in the PVM analysis is the *studies*, in comparison to individual *experiments/contrasts* in the ALE analysis. This further reduces estimation bias caused by studies with multiple contrasts that reporting similar activation patterns. Similar to the ALE approach, we conducted six different PVM analyses using the algorithms implemented in R statistical software (<http://www.R-project.org>) from a previous study (Costafreda et al., 2009), one for the main analysis of all studies, and one for each of the five sub-lists characterizing brain activation by different aspects of reward processing. Two additional PVM analyses were conducted using the same code base to compare between positive and negative rewards as well as between reward anticipation and outcome.

2.3.1. Main analysis of all studies

MNI coordinates (5214) from the same 142 studies used in the ALE analysis were transformed into a text table, with each study identified by a unique study identification label. Computations on the peak map were constrained within a mask in MNI space. The peak map was first smoothed with a uniform kernel ($\rho = 10$ mm) to generate the summary map, which represents the number of studies reporting overlapping activation peaks within a neighborhood of 10 mm radius. Next, random-effects PVM analysis was run to estimate statistical significance associated with each voxel in the summary map. The number of studies in the summary map was converted into the proportion of studies that reported concordant activation. We used the same threshold as used in ALE analysis to identify significant clusters for the proportion map (using the FDR method with $p < 0.05$ and a minimum cluster size of 60 voxels).

2.3.2. Individual analyses of sub-lists

Five other PVM analyses were conducted on the sub-lists for positive and negative rewards, as well as reward anticipation, outcome, and evaluation. The positive reward analysis included 2167 foci from 111 studies whereas the negative reward analysis included 935 foci from 67 studies. The numbers of studies included in the analyses for anticipation, outcome, and choice evaluation were 1553 foci (65 studies), 1977 (86), and 520 (39), respectively. We applied the same analysis and threshold approaches as we did for the main analysis above.

2.3.3. Comparison analyses

We also conducted two PVM analyses to compare the activation patterns between positive and negative rewards as well as between reward anticipation and outcome. Two peak maps (e.g., one for positive and the other for negative) were first smoothed with a uniform kernel ($\rho = 10$ mm) to generate the summary maps, each representing the number of studies with overlapping activation peak within a neighborhood of 10 mm radius. These two summary maps were entered into a Fisher test to estimate the odds ratio and statistical significance p value for each contributing voxel within the MNI space mask. Since the Fisher's test is not specifically developed for

fMRI data analysis and empirically less sensitive than the other methods, we applied a relatively lenient threshold for the direct comparison PVM analysis, using uncorrected $p < 0.01$ and a minimum cluster size of 60 voxels (Xiong et al., 1995), to correct for multiple comparison Type I error.

3. Results

3.1. ALE results

The all-inclusive analysis of 142 studies showed significant activation of a large cluster that encompassed the bilateral nucleus accumbens (NAcc), pallidum, anterior insula, lateral/medial OFC, anterior cingulate cortex (ACC), supplementary motor area (SMA), lateral prefrontal cortex (PFC), right amygdala, left hippocampus, thalamus, and brain stem (Fig. 1A). Other smaller clusters included the right middle frontal gyrus and left middle/inferior frontal gyrus, bilateral inferior/superior parietal lobule, and posterior cingulate cortex (PCC) (Table 1).

Positive rewards activated a subset of the above mentioned networks, including the bilateral pallidum, anterior insula, thalamus, brain stem, medial OFC, ACC, SMA, PCC, and other frontal and parietal areas (Fig. 1B and Table 2, also see [Supplementary Materials – Fig. S1A](#)). Negative rewards showed activation in the bilateral NAcc, caudate, pallidum, anterior insula, amygdala, thalamus, brain stem, rostral ACC, dorsomedial PFC, lateral OFC, and right middle and inferior frontal gyrus (Fig. 1B and Table 2, also see [Supplementary Materials – Fig. S1B](#)). Contrasting activation by positive versus negative rewards, we found that positive rewards significantly activated the following regions to a great degree: bilateral NAcc, anterior insula, medial OFC, hippocampus, left putamen, and thalamus (Fig. 1D and Table 4). None showed more activation by negative than positive rewards.

Different reward processing stages shared similar brain activation patterns in the above-mentioned core networks, including the bilateral NAcc, anterior insula, thalamus, medial OFC, ACC, and dorsomedial PFC (Fig. 1C and Table 3, also see [Supplementary Materials – Figs. S1C–E](#)). Reward anticipation, as compared to reward outcome, revealed greater activation in the bilateral anterior insula, ACC, SMA, left inferior parietal lobule and middle frontal gyrus (Fig. 1E and Table 5). Outcome preferential activation included bilateral NAcc, caudate, thalamus, and medial/lateral OFC (Table 5).

3.2. PVM results

The main analysis of 142 studies showed significant activation in bilateral NAcc, anterior insula, lateral/medial OFC, ACC, PCC, inferior parietal lobule, and middle frontal Gyrus (Fig. 2A and Table 6).

Positive rewards activated the bilateral NAcc, pallidum, putamen, thalamus, medial OFC, pregenual cingulate cortex, SMA, and PCC (Fig. 2B and Table 7, also see [Supplementary Materials – Fig. S2A](#)). Activation by negative rewards was found in the bilateral NAcc and anterior insula, pallidum, ACC, SMA, and middle/inferior frontal gyrus (Fig. 2B and Table 7, also see [Supplementary Materials – Fig. S2B](#)). Direct contrast between positive and negative rewards revealed preferential activation by positive rewards in the NAcc, pallidum, medial OFC, and PCC, and greater activation by negative rewards in ACC and middle/inferior frontal gyrus (Fig. 2D and Table 9).

Different reward processing stages similarly activated the NAcc and ACC whereas they differentially recruited other brain areas such as medial OFC, anterior insula, and amygdala (Fig. 2C and Table 8, also see [Supplementary Materials – Fig. S2C–E](#)). Reward anticipation, as compared to reward outcome, revealed significant activation in the bilateral anterior insula, thalamus, precentral

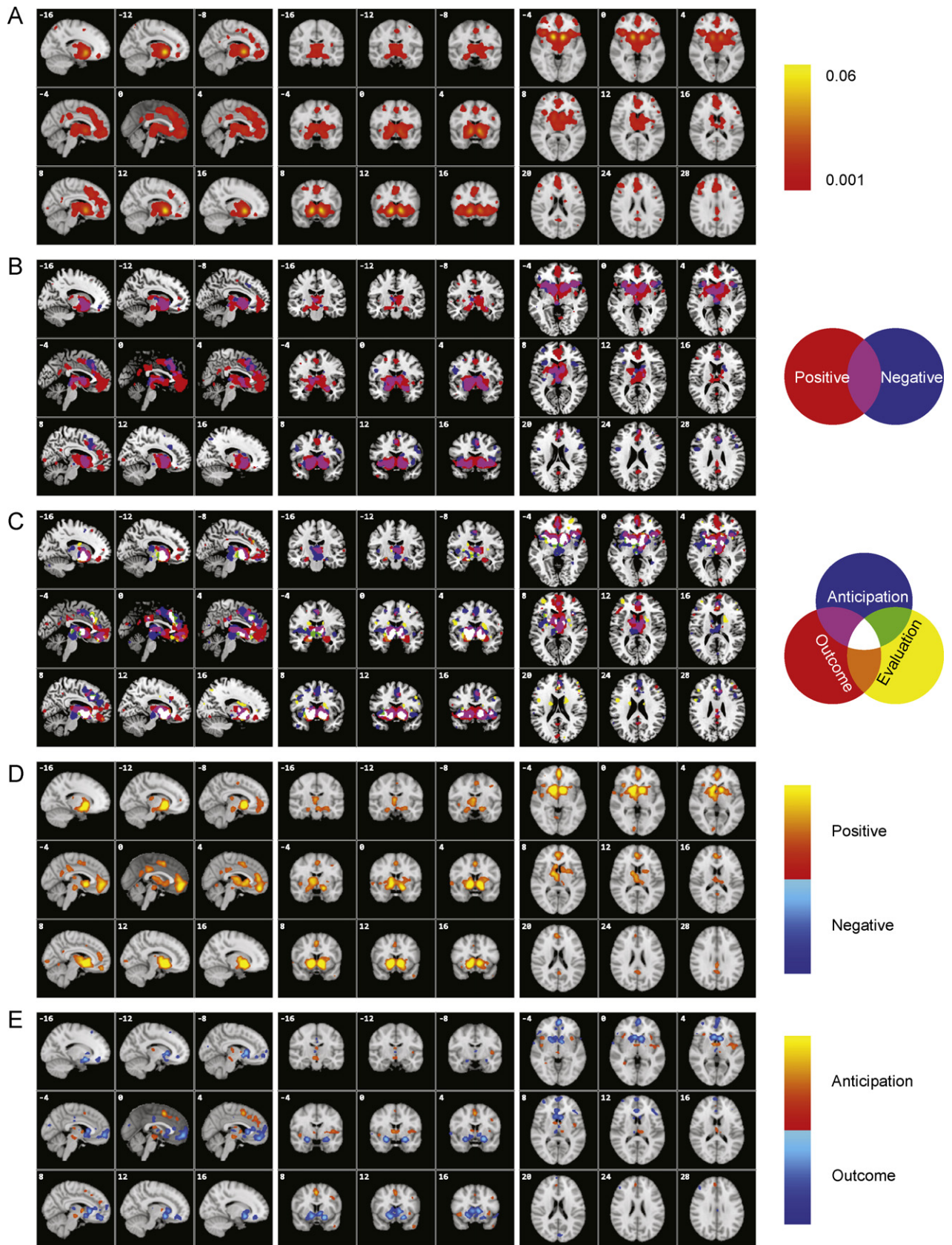


Fig. 1. Concordance of brain activation from the ALE analyses. (A) Core network activated by all contrasts/experiments. (B) Overlay of brain areas separately involved in positive versus negative reward processing. (C) Overlay of brain areas individually activated by different reward processing stages, anticipation, outcome, and evaluation. (D) Direct contrast of brain activation between positive and negative reward processing. (E) Direct contrast of brain activation between reward anticipation and outcome.

Table 1
Brain areas commonly activated by all studies from the ALE analysis (FDR $p < 0.05$ and a minimum cluster size of 60 voxels).

Region	L/R	x	y	z	ALE (10^{-3})	Size
Nucleus accumbens	R	12	10	-6	59	19,461
Pallidum	L	-10	8	-4	56	
Insula	R	36	20	-6	23	
Insula	L	-32	20	-4	21	
Dorsomedial frontal cortex		0	24	40	19	
Medial orbitofrontal cortex		0	54	-8	19	
Amygdala	R	24	-2	-16	15	
Thalamus	R	4	-14	8	15	
Thalamus	L	-6	-16	8	15	
Supplementary motor area		0	8	48	14	
Brain stem	R	8	-18	-10	14	
Anterior cingulate cortex	R	2	44	20	12	
Supplementary motor area	L	-2	-8	50	11	
Brain stem	L	-6	-18	-10	11	
Anterior cingulate cortex		0	44	10	11	
Brain stem	L	-4	-24	-4	10	
Middle frontal gyrus	L	-24	2	52	9	
Insula	L	-38	-4	6	9	
Mid-orbitofrontal cortex	R	24	40	-14	9	
Mid-orbitofrontal cortex	L	-16	42	-14	9	
Middle frontal gyrus	R	40	32	32	10	739
Middle frontal gyrus	R	44	16	30	8	
Inferior parietal lobule	L	-28	-56	48	11	598
Superior parietal lobule	L	-24	-68	56	10	
Angular gyrus	R	28	-58	50	10	475
Angular gyrus	R	44	-52	50	8	
Posterior cingulate cortex		0	-32	32	12	425
Frontal pole	L	-36	50	10	9	337
Lateral orbitofrontal cortex	L	-46	42	-4	7	
Lateral orbitofrontal cortex	L	-42	52	-6	7	
Middle frontal gyrus	R	30	4	50	7	210
Posterior cingulate cortex	R	2	-50	26	8	205
Middle frontal gyrus	L	-44	28	30	7	139
Superior frontal gyrus	L	-22	30	48	9	129

Table 2
Brain areas activated by positive or negative rewards from the ALE analysis (FDR $p < 0.05$ and a minimum cluster size of 60 voxels).

Region	L/R	x	y	z	ALE (10^{-3})	Size
<i>Positive</i>						
Pallidum	R	12	8	-4	35	9254
Pallidum	L	-12	8	-4	33	
Insula	R	36	20	-2	10	
Insula	L	-32	18	-4	8	
Thalamus	R	4	-14	8	7	
Thalamus	L	-10	-22	12	5	
Hippocampus	L	-30	-20	-18	6	
Brain stem	L	-4	-18	-12	5	
Hippocampus	L	-24	-14	-12	5	
Mid-orbitofrontal cortex	L	-28	28	-12	5	
Inferior frontal gyrus	L	-52	18	0	4	
Medial orbitofrontal cortex	L	-2	54	-6	10	3483
Medial orbitofrontal cortex	R	2	48	-14	10	
Supplementary motor area	R	2	8	48	8	
Pregenua cingulate cortex	R	4	42	18	7	
Posterior cingulate cortex		0	-30	32	6	292
Inferior parietal lobule	L	-30	-60	48	5	222
Posterior cingulate cortex	R	2	-50	26	4	166
<i>Negative</i>						
Pallidum	L	-10	6	-2	9	5705
Nucleus accumbens	L	-16	12	-10	8	
Nucleus accumbens	R	12	10	-8	7	
Insula	R	36	20	-6	6	
Caudate	R	10	6	4	5	
Insula	L	-28	24	-8	5	
Amygdala	R	26	0	-18	5	
Anterior cingulate cortex	R	6	24	34	7	1102
Inferior frontal gyrus	R	52	10	22	3	195
Precentral gyrus	L	-48	4	26	4	189
Middle frontal gyrus	R	44	28	36	2	125
Mid-orbitofrontal cortex	L	-18	44	-12	3	98
Frontal pole	L	-36	50	10	4	91

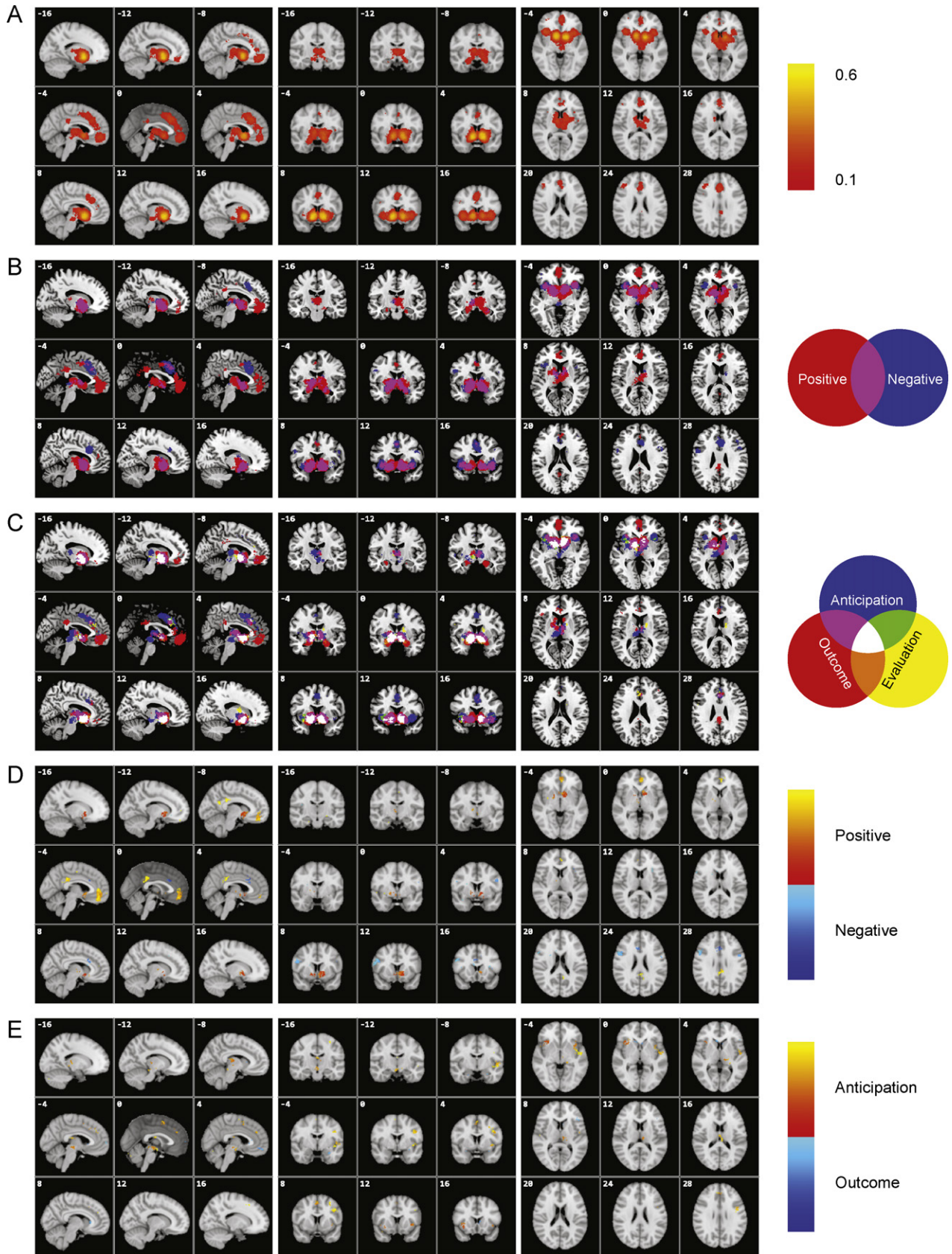


Fig. 2. Concordance of brain activation from the PVM analyses. (A) Core network activated by all contrasts/experiments. (B) Overlay of brain areas separately involved in positive versus negative reward processing. (C) Overlay of brain areas individually activated by different reward processing stages, anticipation, outcome, and evaluation. (D) Direct contrast of brain activation between positive and negative reward processing. (E) Direct contrast of brain activation between reward anticipation and outcome.

Table 3
Brain areas activated by anticipation, outcome, and evaluation from the ALE analysis (FDR $p < 0.05$ and a minimum cluster size of 60 voxels).

Region	L/R	x	y	z	ALE (10^{-3})	Size
<i>Anticipation</i>						
Nucleus accumbens	R	12	10	-4	20	7960
Nucleus accumbens	L	-12	10	-6	20	
Insula	R	38	20	-8	10	8
Insula	L	-32	18	-6	8	
Thalamus	R	4	-12	12	6	6
Thalamus	L	-10	-22	12	6	
Brain stem	R	8	-18	-10	6	5
Brain stem	L	-4	-24	-6	5	
Putamen	R	24	4	0	5	8
Supplementary motor area	R	2	8	48	8	
Anterior cingulate cortex	R	2	24	40	7	2258
Anterior cingulate cortex	R	4	38	38	5	
Anterior cingulate cortex	R	2	28	34	7	4
Supplementary motor area	L	-2	-6	50	4	
Medial orbitofrontal cortex	L	-2	50	-16	5	450
Inferior parietal lobule	L	-28	-58	50	5	
Middle frontal gyrus	R	40	28	34	4	192
Superior parietal lobule	R	34	-52	52	3	
Middle frontal gyrus	L	-26	4	52	4	119
Precentral gyrus	L	-44	6	30	3	
Posterior cingulate cortex		0	-30	32	4	94
<i>Outcome</i>						
Nucleus accumbens	R	12	10	-6	27	11,322
Nucleus accumbens	L	-10	8	-4	26	
Medial orbitofrontal cortex	L	-2	56	-6	10	9
Medial orbitofrontal cortex	R	2	48	-14	9	
Amygdala	R	26	0	-16	10	9
Insula	R	36	22	-8	9	
Insula	L	-28	24	-8	7	7
Thalamus	R	4	-16	6	9	
Anterior cingulate cortex	R	8	24	32	7	6
Supplementary motor area	R	4	22	52	6	
Frontal pole	L	-18	40	-16	6	5
Posterior cingulate cortex		0	-22	32	5	
Superior frontal gyrus	L	-24	30	48	5	345
Supplementary motor area	R	2	-6	50	4	147
Inferior frontal gyrus	L	-54	18	16	3	113
Occipital pole	L	-32	-94	-12	5	111
Middle frontal gyrus	R	44	36	28	4	110
<i>Evaluation</i>						
Pallidum	L	-10	4	-4	7	2846
Putamen	L	-26	6	-8	5	
Nucleus accumbens	R	10	10	-10	5	5
Nucleus accumbens	L	-16	4	-14	5	
Dorsomedial frontal cortex	L	-2	24	42	3	585
Anterior cingulate cortex	R	6	26	34	3	
Anterior cingulate cortex	L	-2	32	30	3	3
Lateral orbitofrontal cortex	R	30	30	-16	3	
Insula	R	38	18	-4	2	363
Caudate	R	20	4	18	2	
Frontal pole	L	-36	50	10	4	202
Frontal pole	R	32	54	-4	2	137
Precentral gyrus	L	-48	4	24	3	132
						100

gyrus, and inferior parietal lobule (Fig. 2E and Table 10). No brain area showed greater activation by reward outcome in comparison to anticipation.

3.3. Comparison of ALE and PVM results

The current study also showed that although ALE and PVM methods treated the coordinate-based data differently and adopted distinct estimation algorithms, the results for a single list of coordinates from these two meta-analysis approaches were very similar and comparable (Figs. 1A–C and 2A–C, Table 11, also see Figs. S1 and S2 in Supplementary Materials). The improved ALE algorithm implemented in GingerALE 2.0, by design, treats experiments (or contrasts) as the random-effects factor, which significantly reduces the bias caused by experiments reporting more loci versus those with fewer loci. Different studies, however, include different number of experiments/contrasts. Therefore, the

results of GingerALE 2.0 may still be affected by the bias that weighs more toward studies reporting more contrasts, potentially overestimating cross-study concordance. However, by choice, users can combine coordinates from different contrasts together so that GingerALE 2.0 can treat each study as a single experiment. This is what PVM implements, pooling coordinates from all contrasts within a study into a single activation map, thus weighing all studies equally to estimate activation overlap across studies.

In contrast, comparison of two lists of coordinates differed significantly between ALE and PVM approaches (Table 11), as a result of their differences in sensitivity to within-study and cross-study convergence. Since the improved ALE algorithm has not been implemented for the subtractive ALE analysis, we used an earlier version, GingerALE 1.2, which treats the coordinates as the random-effects factor and experiments as the fixed-effects variable. Therefore differences in both the numbers of coordinates and experiments in two lists may affect the subtraction results. The sub-

Table 4
Brain areas differentially activated by positive and negative rewards from the ALE subtraction analysis (FDR $p < 0.05$ and a minimum cluster size of 60 voxels).

Region	L/R	x	y	z	ALE (10^{-3})	Size	
<i>Positive > negative</i>							
Nucleus accumbens	R	12	8	-4	177	5951	
Nucleus accumbens	L	-10	10	-4	157		
Putamen	L	-24	4	6	38		
Brain stem	L	-4	-18	-14	37		
Hippocampus	L	-30	-20	-18	36		
Hippocampus	L	-24	-14	-12	35		
Insula	R	42	-4	-4	32		
Thalamus	L	-10	-24	12	32		
Insula	L	-30	18	-2	30		
Hippocampus	R	20	-22	-10	27		
Medial orbitofrontal cortex		0	48	-12	72		1855
Pregenua cingulate cortex	R	2	46	8	52		
Pregenua cingulate cortex	R	4	44	16	45		
Supplementary motor area	R	2	6	48	49		
Posterior cingulate cortex		0	-32	32	43		
Insula	R	36	22	0	38		
Posterior cingulate cortex		0	-50	26	30		
Inferior parietal lobule	L	-30	-62	48	33		
Frontal pole	R	30	46	-10	30		
<i>Positive < negative</i>							
None							

Table 5
Brain areas differentially activated by anticipation and outcome from the ALE subtraction analysis (FDR $p < 0.05$ and a minimum cluster size of 60 voxels).

Region	L/R	x	y	z	ALE (10^{-3})	Size
<i>Anticipation > outcome</i>						
Supplementary motor area	R	2	8	50	52	545
Anterior cingulate cortex	R	4	40	36	30	
Anterior cingulate cortex	R	4	22	40	29	
Anterior cingulate cortex	R	6	46	24	24	
Anterior cingulate cortex	R	2	30	32	21	
Brain stem	R	6	-18	-10	34	
Brain stem	L	-6	-24	-12	23	
Insula	L	-42	-6	4	32	
Pallidum	L	-22	-4	2	19	
Insula	R	40	16	-6	31	
Insula	R	34	26	2	25	
Thalamus	R	6	0	4	37	
Thalamus	L	-10	-22	12	27	
Inferior parietal lobule	L	-28	-60	50	31	
Middle frontal gyrus	L	-44	18	36	22	
<i>Anticipation < outcome</i>						
Nucleus accumbens	L	-18	8	-14	69	4491
Amygdala	R	26	0	-16	61	
Nucleus accumbens	R	14	10	-12	57	
Caudate	L	-8	14	2	56	
Medial orbitofrontal cortex	L	-2	56	-6	54	
Caudate	R	8	20	2	52	
Medial orbitofrontal cortex	R	4	48	-14	50	
Nucleus accumbens	L	-8	8	-4	48	
Pregenua cingulate cortex	R	4	34	10	34	
Mid-orbitofrontal cortex	L	-18	40	-16	33	
Lateral orbitofrontal cortex	L	-40	44	-16	28	
Medial superior frontal cortex	R	4	62	14	27	
Medial orbitofrontal cortex	L	-10	42	-8	27	
Occipital pole	L	-30	-94	-14	34	
Inferior frontal gyrus	L	-38	34	12	25	
Lateral orbitofrontal cortex	L	-50	24	-14	26	
Frontal pole	R	46	34	-6	22	

tractive ALE analysis biased toward the list with more experiments against the other with fewer (Fig. 1D/E). Positive reward studies (2167 foci from 283 experiments) clearly predominated over negative studies (935 foci from 140 experiments). The difference between reward anticipation (1553 foci from 185 experiments) and outcome (1977 foci from 253 experiments) was smaller, but could have also caused the bias toward the outcome phase. On the other hand, the use of the Fisher test to estimate the odds ratio and assign voxels in one of the two lists by PVM seemed to be less sensitive in detecting activation difference between the two lists (Fig. 2D/E).

4. Discussion

We are constantly making decisions in our everyday life. Some decisions involve no apparent positive or negative values of the outcomes whereas others have significant impacts on the valence of the results and our emotional responses toward the choices we make. We may feel happy and satisfied when the outcome is positive or our expectation is fulfilled, or feel frustrated when the outcome is negative or lower than what we anticipated. Moreover, many decisions must be made without advance knowledge

Table 6
Brain areas commonly activated by all studies from the PVM analysis (FDR $p < 0.05$ and a minimum cluster size of 60 voxels).

Label	L/R	x	y	z	PVM (10^{-2})	Size	
Nucleus accumbens	R	12	8	-10	54	9216	
Putamen	L	-16	4	-10	54		
Nucleus accumbens	L	-8	6	-6	51	3032	
Insula	R	38	20	-2	32		
Insula	R	30	18	-8	31		
Anterior cingulate cortex	R	2	22	36	30		
Medial orbitofrontal cortex	L	-4	50	-10	27		
Medial orbitofrontal cortex	L	-8	42	-18	25		
Anterior cingulate cortex		0	34	28	24		
Medial orbitofrontal cortex	L	-6	38	-12	24		
Middle frontal gyrus	R	36	36	30	20		288
Middle frontal gyrus	R	44	34	22	20		
Middle frontal gyrus	R	40	22	34	17	155	
Middle frontal gyrus	R	48	38	16	15		
Inferior parietal lobule	L	-36	-58	48	20		
Superior parietal lobule	L	-26	-66	50	18		
Posterior cingulate cortex	L	-2	-34	30	19		114
Lateral orbitofrontal cortex	R	34	50	-6	21		
Lateral orbitofrontal cortex	R	30	52	0	17		63

of their consequences. Therefore, we need to be able to make predictions about the future reward, and evaluate the reward value and potential risk of obtaining it or being penalized. This requires us to evaluate the choice we make based on the presence of prediction errors and to use these signals to guide our learning and future behaviors. Many neuroimaging studies have examined reward-related decision making. However, given the complex and heterogeneous psychological processes involved in value-based decision making, it is no trivial task to examine neural networks that subserve representation and processing of reward-related information. We have observed a rapid growth in the number of empirical studies in the field of neuroeconomics, yet

thus far it has been hard to see how these studies have converged so as to clearly delineate the reward circuitry in the human brain. In the current meta-analysis study, we have showed concordance across a large number of studies and revealed the common and distinct patterns of brain activation by different aspects of reward processing. In a data-driven fashion, we pooled over all coordinates from different contrasts/experiments of 142 studies, and observed a core reward network, which consists of the NAcc, lateral/medial OFC, ACC, anterior insula, dorsomedial PFC, as well as the lateral frontoparietal areas. A recent meta-analysis study focusing on risk assessment in decision making reported a similar reward circuitry (Mohr et al., 2010). In addition, from

Table 7
Brain areas activated by positive or negative rewards from the PVM analysis (FDR $p < 0.05$ and a minimum cluster size of 60 voxels).

Label	L/R	x	y	z	PVM (10^{-2})	Size	
<i>Positive</i>							
Nucleus accumbens	L	-16	8	-8	46	6609	
Nucleus accumbens	R	14	10	-10	46		
Putamen	L	-18	4	-14	41	1521	
Thalamus	R	10	-8	6	23		
Thalamus	R	6	-12	2	21		
Medial orbitofrontal cortex	L	-4	50	-10	23		
Pregenuar cingulate cortex	L	-6	42	-2	19		
Medial orbitofrontal cortex	L	-8	40	-18	19		
Pregenuar cingulate cortex	R	2	38	10	18		
Medial orbitofrontal cortex	L	-4	58	-2	17		
Middle cingulate cortex		0	2	40	15		343
Supplementary motor area	L	-2	18	42	14		
Supplementary motor area	L	-8	-4	44	12	243	
Middle cingulate cortex	L	-2	10	34	12		
Posterior cingulate cortex	L	-4	-32	32	16		
Posterior cingulate cortex	L	-2	-46	30	14		
Mid-orbitofrontal cortex	R	24	40	-14	14		65
Mid-orbitofrontal cortex	R	16	38	-18	13		
<i>Negative</i>							
Nucleus accumbens	L	-18	4	-10	31		4891
Nucleus accumbens	R	12	2	-10	27		
Nucleus accumbens	R	14	8	-14	27		1166
Pallidum	L	-16	0	-2	25		
Insula	R	36	20	-10	25		
Insula	L	-32	20	-2	22		
Anterior cingulate cortex	R	2	20	36	27		
Anterior cingulate cortex		0	22	28	25		
Supplementary motor area	R	2	12	50	16		
Anterior cingulate cortex		0	36	26	15		
Middle frontal gyrus	R	42	26	28	16	139	
Middle frontal gyrus	R	44	18	30	15		
Inferior frontal gyrus	R	50	6	26	15	82	
Inferior frontal gyrus	L	-52	4	26	15		

Table 8
Brain areas activated by anticipation, outcome, and evaluation from the PVM analysis (FDR $p < 0.05$ and a minimum cluster size of 60 voxels).

Label	L/R	x	y	z	PVM (10^{-2})	Size
<i>Anticipation</i>						
Nucleus accumbens	R	12	2	-4	46	5623
Nucleus accumbens	L	-16	4	-10	46	
Insula	R	34	20	-6	40	1003
Thalamus	L	-8	-20	8	29	
Thalamus	R	8	-6	6	29	
Thalamus	L	-2	-16	6	26	
Anterior cingulate cortex		0	20	42	28	
Anterior cingulate cortex	R	2	30	34	25	
Supplementary motor area	L	-4	4	50	20	
Supplementary motor area		0	0	46	20	
Supplementary motor area	L	-8	-4	44	18	
<i>Outcome</i>						
Nucleus accumbens	R	12	12	-6	51	5288
Nucleus accumbens	R	14	8	-12	48	
Nucleus accumbens	L	-16	8	-10	45	1254
Nucleus accumbens	L	-10	8	-4	43	
Amygdala	L	-18	0	-18	29	
Medial orbitofrontal cortex		0	44	-10	27	
Medial orbitofrontal cortex	L	-8	46	-12	23	
Medial orbitofrontal cortex	L	-8	38	-16	23	
Medial orbitofrontal cortex	L	-2	60	-6	21	
Anterior cingulate cortex	R	2	24	30	21	
Anterior cingulate cortex	R	2	18	38	17	
Supplementary motor area	L	-4	16	46	15	
Posterior cingulate cortex	L	-2	-34	30	20	210
Posterior cingulate cortex	R	2	-46	24	15	
<i>Evaluation</i>						
Nucleus accumbens	L	-20	6	-12	38	1796
Nucleus accumbens	R	12	2	-10	36	
Amygdala	L	-12	0	-14	33	115
Pallidum	L	-12	2	-2	28	
Anterior cingulate cortex		0	26	24	23	
Anterior cingulate cortex	R	2	22	38	20	
Anterior cingulate cortex		0	36	26	20	
Anterior cingulate cortex	L	-6	32	22	18	

a theory-driven perspective, we contrasted neural networks that were involved in positive and negative valence across anticipation and outcome stages of reward processing, and elucidated distinct neural substrates subserving valence-related assessment as well as their preferential involvement in anticipation and outcome.

4.1. Core reward areas: NAcc and OFC

The NAcc and OFC have long been conceived as the major players in reward processing because they are the main projection areas of two distinct dopaminergic pathways, the mesolimbic and mesocortical pathways, respectively. However, it remains unknown how

Table 9
Brain areas differentially activated by positive and negative rewards from the PVM Fisher odds ratio analysis (voxel $p < 0.01$ and a minimum cluster size of 60 voxels).

Label	L/R	x	y	z	OR	Size
<i>Positive > negative</i>						
Medial orbitofrontal cortex	L	-12	48	-22	0.001	371
Medial orbitofrontal cortex	L	-4	38	-22	0.097	
Medial orbitofrontal cortex	L	-6	52	-12	0.202	192
Medial orbitofrontal cortex	L	-8	42	-18	0.202	
Medial orbitofrontal cortex	L	-6	48	-6	0.244	
Nucleus accumbens	L	-6	4	-10	0.352	
Pallidum	L	-12	4	-2	0.409	
Posterior cingulate cortex	R	4	-30	38	0.001	
Posterior cingulate cortex	R	6	-34	30	0.001	
Posterior cingulate cortex	L	-8	-38	34	0.097	
Posterior cingulate cortex	L	-2	-46	30	0.097	
Posterior cingulate cortex	L	-4	-34	28	0.097	
Pallidum	R	16	2	-2	0.336	60
Nucleus accumbens	R	8	12	-8	0.409	
<i>Positive < negative</i>						
Middle frontal gyrus	R	46	18	32	1724.2	149
Inferior frontal gyrus	R	52	12	24	1724.2	
Middle frontal gyrus	R	50	24	32	1093.5	65
Inferior frontal gyrus	R	60	12	16	896.9	
Precentral gyrus	R	50	6	26	19.0	
Anterior cingulate cortex	R	8	24	24	7.8	
Anterior cingulate cortex	R	6	16	30	5.2	
Anterior cingulate cortex	L	-4	20	28	4.2	
Anterior cingulate cortex	R	4	24	34	3.4	

Table 10
Brain areas differentially activated by anticipation and outcome from the PVM Fisher odds ratio analysis (voxel $p < 0.01$ and a minimum cluster size of 60 voxels).

Label	L/R	x	y	z	OR	Size
<i>Anticipation > outcome</i>						
Superior temporal gyrus	L	-58	-6	0	0.149	143
Heschl gyrus	L	-50	-10	0	0.149	
Insula	L	-40	-2	-2	0.149	
Rolandic opercular	L	-46	-4	6	0.179	
Insula	L	-34	6	-4	0.217	
Angular gyrus	L	-36	-68	42	0.149	117
Angular gyrus	L	-42	-56	36	0.149	
Inferior parietal lobule	L	-32	-62	46	0.179	
Angular gyrus	L	-42	-66	38	0.179	
Insula	R	38	22	4	0.307	116
Insula	R	28	24	-6	0.307	
Insula	R	36	20	-4	0.357	
Precentral gyrus	L	-42	2	38	0.001	106
Precentral gyrus	L	-48	0	30	0.149	
Brain stem		0	-24	-10	0.273	79
Thalamus	L	-4	-16	14	0.217	78
Thalamus	L	-8	-18	8	0.270	
Thalamus	L	-10	-24	4	0.273	
<i>Anticipation < outcome</i>						
None						

dopamine neurons distinctively modulate activity in these limbic and cortical areas. Previous studies have tried to differentiate the roles of these two structures in terms of temporal stages, associating the NAcc with reward anticipation and relating the medial OFC to receipt of reward (Knutson et al., 2001b, 2003; Ramnani et al., 2004). Results from other studies questioned such a distinction (Breiter et al., 2001; Delgado et al., 2005; Rogers et al., 2004). Many studies also implied that the NAcc was responsible for detecting prediction error, a crucial signal in incentive learning and reward association (McClure et al., 2003; O'Doherty et al., 2003b; Pagnoni et al., 2002). Studies also found that the NAcc showed a biphasic response, such that activity in the NAcc would decrease and drop below the baseline in response to negative prediction errors (Knutson et al., 2001b; McClure et al., 2003; O'Doherty et al., 2003b). Although the OFC usually displays similar patterns of activity as the NAcc, previous neuroimaging studies in humans have suggested that the OFC serves to convert a variety of stimuli into a common currency in terms of their reward values (Arana et al., 2003; Cox et al., 2005; Elliott et al., 2010; FitzGerald et al., 2009; Gottfried et al., 2003; Kringelbach et al., 2003; O'Doherty et al., 2001; Plassmann et al., 2007). These findings paralleled those obtained from single cell recording and lesion studies in animals (Schoenbaum and Roesch, 2005; Schoenbaum et al., 2003, 2009; Schultz et al., 2000; Tremblay and Schultz, 1999, 2000; Wallis, 2007).

Our overall analyses showed that the NAcc and OFC responded to general reward processing (Figs. 1A and 2A). Activation in the NAcc largely overlapped across different stages, whereas the medial OFC was more tuned to reward receipt (Figs. 1C/E and 2C). These findings highlighted that the NAcc may be responsible for track-

ing both positive and negative signals of reward and using them to modulate learning of reward association, whereas the OFC mostly monitors and evaluates reward outcomes. Further investigation is needed to better differentiate the roles of the NAcc and OFC in reward-related decision making (Frank and Claus, 2006; Hare et al., 2008).

4.2. Valence-related assessment

In addition to converting various reward options into common currency and representing their reward values, distinct brain regions in the reward circuitry may separately encode positive and negative valences of reward. Direct comparisons across reward valence revealed that both the NAcc and medial OFC were more active in response to positive versus negative rewards (Figs. 1B/D and 2B/D). In contrast, the anterior insular cortex was involved in the processing of negative reward information (Fig. 1B and 2B). These results confirmed the medial-lateral distinction for positive versus negative rewards (Kringelbach, 2005; Kringelbach and Rolls, 2004), and were consistent with what we observed in our previous study on a reward task (Liu et al., 2007). Sub-regions of the ACC uniquely responded to positive and negative rewards. Pregenual and rostral ACC, close to the medial OFC, were activated by positive rewards whereas the caudal ACC responded to negative rewards (Figs. 1B and 2B). ALE and PVM meta-analyses also revealed that the PCC was consistently activated by positive rewards (Fig. 1B and 2B).

Interestingly, separate networks encoding positive and negative valences are similar to the distinction between two anti-correlated

Table 11
Summary of ALE and PVM results on key regions of interest.

	VS	aINS	mOFC	lOFC	AMY	ACC	IPL	dIPFC	dmPFC
Overall	ALE, PVM	ALE, PVM	ALE, PVM	ALE, PVM	ALE	ALE, PVM	ALE, PVM	ALE, PVM	ALE
Positive	ALE, PVM	ALE	ALE, PVM				ALE	ALE	
Negative	ALE, PVM	ALE, PVM			ALE	ALE, PVM		ALE, PVM	
Anticipation	ALE, PVM	ALE, PVM	ALE			ALE, PVM	ALE	ALE	
Outcome	ALE, PVM	ALE	ALE, PVM		ALE, PVM	ALE, PVM		ALE	
Evaluation	ALE, PVM	ALE		ALE	ALE, PVM	ALE, PVM			ALE
Positive > negative	ALE, PVM	ALE	ALE, PVM				ALE		
Positive < negative						PVM		PVM	
Anticipation > outcome		ALE, PVM				ALE	ALE, PVM	ALE	
Anticipation < outcome	ALE		ALE	ALE	ALE			ALE	

VS – ventral striatum; aINS – anterior insula; mOFC – medial orbitofrontal cortex; lOFC – lateral orbitofrontal cortex; AMY – amygdala; ACC – anterior cingulate cortex; IPL – inferior parietal lobule; dIPFC – dorsolateral prefrontal cortex; dmPFC – dorsomedial prefrontal cortex.

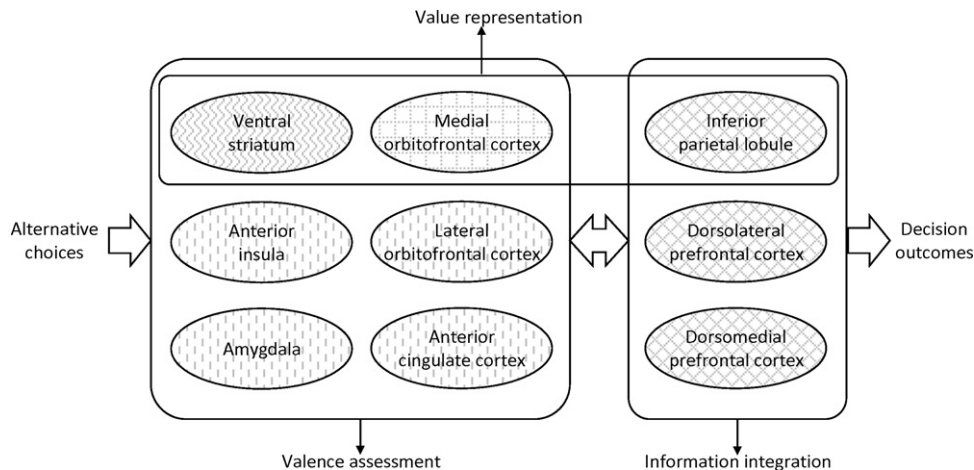


Fig. 3. A schematic framework illustrates the roles of core brain areas involved in different aspects of reward-related decision making. The grid pattern denotes the medial orbitofrontal cortex encoding positive valence; the dash pattern denotes the anterior insula, lateral orbitofrontal cortex, anterior cingulate cortex, and amygdala encoding negative valence; the wave pattern denotes the ventral striatum encoding both positive and negative valence; the diamond pattern denotes the frontoparietal network being involved in information integration.

networks, the default-mode network and task-related network (Fox et al., 2005; Raichle et al., 2001; Raichle and Snyder, 2007). Recent meta-analyses found that the default-mode network mainly involved the medial prefrontal regions (including the medial OFC) and medial posterior cortex (including the PCC and precuneus), and the task-related network includes the ACC, insula, and lateral frontoparietal regions (Laird et al., 2009; Toro et al., 2008). Activation in the medial OFC and PCC by positive rewards mirrored the default-mode network commonly observed during the resting state, whereas activation in the ACC, insula, lateral prefrontal cortex by negative rewards paralleled the task-related network. This intrinsic functional organization of the brain was found to influence reward and risky decision making and account for individual differences in risk-taking traits (Cox et al., 2010).

4.3. Anticipation versus outcome

The bilateral anterior insula, ACC/SMA, inferior parietal lobule, and brain stem showed more consistent activation in anticipation in comparison to the outcome phase (Figs. 1C/E and 2C/E). The anterior insula and ACC have previously been implicated in interoception, emotion and empathy (Craig, 2002, 2009; Gu et al., 2010; Phan et al., 2002), and risk and uncertainty assessment (Critchley et al., 2001; Kuhnen and Knutson, 2005; Paulus et al., 2003), lending its role in anticipation. The anterior insula was consistently involved in risk processing, especially in anticipation of loss, as revealed by a recent meta-analysis (Mohr et al., 2010). Similar to the role of the OFC, the parietal lobule has been associated with valuation of different options (Sugrue et al., 2005), numerical representation (Cohen Kadosh et al., 2005; Hubbard et al., 2005), and information integration (Gold and Shadlen, 2007; Yang and Shadlen, 2007). Therefore, it is crucial for the parietal lobule to be involved in the anticipation stage of reward processing so as to plan and prepare for an informed action (Andersen and Cui, 2009; Lau et al., 2004a,b).

On the other hand, the ventral striatum, medial OFC, and amygdala showed preferential activation during reward outcome in comparison to the anticipation stage (Figs. 1C/E and 2C). These patterns were consistent with what we and other investigators found previously (Breiter et al., 2001; Delgado et al., 2005; Liu et al., 2007; Rogers et al., 2004), standing against the functional dissociation between the ventral striatum and medial OFC in terms of their respective roles in reward anticipation and reward outcome (Knutson et al., 2001a,b, 2003).

4.4. A schematic illustration of reward processing

Based on the findings of common and distinct networks involved in various aspects of reward decision making, we have come up with a schematic illustration to summarize the distributed representations of valuation and valence in reward processing (Fig. 3). We tentatively group different brain regions based on their roles in different processes, although each region may serve multiple functions and interact with other brain areas in a far more complex way. When facing alternative choices, each of which has distinctive characteristics such as magnitude and probability, these properties need to be converted into comparable value-based information, a “common currency”. Not only do we compare the values of these alternative choices, but we also compare the factual and projected values as well as the fictional values associated with the un-chosen choice (e.g., the prediction error signal). The ventral striatum and medial OFC have been implicated in this value-based representation. The inferior parietal lobule has also been found to be involved in representing and comparing numerical information. In addition, value-based decision making inevitably results in evaluation of the choices, based on the valence of the outcomes and associated emotional responses. While the ventral striatum and medial OFC are also involved in detecting the positive reward valence, the lateral OFC, anterior insula, ACC and amygdala are mostly implicated in processing of the negative reward valence, most likely linked to their evaluative roles in negative emotional responses. Because of the negative affect usually associated with risk, the anterior insula and ACC are also involved in reward anticipation of risky decisions, especially for uncertainty-averse responses in anticipation of loss. Finally, the frontoparietal regions serve to integrate and act upon these signals in order to produce optimal decisions (e.g., win-stay-loss-switch).

4.5. Caveats

A couple of methodological caveats need to be noted. The first is related to the bias in reporting the results in different studies. Some studies are purely ROI-based, which were excluded from the current study. Still, others singled out or put more emphasis on *a priori* regions by reporting more coordinates or contrasts related to those regions. They could bias the results toward confirming the “hotspots”. Secondly, we want to caution about conceptual distinction of different aspects of reward processing. We classified various contrasts into different categories of theoretical interest.

However, with real life decisions or in many experimental tasks, these aspects do not necessarily have clear divisions. For example, evaluation of the previous choice and reward outcome may intermingle with upcoming reward anticipation and decision making. There is no clear boundary across different stages of reward processing, leaving our current classification open for discussion. Nonetheless, this hypothesis-driven approach is greatly needed (Caspers et al., 2010; Mohr et al., 2010; Richlan et al., 2009), which complements the data-driven nature of meta-analysis. Many factors related to reward decision making, such as risk assessment and types of reward (e.g., primary vs. secondary, monetary vs. social), call for additional meta-analyses.

Contributions

XL designed and supervised the whole study. JH and MS made equal contributions to this study, performing literature search, data extraction and organization. JF participated in discussion and manuscript preparation.

Acknowledgements

This study is supported by the Hundred-Talent Project of the Chinese Academy of Sciences, NARSAD Young Investigator Award (XL), and NIH Grant R21MH083164 (JF). The authors wish to thank the development team of BrainMap and Sergi G. Costafreda for providing excellent tools for this study.

Appendix A.

List of articles included in the meta-analyses of the current study:

- 1 Abler, B., Walter, H., Erk, S., Kammerer, H., Spitzer, M., 2006. Prediction error as a linear function of reward probability is coded in human nucleus accumbens. *Neuroimage* 31, 790–795.
- 2 Adcock, R.A., Thangavel, A., Whitfield-Gabrieli, S., Knutson, B., Gabrieli, J.D., 2006. Reward-motivated learning: mesolimbic activation precedes memory formation. *Neuron* 50, 507–517.
- 3 Akitsuki, Y., Sugiura, M., Watanabe, J., Yamashita, K., Sassa, Y., Awata, S., Matsuoka, H., Maeda, Y., Matsue, Y., Fukuda, H., Kawashima, R., 2003. Context-dependent cortical activation in response to financial reward and penalty: an event-related fMRI study. *Neuroimage* 19, 1674–1685.
- 4 Ballard, K., Knutson, B., 2009. Dissociable neural representations of future reward magnitude and delay during temporal discounting. *Neuroimage* 45, 143–150.
- 5 Behrens, T.E., Woolrich, M.W., Walton, M.E., Rushworth, M.F., 2007. Learning the value of information in an uncertain world. *Nature Neuroscience* 10, 1214–1221.
- 6 Bjork, J.M., Hommer, D.W., 2007. Anticipating instrumentally obtained and passively-received rewards: a factorial fMRI investigation. *Behavioural Brain Research* 177, 165–170.
- 7 Bjork, J.M., Knutson, B., Fong, G.W., Caggiano, D.M., Bennett, S.M., Hommer, D.W., 2004. Incentive-elicited brain activation in adolescents: similarities and differences from young adults. *Journal of Neuroscience* 24, 1793–1802.
- 8 Bjork, J.M., Momenan, R., Smith, A.R., Hommer, D.W., 2008. Reduced posterior mesofrontal cortex activation by risky rewards in substance-dependent patients. *Drug and Alcohol Dependence* 95, 115–128.
- 9 Bjork, J.M., Smith, A.R., Danube, C.L., Hommer, D.W., 2007. Developmental differences in posterior mesofrontal cortex recruitment by risky rewards. *Journal of Neuroscience* 27, 4839–4849.
- 10 Blair, K., Marsh, A.A., Morton, J., Vythilingam, M., Jones, M., Mondillo, K., Pine, D.C., Drevets, W.C., Blair, J.R., 2006. Choosing the lesser of two evils, the better of two goods: specifying the roles of ventromedial prefrontal cortex and dorsal anterior cingulate in object choice. *Journal of Neuroscience* 26, 11379–11386.
- 11 Breiter, H.C., Aharon, I., Kahneman, D., Dale, A., Shizgal, P., 2001. Functional imaging of neural responses to expectancy and experience of monetary gains and losses. *Neuron* 30, 619–639.

- 12 Budhani, S., Marsh, A.A., Pine, D.S., Blair, R.J., 2007. Neural correlates of response reversal: considering acquisition. *Neuroimage* 34, 1754–1765.
- 13 Bush, G., Vogt, B.A., Holmes, J., Dale, A.M., Greve, D., Jenike, M.A., Rosen, B.R., 2002. Dorsal anterior cingulate cortex: a role in reward-based decision making. *Proceedings of the National Academy of Sciences of the United States of America* 99, 523–528.
- 14 Camara, E., Rodriguez-Fornells, A., Munte, T.F., 2008. Functional connectivity of reward processing in the brain. *Frontiers in Human Neuroscience* 2, 19.
- 15 Campbell-Meiklejohn, D.K., Woolrich, M.W., Passingham, R.E., Rogers, R.D., 2008. Knowing when to stop: the brain mechanisms of chasing losses. *Biological Psychiatry* 63, 293–300.
- 16 Chiu, P.H., Lohrenz, T.M., Montague, P.R., 2008. Smokers' brains compute, but ignore, a fictive error signal in a sequential investment task. *Nature Neuroscience* 11, 514–520.
- 17 Clithero, J.A., Carter, R.M., Huettel, S.A., 2009. Local pattern classification differentiates processes of economic valuation. *Neuroimage* 45, 1329–1338.
- 18 Cohen, M.X., 2007. Individual differences and the neural representations of reward expectation and reward prediction error. *Social Cognitive and Affective Neuroscience* 2, 20–30.
- 19 Cohen, M.X., Elger, C.E., Weber, B., 2008. Amygdala tractography predicts functional connectivity and learning during feedback-guided decision-making. *Neuroimage* 39, 1396–1407.
- 20 Cohen, M.X., Heller, A.S., Ranganath, C., 2005a. Functional connectivity with anterior cingulate and orbitofrontal cortices during decision-making. *Brain Research. Cognitive Brain Research* 23, 61–70.
- 21 Cohen, M.X., Ranganath, C., 2005. Behavioral and neural predictors of upcoming decisions. *Cognitive, Affective, & Behavioral Neuroscience* 5, 117–126.
- 22 Cohen, M.X., Young, J., Baek, J.M., Kessler, C., Ranganath, C., 2005b. Individual differences in extraversion and dopamine genetics predict neural reward responses. *Brain Research. Cognitive Brain Research* 25, 851–861.
- 23 Cooper, J.C., Knutson, B., 2008. Valence and salience contribute to nucleus accumbens activation. *Neuroimage* 39, 538–547.
- 24 Coricelli, G., Critchley, H.D., Joffily, M., O'Doherty, J.P., Sirigu, A., Dolan, R.J., 2005. Regret and its avoidance: a neuroimaging study of choice behavior. *Nature Neuroscience* 8, 1255–1262.
- 25 Cox, S.M., Andrade, A., Johnsrude, I.S., 2005. Learning to like: a role for human orbitofrontal cortex in conditioned reward. *Journal of Neuroscience* 25, 2733–2740.
- 26 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.
- 27 D'Ardenne, K., McClure, S.M., Nystrom, L.E., Cohen, J.D., 2008. BOLD responses reflecting dopaminergic signals in the human ventral tegmental area. *Science* 319, 1264–1267.
- 28 Daw, N.D., O'Doherty, J.P., Dayan, P., Seymour, B., Dolan, R.J., 2006. Cortical substrates for exploratory decisions in humans. *Nature* 441, 876–879.
- 29 Delgado, M.R., Locke, H.M., Stenger, V.A., Fiez, J.A., 2003. Dorsal striatum responses to reward and punishment: effects of valence and magnitude manipulations. *Cognitive, Affective, & Behavioral Neuroscience* 3, 27–38.
- 30 Delgado, M.R., Miller, M.M., Inati, S., Phelps, E.A., 2005. An fMRI study of reward-related probability learning. *Neuroimage* 24, 862–873.
- 31 Delgado, M.R., Nystrom, L.E., Fissell, C., Noll, D.C., Fiez, J.A., 2000. Tracking the hemodynamic responses to reward and punishment in the striatum. *Journal of Neurophysiology* 84, 3072–3077.
- 32 Delgado, M.R., Schotter, A., Ozbay, E.Y., Phelps, E.A., 2008. Understanding overbidding: using the neural circuitry of reward to design economic auctions. *Science* 321, 1849–1852.
- 33 Dillon, D.G., Holmes, A.J., Jahn, A.L., Bogdan, R., Wald, L.L., Pizzagalli, D.A., 2008. Dissociation of neural regions associated with anticipatory versus consummatory phases of incentive processing. *Psychophysiology* 45, 36–49.
- 34 Elliott, R., Agnew, Z., Deakin, J.F., 2008. Medial orbitofrontal cortex codes relative rather than absolute value of financial rewards in humans. *European Journal of Neuroscience* 27, 2213–2218.
- 35 Elliott, R., Agnew, Z., Deakin, J.F., 2009. Hedonic and Informational Functions of the Human Orbitofrontal Cortex. *Cerebral Cortex*.
- 36 Elliott, R., Friston, K.J., Dolan, R.J., 2000. Dissociable neural responses in human reward systems. *Journal of Neuroscience* 20, 6159–6165.
- 37 Elliott, R., Newman, J.L., Longe, O.A., Deakin, J.F., 2003. Differential response patterns in the striatum and orbitofrontal cortex to financial reward in humans: a parametric functional magnetic resonance imaging study. *Journal of Neuroscience* 23, 303–307.

- 38 Elliott, R., Newman, J.L., Longe, O.A., William Deakin, J.F., 2004. Instrumental responding for rewards is associated with enhanced neuronal response in subcortical reward systems. *Neuroimage* 21, 984–990.
- 39 Ernst, M., Nelson, E.E., Jazbec, S., McClure, E.B., Monk, C.S., Leibenluft, E., Blair, J., Pine, D.S., 2005. Amygdala and nucleus accumbens in responses to receipt and omission of gains in adults and adolescents. *Neuroimage* 25, 1279–1291.
- 40 Ernst, M., Nelson, E.E., McClure, E.B., Monk, C.S., Munson, S., Eshel, N., Zarah, E., Leibenluft, E., Zametkin, A., Towbin, K., Blair, J., Charney, D., Pine, D.S., 2004. Choice selection and reward anticipation: an fMRI study. *Neuropsychologia* 42, 1585–1597.
- 41 Fujiwara, J., Tobler, P.N., Taira, M., Iijima, T., Tsutsui, K., 2009a. A parametric relief signal in human ventrolateral prefrontal cortex. *Neuroimage* 44, 1163–1170.
- 42 Fujiwara, J., Tobler, P.N., Taira, M., Iijima, T., Tsutsui, K., 2009b. Segregated and integrated coding of reward and punishment in the cingulate cortex. *Journal of Neurophysiology* 101, 3284–3293.
- 43 Fukui, H., Murai, T., Fukuyama, H., Hayashi, T., Hanakawa, T., 2005. Functional activity related to risk anticipation during performance of the Iowa Gambling Task. *Neuroimage* 24, 253–259.
- 44 Glascher, J., Hampton, A.N., O'Doherty, J.P., 2009. Determining a role for ventromedial prefrontal cortex in encoding action-based value signals during reward-related decision making. *Cerebral Cortex* 19, 483–495.
- 45 Gottfried, J.A., O'Doherty, J., Dolan, R.J., 2003. Encoding predictive reward value in human amygdala and orbitofrontal cortex. *Science* 301, 1104–1107.
- 46 Hare, T.A., O'Doherty, J., Camerer, C.F., Schultz, W., Rangel, A., 2008. Dissociating the role of the orbitofrontal cortex and the striatum in the computation of goal values and prediction errors. *Journal of Neuroscience* 28, 5623–5630.
- 47 Hariri, A.R., Brown, S.M., Williamson, D.E., Flory, J.D., de Wit, H., Manuck, S.B., 2006. Preference for immediate over delayed rewards is associated with magnitude of ventral striatal activity. *Journal of Neuroscience* 26, 13213–13217.
- 48 Haruno, M., Kawato, M., 2006. Different neural correlates of reward expectation and reward expectation error in the putamen and caudate nucleus during stimulus-action-reward association learning. *Journal of Neurophysiology* 95, 948–959.
- 49 Haruno, M., Kuroda, T., Doya, K., Toyama, K., Kimura, M., Samejima, K., Imamizu, H., Kawato, M., 2004. A neural correlate of reward-based behavioral learning in caudate nucleus: a functional magnetic resonance imaging study of a stochastic decision task. *Journal of Neuroscience* 24, 1660–1665.
- 50 Heekeren, H.R., Wartenburger, I., Marschner, A., Mell, T., Villringer, A., Reischies, F.M., 2007. Role of ventral striatum in reward-based decision making. *Neuroreport* 18, 951–955.
- 51 Hewig, J., Straube, T., Trippe, R.H., Kretschmer, N., Hecht, H., Coles, M.G., Miltner, W.H., 2008. Decision-making under risk: an fMRI study. *Journal of Cognitive Neuroscience*.
- 52 Hommer, D.W., Knutson, B., Fong, G.W., Bennett, S., Adams, C.M., Varnera, J.L., 2003. Amygdalar recruitment during anticipation of monetary rewards: an event-related fMRI study. *Annals of the New York Academy of Sciences* 985, 476–478.
- 53 Hsu, M., Krajbich, I., Zhao, C., Camerer, C.F., 2009. Neural response to reward anticipation under risk is nonlinear in probabilities. *Journal of Neuroscience* 29, 2231–2237.
- 54 Huettel, S.A., 2006. Behavioral, but not reward, risk modulates activation of prefrontal, parietal, and insular cortices. *Cognitive, Affective, & Behavioral Neuroscience* 6, 141–151.
- 55 Huettel, S.A., Stowe, C.J., Gordon, E.M., Warner, B.T., Platt, M.L., 2006. Neural signatures of economic preferences for risk and ambiguity. *Neuron* 49, 765–775.
- 56 Ino, T., Nakai, R., Azuma, T., Kimura, T., Fukuyama, H., 2009. Differential activation of the striatum for decision making and outcomes in a monetary task with gain and loss. *Cortex*.
- 57 Izuma, K., Saito, D.N., Sadato, N., 2008. Processing of social and monetary rewards in the human striatum. *Neuron* 58, 284–294.
- 58 Izuma, K., Saito, D.N., Sadato, N., 2009. Processing of the Incentive for Social Approval in the Ventral Striatum during Charitable Donation. *Journal of Cognitive Neuroscience*.
- 59 Juckel, G., Schlagenhauf, F., Koslowski, M., Wustenberg, T., Villringer, A., Knutson, B., Wrase, J., Heinz, A., 2006. Dysfunction of ventral striatal reward prediction in schizophrenia. *Neuroimage* 29, 409–416.
- 60 Kable, J.W., Glimcher, P.W., 2007. The neural correlates of subjective value during intertemporal choice. *Nature Neuroscience* 10, 1625–1633.
- 61 Kahnt, T., Park, S.Q., Cohen, M.X., Beck, A., Heinz, A., Wrase, J., 2009. Dorsal Striatal-midbrain Connectivity in Humans Predicts How Reinforcements Are Used to Guide Decisions. *Journal of Cognitive Neuroscience* 21, 1332–1345.
- 62 Kim, H., Shimojo, S., O'Doherty, J.P., 2006. Is avoiding an aversive outcome rewarding? Neural substrates of avoidance learning in the human brain. *PLoS Biology* 4, e233.
- 63 Kirsch, P., Schienle, A., Stark, R., Sammer, G., Blecker, C., Walter, B., Ott, U., Burkart, J., Vaitl, D., 2003. Anticipation of reward in a nonaversive differential conditioning paradigm and the brain reward system: an event-related fMRI study. *Neuroimage* 20, 1086–1095.
- 64 Knutson, B., Adams, C.M., Fong, G.W., Hommer, D., 2001a. Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *Journal of Neuroscience* 21, RC159.
- 65 Knutson, B., Fong, G.W., Adams, C.M., Varner, J.L., Hommer, D., 2001b. Dissociation of reward anticipation and outcome with event-related fMRI. *Neuroreport* 12, 3683–3687.
- 66 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.
- 67 Knutson, B., Rick, S., Wimmer, G.E., Prelec, D., Loewenstein, G., 2007. Neural predictors of purchases. *Neuron* 53, 147–156.
- 68 Knutson, B., Taylor, J., Kaufman, M., Peterson, R., Glover, G., 2005. Distributed neural representation of expected value. *Journal of Neuroscience* 25, 4806–4812.
- 69 Knutson, B., Westdorp, A., Kaiser, E., Hommer, D., 2000. fMRI visualization of brain activity during a monetary incentive delay task. *Neuroimage* 12, 20–27.
- 70 Knutson, B., Wimmer, G.E., 2007. Splitting the difference: how does the brain code reward episodes? *Annals of the New York Academy of Sciences* 1104, 54–69.
- 71 Knutson, B., Wimmer, G.E., Rick, S., Hollon, N.G., Prelec, D., Loewenstein, G., 2008. Neural antecedents of the endowment effect. *Neuron* 58, 814–822.
- 72 Koch, K., Schachtzabel, C., Wagner, G., Reichenbach, J.R., Sauer, H., Schlosser, R., 2008. The neural correlates of reward-related trial-and-error learning: an fMRI study with a probabilistic learning task. *Learning & Memory* 15, 728–732.
- 73 Kuhnen, C.M., Knutson, B., 2005. The neural basis of financial risk taking. *Neuron* 47, 763–770.
- 74 Landmann, C., Dehaene, S., Pappata, S., Jobert, A., Bottlaender, M., Roumenov, D., Le Bihan, D., 2007. Dynamics of prefrontal and cingulate activity during a reward-based logical deduction task. *Cerebral Cortex* 17, 749–759.
- 75 Liu, X., Powell, D.K., Wang, H., Gold, B.T., Corbly, C.R., Joseph, J.E., 2007. Functional dissociation in frontal and striatal areas for processing of positive and negative reward information. *Journal of Neuroscience* 27, 4587–4597.
- 76 Lohrenz, T., McCabe, K., Camerer, C.F., Montague, P.R., 2007. Neural signature of fictive learning signals in a sequential investment task. *Proceedings of the National Academy of Sciences of the United States of America* 104, 9493–9498.
- 77 Longe, O., Senior, C., Rippon, G., 2009. The lateral and ventromedial prefrontal cortex work as a dynamic integrated system: evidence from fMRI connectivity analysis. *Journal of Cognitive Neuroscience* 21, 141–154.
- 78 Luhmann, C.C., Chun, M.M., Yi, D.J., Lee, D., Wang, X.J., 2008. Neural dissociation of delay and uncertainty in intertemporal choice. *Journal of Neuroscience* 28, 14459–14466.
- 79 Marsh, A.A., Blair, K.S., Vythilingam, M., Busis, S., Blair, R.J., 2007. Response options and expectations of reward in decision-making: the differential roles of dorsal and rostral anterior cingulate cortex. *Neuroimage* 35, 979–988.
- 80 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.
- 81 McLean, J., Brennan, D., Wyper, D., Condon, B., Hadley, D., Cavanagh, J., 2009. Localisation of regions of intense pleasure response evoked by soccer goals. *Psychiatry Research* 171, 33–43.
- 82 Nieuwenhuis, S., Heslenfeld, D.J., von Geusau, N.J., Mars, R.B., Holroyd, C.B., Yeung, N., 2005a. Activity in human reward-sensitive brain areas is strongly context dependent. *Neuroimage* 25, 1302–1309.
- 83 Nieuwenhuis, S., Slagter, H.A., von Geusau, N.J., Heslenfeld, D.J., Holroyd, C.B., 2005b. Knowing good from bad: differential activation of human cortical areas by positive and negative outcomes. *European Journal of Neuroscience* 21, 3161–3168.
- 84 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. *Journal of Neuroscience* 23, 7931–7939.
- 85 O'Doherty, J., Dayan, P., Schultz, J., Deichmann, R., Friston, K., Dolan, R.J., 2004. Dissociable roles of ventral and dorsal striatum in instrumental conditioning. *Science* 304, 452–454.

- 86 O'Doherty, J., Kringelbach, M.L., Rolls, E.T., Hornak, J., Andrews, C., 2001. Abstract reward and punishment representations in the human orbitofrontal cortex. *Nature Neuroscience* 4, 95–102.
- 87 O'Doherty, J.P., Dayan, P., Friston, K., Critchley, H., Dolan, R.J., 2003b. Temporal difference models and reward-related learning in the human brain. *Neuron* 38, 329–337.
- 88 O'Doherty, J.P., Deichmann, R., Critchley, H.D., Dolan, R.J., 2002. Neural responses during anticipation of a primary taste reward. *Neuron* 33, 815–826.
- 89 Paulus, M.P., Frank, L.R., 2006. Anterior cingulate activity modulates nonlinear decision weight function of uncertain prospects. *Neuroimage* 30, 668–677.
- 90 Paulus, M.P., Rogalsky, C., Simmons, A., Feinstein, J.S., Stein, M.B., 2003. Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. *Neuroimage* 19, 1439–1448.
- 91 Pessiglione, M., Petrovic, P., Daunizeau, J., Palminteri, S., Dolan, R.J., Frith, C.D., 2008. Subliminal instrumental conditioning demonstrated in the human brain. *Neuron* 59, 561–567.
- 92 Petrovic, P., Pleger, B., Seymour, B., Kloppel, S., De Martino, B., Critchley, H., Dolan, R.J., 2008. Blocking central opiate function modulates hedonic impact and anterior cingulate response to rewards and losses. *Journal of Neuroscience* 28, 10509–10516.
- 93 Plassmann, H., O'Doherty, J., Rangel, A., 2007. Orbitofrontal cortex encodes willingness to pay in everyday economic transactions. *Journal of Neuroscience* 27, 9984–9988.
- 94 Pleger, B., Blankenburg, F., Ruff, C.C., Driver, J., Dolan, R.J., 2008. Reward facilitates tactile judgments and modulates hemodynamic responses in human primary somatosensory cortex. *Journal of Neuroscience* 28, 8161–8168.
- 95 Pochon, J.B., Levy, R., Fossati, P., Lehericy, S., Poline, J.B., Pillon, B., Le Bihan, D., Dubois, B., 2002. The neural system that bridges reward and cognition in humans: an fMRI study. *Proceedings of the National Academy of Sciences of the United States of America* 99, 5669–5674.
- 96 Preusschoff, K., Bossaerts, P., Quartz, S.R., 2006. Neural differentiation of expected reward and risk in human subcortical structures. *Neuron* 51, 381–390.
- 97 Preusschoff, K., Quartz, S.R., Bossaerts, P., 2008. Human insula activation reflects risk prediction errors as well as risk. *Journal of Neuroscience* 28, 2745–2752.
- 98 Ramnani, N., Elliott, R., Athwal, B.S., Passingham, R.E., 2004. Prediction error for free monetary reward in the human prefrontal cortex. *Neuroimage* 23, 777–786.
- 99 Ramnani, N., Miall, R.C., 2003. Instructed delay activity in the human prefrontal cortex is modulated by monetary reward expectation. *Cerebral Cortex* 13, 318–327.
- 100 Remijne, P.L., Nielen, M.M., Uylings, H.B., Veltman, D.J., 2005. Neural correlates of a reversal learning task with an affectively neutral baseline: an event-related fMRI study. *Neuroimage* 26, 609–618.
- 101 Remijne, P.L., Nielen, M.M., van Balkom, A.J., Cath, D.C., van Oppen, P., Uylings, H.B., Veltman, D.J., 2006. Reduced orbitofrontal-striatal activity on a reversal learning task in obsessive-compulsive disorder. *Archives of General Psychiatry* 63, 1225–1236.
- 102 Reuter, J., Raedler, T., Rose, M., Hand, I., Glascher, J., Buchel, C., 2005. Pathological gambling is linked to reduced activation of the mesolimbic reward system. *Nature Neuroscience* 8, 147–148.
- 103 Rilling, J.K., Gutman, D., Zeh, T., Pagnoni, G., Berns, G., Kilts, C., 2002. A neural basis for social cooperation. *Neuron* 35, 395–405.
- 104 Rilling, J.K., Sanfey, A.G., Aronson, J.A., Nystrom, L.E., Cohen, J.D., 2004. Opposing BOLD responses to reciprocated and unreciprocated altruism in putative reward pathways. *Neuroreport* 15, 2539–2543.
- 105 Rogers, R.D., Ramnani, N., Mackay, C., Wilson, J.L., Jezzard, P., Carter, C.S., Smith, S.M., 2004. Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. *Biological Psychiatry* 55, 594–602.
- 106 Rolls, E.T., McCabe, C., Redoute, J., 2008. Expected value, reward outcome, and temporal difference error representations in a probabilistic decision task. *Cerebral Cortex* 18, 652–663.
- 107 Sailer, U., Robinson, S., Fischmeister, F.P., Konig, D., Oppenauer, C., Lueger-Schuster, B., Moser, E., Kryspin-Exner, I., Bauer, H., 2008. Altered reward processing in the nucleus accumbens and mesial prefrontal cortex of patients with posttraumatic stress disorder. *Neuropsychologia* 46, 2836–2844.
- 108 Sailer, U., Robinson, S., Fischmeister, F.P., Moser, E., Kryspin-Exner, I., Bauer, H., 2007. Imaging the changing role of feedback during learning in decision-making. *Neuroimage* 37, 1474–1486.
- 109 Samanez-Larkin, G.R., Gibbs, S.E., Khanna, K., Nielsen, L., Carstensen, L.L., Knutson, B., 2007. Anticipation of monetary gain but not loss in healthy older adults. *Nature Neuroscience* 10, 787–791.
- 110 Sanfey, A.G., Rilling, J.K., Aronson, J.A., Nystrom, L.E., Cohen, J.D., 2003. The neural basis of economic decision-making in the Ultimatum Game. *Science* 300, 1755–1758.
- 111 Satterthwaite, T.D., Green, L., Myerson, J., Parker, J., Ramaratnam, M., Buckner, R.L., 2007. Dissociable but inter-related systems of cognitive control and reward during decision making: evidence from pupillometry and event-related fMRI. *Neuroimage* 37, 1017–1031.
- 112 Schonberg, T., Daw, N.D., Joel, D., O'Doherty, J.P., 2007. Reinforcement learning signals in the human striatum distinguish learners from nonlearners during reward-based decision making. *Journal of Neuroscience* 27, 12860–12867.
- 113 Smith, B.W., Mitchell, D.G., Hardin, M.G., Jazbec, S., Fridberg, D., Blair, R.J., Ernst, M., 2009. Neural substrates of reward magnitude, probability, and risk during a wheel of fortune decision-making task. *Neuroimage* 44, 600–609.
- 114 Spicer, J., Galvan, A., Hare, T.A., Voss, H., Glover, G., Casey, B., 2007. Sensitivity of the nucleus accumbens to violations in expectation of reward. *Neuroimage* 34, 455–461.
- 115 Staudinger, M.R., Erk, S., Abler, B., Walter, H., 2009. Cognitive reappraisal modulates expected value and prediction error encoding in the ventral striatum. *Neuroimage* 47, 713–721.
- 116 Strohle, A., Stoy, M., Wrase, J., Schwarzer, S., Schlagenhauf, F., Huss, M., Hein, J., Nedderhut, A., Neumann, B., Gregor, A., Juckel, G., Knutson, B., Lehmkuhl, U., Bauer, M., Heinz, A., 2008. Reward anticipation and outcomes in adult males with attention-deficit/hyperactivity disorder. *Neuroimage* 39, 966–972.
- 117 Tanaka, S.C., Doya, K., Okada, G., Ueda, K., Okamoto, Y., Yamawaki, S., 2004. Prediction of immediate and future rewards differentially recruits cortico-basal ganglia loops. *Nature Neuroscience* 7, 887–893.
- 118 Tanaka, S.C., Samejima, K., Okada, G., Ueda, K., Okamoto, Y., Yamawaki, S., Doya, K., 2006. Brain mechanism of reward prediction under predictable and unpredictable environmental dynamics. *Neural Networks* 19, 1233–1241.
- 119 Taylor, S.F., Welsh, R.C., Wager, T.D., Phan, K.L., Fitzgerald, K.D., Gehring, W.J., 2004. A functional neuroimaging study of motivation and executive function. *Neuroimage* 21, 1045–1054.
- 120 Tobler, P.N., Christopoulos, G.I., O'Doherty, J.P., Dolan, R.J., Schultz, W., 2008. Neuronal distortions of reward probability without choice. *Journal of Neuroscience* 28, 11703–11711.
- 121 Tobler, P.N., O'Doherty, J.P., Dolan, R.J., Schultz, W., 2007. Reward value coding distinct from risk attitude-related uncertainty coding in human reward systems. *Journal of Neurophysiology* 97, 1621–1632.
- 122 Tom, S.M., Fox, C.R., Trepel, C., Poldrack, R.A., 2007. The neural basis of loss aversion in decision-making under risk. *Science* 315, 515–518.
- 123 Tricomi, E.M., Delgado, M.R., Fiez, J.A., 2004. Modulation of caudate activity by action contingency. *Neuron* 41, 281–292.
- 124 Ullsperger, M., von Cramon, D.Y., 2003. Error monitoring using external feedback: specific roles of the habenular complex, the reward system, and the cingulate motor area revealed by functional magnetic resonance imaging. *Journal of Neuroscience* 23, 4308–4314.
- 125 Ursu, S., Carter, C.S., 2005. Outcome representations, counterfactual comparisons and the human orbitofrontal cortex: implications for neuroimaging studies of decision-making. *Brain Research. Cognitive Brain Research* 23, 51–60.
- 126 van den Bos, W., McClure, S.M., Harris, L.T., Fiske, S.T., Cohen, J.D., 2007. Dissociating affective evaluation and social cognitive processes in the ventral medial prefrontal cortex. *Cognitive, Affective, & Behavioral Neuroscience* 7, 337–346.
- 127 Vollm, B., Richardson, P., McKie, S., Elliott, R., Dolan, M., Deakin, B., 2007. Neuronal correlates of reward and loss in Cluster B personality disorders: a functional magnetic resonance imaging study. *Psychiatry Research* 156, 151–167.
- 128 Volz, K.G., Schubotz, R.I., von Cramon, D.Y., 2003. Predicting events of varying probability: uncertainty investigated by fMRI. *Neuroimage* 19, 271–280.
- 129 Volz, K.G., Schubotz, R.I., von Cramon, D.Y., 2005. Variants of uncertainty in decision-making and their neural correlates. *Brain Research Bulletin* 67, 403–412.
- 130 Weber, B., Aholt, A., Neuhaus, C., Trautner, P., Elger, C.E., Teichert, T., 2007. Neural evidence for Reference-dependence in real-market-transactions. *Neuroimage* 35, 441–447.
- 131 Weber, B.J., Huettel, S.A., 2008. The neural substrates of probabilistic and intertemporal decision making. *Brain Research* 1234, 104–115.
- 132 Wittmann, M., Leland, D.S., Paulus, M.P., 2007. Time and decision making: differential contribution of the posterior insular cortex and the striatum during a delay discounting task. *Experimental Brain Research* 179, 643–653.
- 133 Wrase, J., Kahnt, T., Schlagenhauf, F., Beck, A., Cohen, M.X., Knutson, B., Heinz, A., 2007a. Different neural systems adjust motor behavior in response to reward and punishment. *Neuroimage* 36, 1253–1262.

- 134 Wrase, J., Schlagenhauf, F., Kienast, T., Wustenberg, T., Bermpohl, F., Kahnt, T., Beck, A., Strohle, A., Juckel, G., Knutson, B., Heinz, A., 2007b. Dysfunction of reward processing correlates with alcohol craving in detoxified alcoholics. *Neuroimage* 35, 787–794.
- 135 Xu, L., Liang, Z.Y., Wang, K., Li, S., Jiang, T., 2009. Neural mechanism of intertemporal choice: from discounting future gains to future losses. *Brain Research* 1261, 65–74.
- 136 Xue, G., Lu, Z., Levin, I.P., Weller, J.A., Li, X., Bechara, A., 2009. Functional dissociations of risk and reward processing in the medial prefrontal cortex. *Cerebral Cortex* 19, 1019–1027.
- 137 Yacubian, J., Glascher, J., Schroeder, K., Sommer, T., Braus, D.F., Buchel, C., 2006. Dissociable systems for gain- and loss-related value predictions and errors of prediction in the human brain. *Journal of Neuroscience* 26, 9530–9537.
- 138 Yacubian, J., Sommer, T., Schroeder, K., Glascher, J., Kalisch, R., Leuenberger, B., Braus, D.F., Buchel, C., 2007. Gene-gene interaction associated with neural reward sensitivity. *Proceedings of the National Academy of Sciences of the United States of America* 104, 8125–8130.
- 139 Yarkoni, T., Braver, T.S., Gray, J.R., Green, L., 2005a. Prefrontal brain activity predicts temporally extended decision-making behavior. *Journal of the Experimental Analysis of Behavior* 84, 537–554.
- 140 Yarkoni, T., Gray, J.R., Chrostil, E.R., Barch, D.M., Green, L., Braver, T.S., 2005b. Sustained neural activity associated with cognitive control during temporally extended decision making. *Brain Research. Cognitive Brain Research* 23, 71–84.
- 141 Zalla, T., Koechlin, E., Pietrini, P., Basso, G., Aquino, P., Sirigu, A., Grafman, J., 2000. Differential amygdala responses to winning and losing: a functional magnetic resonance imaging study in humans. *European Journal of Neuroscience* 12, 1764–1770.
- 142 Zink, C.F., Pagnoni, G., Martin-Skurski, M.E., Chappel, J.C., Berns, G.S., 2004. Human striatal responses to monetary reward depend on saliency. *Neuron* 42, 509–517.
- Delgado, M.R., Miller, M.M., Inati, S., Phelps, E.A., 2005. An fMRI study of reward-related probability learning. *Neuroimage* 24, 862–873.
- Drevets, W.C., 2001. Neuroimaging and neuropathological studies of depression: implications for the cognitive-emotional features of mood disorders. *Curr. Opin. Neurobiol.* 11, 240–249.
- Eickhoff, S.B., Laird, A.R., Grefkes, C., Wang, L.E., Zilles, K., Fox, P.T., 2009. Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: a random-effects approach based on empirical estimates of spatial uncertainty. *Hum. Brain Mapp.* 30, 2907–2926.
- Elliott, R., Agnew, Z., Deakin, J.F., 2010. Hedonic and informational functions of the human orbitofrontal cortex. *Cereb. Cortex* 20, 198–204.
- Elliott, R., Friston, K.J., Dolan, R.J., 2000. Dissociable neural responses in human reward systems. *J. Neurosci.* 20, 6159–6165.
- Ernst, M., Nelson, E.E., Jazbec, S., McClure, E.B., Monk, C.S., Leibenluft, E., Blair, J., Pine, D.S., 2005. Amygdala and nucleus accumbens in responses to receipt and omission of gains in adults and adolescents. *Neuroimage* 25, 1279–1291.
- Fellows, L.K., 2004. The cognitive neuroscience of human decision making: a review and conceptual framework. *Behav. Cogn. Neurosci. Rev.* 3, 159–172.
- FitzGerald, T.H., Seymour, B., Dolan, R.J., 2009. The role of human orbitofrontal cortex in value comparison for incommensurable objects. *J. Neurosci.* 29, 8388–8395.
- Fox, M.D., Snyder, A.Z., Vincent, J.L., Corbetta, M., Van Essen, D.C., Raichle, M.E., 2005. The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proc. Natl. Acad. Sci. U.S.A.* 102, 9673–9678.
- Frank, M.J., Claus, E.D., 2006. Anatomy of a decision: striato-orbitofrontal interactions in reinforcement learning, decision making, and reversal. *Psychol. Rev.* 113, 300–326.
- Garavan, H., Stout, J.C., 2005. Neurocognitive insights into substance abuse. *Trends Cogn. Sci.* 9, 195–201.
- Gold, J.I., Shadlen, M.N., 2007. The neural basis of decision making. *Annu. Rev. Neurosci.* 30, 535–574.
- Gottfried, J.A., O'Doherty, J., Dolan, R.J., 2003. Encoding predictive reward value in human amygdala and orbitofrontal cortex. *Science* 301, 1104–1107.
- Gu, X., Liu, X., Guise, K.G., Naidich, T.P., Hof, P.R., Fan, J., 2010. Functional dissociation of the fronto-insular and anterior cingulate cortices in empathy for pain. *J. Neurosci.* 30, 3739–3744.
- Hare, T.A., O'Doherty, J., Camerer, C.F., Schultz, W., Rangel, A., 2008. Dissociating the role of the orbitofrontal cortex and the striatum in the computation of goal values and prediction errors. *J. Neurosci.* 28, 5623–5630.
- Hsu, M., Krajbich, I., Zhao, C., Camerer, C.F., 2009. Neural response to reward anticipation under risk is nonlinear in probabilities. *J. Neurosci.* 29, 2231–2237.
- Hubbard, E.M., Piazza, M., Pinel, P., Dehaene, S., 2005. Interactions between number and space in parietal cortex. *Nat. Rev. Neurosci.* 6, 435–448.
- Huettel, S.A., 2006. Behavioral, but not reward, risk modulates activation of prefrontal, parietal, and insular cortices. *Cogn. Affect. Behav. Neurosci.* 6, 141–151.
- Kim, H., Shimojo, S., O'Doherty, J.P., 2006. Is avoiding an aversive outcome rewarding? Neural substrates of avoidance learning in the human brain. *PLoS Biol.* 4, e233.
- Knutson, B., Adams, C.M., Fong, G.W., Hommer, D., 2001a. Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *J. Neurosci.* 21, RC159.
- Knutson, B., Fong, G.W., Adams, C.M., Varner, J.L., Hommer, D., 2001b. Dissociation of reward anticipation and outcome with event-related fMRI. *Neuroreport* 12, 3683–3687.
- Knutson, B., Fong, G.W., Bennett, S.M., Adams, C.M., Hommer, D., 2003. A region of mesial prefrontal cortex monetarily rewarding outcomes: characterization with rapid event-related fMRI. *Neuroimage* 18, 263–272.
- Kringelbach, M.L., 2005. The human orbitofrontal cortex: linking reward to hedonic experience. *Nat. Rev. Neurosci.* 6, 691–702.
- Kringelbach, M.L., O'Doherty, J., Rolls, E.T., Andrews, C., 2003. Activation of the human orbitofrontal cortex to a liquid food stimulus is correlated with its subjective pleasantness. *Cereb. Cortex* 13, 1064–1071.
- Kringelbach, M.L., Rolls, E.T., 2004. The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology. *Prog. Neurobiol.* 72, 341–372.
- Kuhnen, C.M., Knutson, B., 2005. The neural basis of financial risk taking. *Neuron* 47, 763–770.
- Laird, A.R., Eickhoff, S.B., Li, K., Robin, D.A., Glahn, D.C., Fox, P.T., 2009. Investigating the functional heterogeneity of the default mode network using coordinate-based meta-analytic modeling. *J. Neurosci.* 29, 14496–14505.
- Laird, A.R., Fox, P.M., Price, C.J., Glahn, D.C., Uecker, A.M., Lancaster, J.L., Turkeltaub, P.E., Kochunov, P., Fox, P.T., 2005. ALE meta-analysis: controlling the false discovery rate and performing statistical contrasts. *Hum. Brain Mapp.* 25, 155–164.
- Lau, H.C., Rogers, R.D., Haggard, P., Passingham, R.E., 2004a. Attention to intention. *Science* 303, 1208–1210.
- Lau, H.C., Rogers, R.D., Ramnani, N., Passingham, R.E., 2004b. Willed action and attention to the selection of action. *Neuroimage* 21, 1407–1415.
- Liu, X., Powell, D.K., Wang, H., Gold, B.T., Corbly, C.R., Joseph, J.E., 2007. Functional dissociation in frontal and striatal areas for processing of positive and negative reward information. *J. Neurosci.* 27, 4587–4597.
- 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.
- Mohr, P.N., Biele, G., Heekeren, H.R., 2010. Neural processing of risk. *J. Neurosci.* 30, 6613–6619.
- Nieuwenhuis, S., Slagter, H.A., von Geusau, N.J., Heslenfeld, D.J., Holroyd, C.B., 2005. Knowing good from bad: differential activation of human cortical areas by positive and negative outcomes. *Eur. J. Neurosci.* 21, 3161–3168.

Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neubiorev.2010.12.012.

References

- Andersen, R.A., Cui, H., 2009. Intention, action planning, and decision making in parietal-frontal circuits. *Neuron* 63, 568–583.
- Arana, F.S., Parkinson, J.A., Hinton, E., Holland, A.J., Owen, A.M., Roberts, A.C., 2003. Dissociable contributions of the human amygdala and orbitofrontal cortex to incentive motivation and goal selection. *J. Neurosci.* 23, 9632–9638.
- Bach, D.R., Seymour, B., Dolan, R.J., 2009. Neural activity associated with the passive prediction of ambiguity and risk for aversive events. *J. Neurosci.* 29, 1648–1656.
- Bechara, A., 2005. Decision making, impulse control and loss of willpower to resist drugs: a neurocognitive perspective. *Nat. Neurosci.* 8, 1458–1463.
- Bjork, J.M., Knutson, B., Fong, G.W., Caggiano, D.M., Bennett, S.M., Hommer, D.W., 2004. Incentive-elicited brain activation in adolescents: similarities and differences from young adults. *J. Neurosci.* 24, 1793–1802.
- Breiter, H.C., Aharon, I., Kahneman, D., Dale, A., Shizgal, P., 2001. Functional imaging of neural responses to expectancy and experience of monetary gains and losses. *Neuron* 30, 619–639.
- Brett, M., Johnsrude, I.S., Owen, A.M., 2002. The problem of functional localization in the human brain. *Nat. Rev. Neurosci.* 3, 243–249.
- Caspers, S., Zilles, K., Laird, A.R., Eickhoff, S.B., 2010. ALE meta-analysis of action observation and imitation in the human brain. *Neuroimage* 50, 1148–1167.
- Cohen Kadosh, R., Henik, A., Rubinsten, O., Mohr, H., Dori, H., van de Ven, V., Zorzi, M., Hendler, T., Goebel, R., Linden, D.E., 2005. Are numbers special? The comparison systems of the human brain investigated by fMRI. *Neuropsychologia* 43, 1238–1248.
- Cohen, M.X., Ranganath, C., 2005. Behavioral and neural predictors of upcoming decisions. *Cogn. Affect. Behav. Neurosci.* 5, 117–126.
- Costafreda, S.G., David, A.S., Brammer, M.J., 2009. A parametric approach to voxel-based meta-analysis. *Neuroimage* 46, 115–122.
- Cox, C.L., Gotimer, K., Roy, A.K., Castellanos, F.X., Milham, M.P., Kelly, C., 2010. Your resting brain CAREs about your risky behavior. *PLoS One* 5, e12296.
- Cox, S.M., Andrade, A., Johnsrude, I.S., 2005. Learning to like: a role for human orbitofrontal cortex in conditioned reward. *J. Neurosci.* 25, 2733–2740.
- Craig, A.D., 2002. How do you feel? Interoception: the sense of the physiological condition of the body. *Nat. Rev. Neurosci.* 3, 655–666.
- Craig, A.D., 2009. How do you feel – now? The anterior insula and human awareness. *Nat. Rev. Neurosci.* 10, 59–70.
- 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.
- d'Acromont, M., Bossaerts, P., 2008. Neurobiological studies of risk assessment: a comparison of expected utility and mean-variance approaches. *Cogn. Affect. Behav. Neurosci.* 8, 363–374.

- O'Doherty, J.P., 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.P., Dayan, P., Friston, K., Critchley, H., Dolan, R.J., 2003b. Temporal difference models and reward-related learning in the human brain. *Neuron* 38, 329–337.
- O'Doherty, J.P., Deichmann, R., Critchley, H.D., Dolan, R.J., 2002. Neural responses during anticipation of a primary taste reward. *Neuron* 33, 815–826.
- O'Doherty, J.P., Kringsbach, M.L., Rolls, E.T., Hornak, J., Andrews, C., 2001. Abstract reward and punishment representations in the human orbitofrontal cortex. *Nat. Neurosci.* 4, 95–102.
- Pagnoni, G., Zink, C.F., Montague, P.R., Berns, G.S., 2002. Activity in human ventral striatum locked to errors of reward prediction. *Nat. Neurosci.* 5, 97–98.
- Paulus, M.P., Rogalsky, C., Simmons, A., Feinstein, J.S., Stein, M.B., 2003. Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. *Neuroimage* 19, 1439–1448.
- Phan, K.L., Wager, T., Taylor, S.F., Liberzon, I., 2002. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage* 16, 331–348.
- Plassmann, H., O'Doherty, J., Rangel, A., 2007. Orbitofrontal cortex encodes willingness to pay in everyday economic transactions. *J. Neurosci.* 27, 9984–9988.
- Raichle, M.E., MacLeod, A.M., Snyder, A.Z., Powers, W.J., Gusnard, D.A., Shulman, G.L., 2001. A default mode of brain function. *Proc. Natl. Acad. Sci. U.S.A.* 98, 676–682.
- Raichle, M.E., Snyder, A.Z., 2007. A default mode of brain function: a brief history of an evolving idea. *Neuroimage* 37, 1083–1090.
- Ramnani, N., Elliott, R., Athwal, B.S., Passingham, R.E., 2004. Prediction error for free monetary reward in the human prefrontal cortex. *Neuroimage* 23, 777–786.
- Richlan, F., Kronbichler, M., Wimmer, H., 2009. Functional abnormalities in the dyslexic brain: a quantitative meta-analysis of neuroimaging studies. *Hum. Brain Mapp.* 30, 3299–3308.
- Rogers, R.D., Ramnani, N., Mackay, C., Wilson, J.L., Jezard, P., Carter, C.S., Smith, S.M., 2004. Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. *Biol. Psychiatry* 55, 594–602.
- Salimi-Khorshidi, G., Smith, S.M., Keltner, J.R., Wager, T.D., Nichols, T.E., 2009. Meta-analysis of neuroimaging data: a comparison of image-based and coordinate-based pooling of studies. *Neuroimage* 45, 810–823.
- Schoenbaum, G., Roesch, M., 2005. Orbitofrontal cortex, associative learning, and expectancies. *Neuron* 47, 633–636.
- Schoenbaum, G., Roesch, M.R., Stalnaker, T.A., Takahashi, Y.K., 2009. A new perspective on the role of the orbitofrontal cortex in adaptive behaviour. *Nat. Rev. Neurosci.*
- Schoenbaum, G., Setlow, B., Saddoris, M.P., Gallagher, M., 2003. Encoding predicted outcome and acquired value in orbitofrontal cortex during cue sampling depends upon input from basolateral amygdala. *Neuron* 39, 855–867.
- Schultz, W., Tremblay, L., Hollerman, J.R., 2000. Reward processing in primate orbitofrontal cortex and basal ganglia. *Cereb. Cortex* 10, 272–284.
- Sugrue, L.P., Corrado, G.S., Newsome, W.T., 2005. Choosing the greater of two goods: neural currencies for valuation and decision making. *Nat. Rev. Neurosci.* 6, 363–375.
- Tom, S.M., Fox, C.R., Trepel, C., Poldrack, R.A., 2007. The neural basis of loss aversion in decision-making under risk. *Science* 315, 515–518.
- Toro, R., Fox, P.T., Paus, T., 2008. Functional coactivation map of the human brain. *Cereb. Cortex* 18, 2553–2559.
- Tremblay, L., Schultz, W., 1999. Relative reward preference in primate orbitofrontal cortex. *Nature* 398, 704–708.
- Tremblay, L., Schultz, W., 2000. Modifications of reward expectation-related neuronal activity during learning in primate orbitofrontal cortex. *J. Neurophysiol.* 83, 1877–1885.
- Trepel, C., Fox, C.R., Poldrack, R.A., 2005. Prospect theory on the brain? Toward a cognitive neuroscience of decision under risk. *Brain Res. Cogn. Brain Res.* 23, 34–50.
- Turkeltaub, P.E., Eden, G.F., Jones, K.M., Zeffiro, T.A., 2002. Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *Neuroimage* 16, 765–780.
- Ullsperger, M., von Cramon, D.Y., 2003. Error monitoring using external feedback: specific roles of the habenular complex, the reward system, and the cingulate motor area revealed by functional magnetic resonance imaging. *J. Neurosci.* 23, 4308–4314.
- Volkow, N.D., Fowler, J.S., Wang, G.J., 2003. The addicted human brain: insights from imaging studies. *J. Clin. Invest.* 111, 1444–1451.
- Volkow, N.D., Wise, R.A., 2005. How can drug addiction help us understand obesity? *Nat. Neurosci.* 8, 555–560.
- Wallis, J.D., 2007. Orbitofrontal cortex and its contribution to decision-making. *Annu. Rev. Neurosci.* 30, 31–56.
- Xiong, J., Gao, J.H., Lancaster, J.L., Fox, P.T., 1995. Clustered pixels analysis for functional MRI activation studies of the human brain. *Hum. Brain Mapp.* 3, 287–301.
- Yang, T., Shadlen, M.N., 2007. Probabilistic reasoning by neurons. *Nature* 447, 1075–1080.
- Zalla, T., Koehlin, E., Pietrini, P., Basso, G., Aquino, P., Sirigu, A., Grafman, J., 2000. Differential amygdala responses to winning and losing: a functional magnetic resonance imaging study in humans. *Eur. J. Neurosci.* 12, 1764–1770.