Neuropsychologia 50 (2012) 1252–1266

Contents lists available at SciVerse ScienceDirect

Neuropsychologia

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

The role of the human ventral striatum and the medial orbitofrontal cortex in the representation of reward magnitude – An activation likelihood estimation meta-analysis of neuroimaging studies of passive reward expectancy and outcome processing

Esther Kristina Diekhof[a,b,*], Lisa Kaps[b], Peter Falkai[b], Oliver Gruber[b]

[a] University of Hamburg, Biocenter Grindel and Zoological Museum, Institute for Human Biology, Hamburg, Germany
[b] Centre for Translational Research in Systems Neuroscience and Psychiatry, Department of Psychiatry & Psychotherapy, Georg August University Göttingen, Germany

ARTICLE INFO

Article history:
Received 29 August 2011
Received in revised form 1 February 2012
Accepted 9 February 2012
Available online 18 February 2012

Keywords:
Orbitofrontal cortex
Nucleus accumbens
fMRI
PET
Reward value
GingerALE

ABSTRACT

Reward maximization is a core motivation of every organism. In humans, several brain regions have been implicated in the representation of reward magnitude. Still, it is unclear whether identical brain regions consistently play a role in reward prediction and its consumption. In this study we used coordinate-based ALE meta-analysis to determine the individual roles of the ventral striatum (vSTR) and the medial orbitofrontal cortex (mOFC/VMPFC) in the representation of reward in general and of reward magnitude in particular. Specifically, we wanted to assess commonalities and differences in regional brain activation during the passive anticipation and consumption of rewards. Two independent meta-analyses of neuroimaging data from the past decade revealed a general role for the vSTR in reward anticipation and consumption. This was the case particularly when the consumed rewards occurred unexpectedly or were uncertain. In contrast, for the mOFC/VMPFC the present meta-analytic data suggested a rather specific function in reward consumption as opposed to passive anticipation. Importantly, when considering only coordinates that compared different reward magnitudes, the same parts of the vSTR and the mOFC/VMPFC showed concordant responses across studies, although areas of coherence were regionally more confined. These meta-analytic data suggest that the vSTR may be involved in both prediction and consumption of salient rewards, and may also be sensitive to different reward magnitudes, while the mOFC/VMPFC may rather process the magnitude during reward receipt. Collectively, our meta-analytic data conform with the notion that these two brain regions may subserve different roles in processing of reward magnitude.

1. Introduction

Organisms preferentially seek out locations or initiate motor actions that promise the highest amount of reward. Animal studies have shown that expectations of different reward magnitudes significantly impact on behavioral choice (e.g., Flaherty & Mitchall, 1999). For example, animals performed more accurately in trials with larger rewards and consistently chose larger over smaller incentives (e.g., Cromwell & Schultz, 2003), also when being in a food-deprived state (Collier, 1982). In the same way, the expectancy for higher rewards improved tactile performance in humans and enhanced discrimination accuracy in subsequent trials (Pleger, Blankenburg, Ruff, Driver, & Dolan, 2008). Even when reward predictors were presented subliminally, the magnitude of the available reward influenced the physical effort exerted during the current trial (Pessiglione et al., 2007). These data thus suggest that reward magnitude may be one important driving source that energizes behavior.

Behavioral optimization in terms of reward maximization strongly depends on the neural capacity to represent the expected magnitude of each reward option and to compare the size of all available rewards (Kable & Glimcher, 2009). Reward magnitude is an objective property of reward value that refers to the invariant ratio of different reward sizes (i.e., "less versus more"; see Peters & Büchel, 2010; Schultz, 2006). The present meta-analysis was intended to further dip into the neural substrates involved in the representation of reward magnitude. Neuroimaging research from the past decade identified two functionally related brain regions that probably form the core network for processing of reward magnitude. One of these neural structures is the

* Corresponding author at: University of Hamburg, Biocenter Grindel and Zoological Museum, Institute for Human Biology, Martin-Luther-King Platz 3, D-20146 Hamburg, Germany. Tel.: +49 40 42838 3931; fax: +49 40 42838 3937.
E-mail address: esther.diekhof@uni-hamburg.de (E.K. Diekhof).

0028-3932/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuropsychologia.2012.02.007

human ventral striatum (vSTR) (i.e., the brain region comprising the nucleus accumbens, ventral caudate nucleus and ventral putamen; Haber & Knutson, 2009; Haber & McFarland, 1999). Abundant neuroimaging evidence suggests that this brain region is preferentially activated by reliable predictors of reward (e.g., Cohen, Young, Baek, Kessler, & Ranganath, 2005; Knutson, Fong, Adams, Varner, & Hommer, 2001; Rademacher et al., 2010). Activity changes in the vSTR thereby specifically scaled with the magnitude of expected reward in both humans (e.g., Abler, Herrnberger, Grön, & Spitzer, 2009; Knutson, Adams, Fong, & Hommer, 2001; Tobler, O'Doherty, Dolan, & Schultz, 2007; Yacubian et al., 2007) and non-human primates (Cromwell & Schultz, 2003), and ventral striatal activity was further predictive of subsequent behavioral performance (Cromwell & Schultz, 2003; Pleger et al., 2008). Apart from that, some studies that were interested in outcome-related brain activation also reported increased ventral striatal activation during reward consumption (e.g., Yacubian et al., 2006), whereby the observed increase also scaled with the magnitude of the currently received reward (e.g., Elliott, Friston, & Dolan, 2000). However, the consummatory response of the vSTR was more pronounced in situations in which reward was uncertain, namely when a reward occurred either unpredictably after a risky gamble (e.g., Cohen et al., 2005) or was presented randomly in a sequence of rewards and neutral stimuli (e.g., Berns, McClure, Pagnoni, & Montague, 2001). Finally, studies that tested for both anticipatory and outcome-related activation in the vSTR within the same experiment produced rather heterogeneous results. While some of these studies demonstrated a specific function for the vSTR in the anticipation of reward (e.g., Knutson, Fong, Bennett, Adams, & Hommer, 2003), others observed phase-independent activation in this brain region during both anticipatory and consummatory periods (e.g., Breiter, Aharon, Kahneman, Dale, & Shizgal, 2001; Kim, Shimojo, & O'Doherty, 2010). It therefore remains unclear whether activation in the vSTR can be consistently associated with the representation of reward magnitude across neuroimaging studies during both reward expectancy and its consumption.

The second brain region that has been implicated in reward valuation and in the representation of reward magnitude encompasses the medial orbitofrontal cortex and adjacent parts of the ventromedial prefrontal cortex (i.e., the mOFC/VMPFC). The majority of previous studies found increased activation in this brain region during the consummatory phase of reward processing (e.g., Cohen et al., 2005; Knutson et al., 2003). Activity in the medial OFC was thereby significantly enhanced for larger amounts of reward (e.g., Grabenhorst et al., 2010; O'Doherty, Winston, et al., 2003). In addition, a much small number of previous studies also reported medial orbitofrontal activation in response to passive reward predictors (Tobler, O'Doherty, Dolan, & Schultz, 2006) or during the anticipatory period in general (e.g., Rolls, McCabe, & Redoute, 2008), whereby activation scaled with the anticipated reward size (Smith et al., 2009). Yet, anticipatory reward-related activation during passive evaluation was by far more common in the lateral orbitofrontal cortex (e.g., Gottfried, O'Doherty, & Dolan, 2003; Koeneke, Pedroni, Dieckmann, Bosch, & Jäncke, 2008; O'Doherty, Deichmann, Critchley, & Dolan, 2002; Schienle et al., 2009). In addition, more complex forms of reward valuation that require an integration of multiple dimensions including various decision costs (e.g., behavioral effort or temporal delay) and expected benefits (e.g., expected reward size) have been shown to activate the mOFC/VMPFC in numerous studies (see Peters & Büchel, 2010 and Grabenhorst & Rolls, 2011 for overview). For example Plassmann, O'Doherty, & Rangel (2007) found that the mOFC/VMPFC represented predicted reward value in a Becker–DeGroot–Marschak (BDM) auction during active decision making rather than during forced choice control trials. Finally, a positive deflection of medial orbitofrontal activity could also be observed during the relative down-regulation of negative affect (e.g., Diekhof, Kipshagen, et al., 2011; Diekhof, Geier, Falkai, & Gruber, 2011) and during the evaluation of simulated or hypothetical rewards (e.g., Bray, Shimojo, & O'Doherty, 2010; Coricelli et al., 2005).[1] In sum, the mOFC/VMPFC may thus contribute to the hedonic experience (and/or current mood) associated with processing of highly valued rewards (see Grabenhorst & Rolls, 2011; Kringelbach, 2005; Kringelbach & Rolls, 2004; Peters & Büchel, 2010).

Taken together, these previous neuroimaging findings suggest that the human vSTR and the mOFC/VMPFC represent the core system for the processing of reward in general, and of reward magnitude in particular. Still, the heterogeneity of previous findings to some extent precludes a conclusive judgment on the particular roles of these brain regions in either the passive anticipation or the consumption of rewards with different sizes. For this reason, it needs to be determined (1.) whether the vSTR was indeed consistently activated during passive reward prediction and also during reward receipt, (2.) whether its response also represents reward magnitude, and (3.) whether the medial OFC is activated during both passive reward prediction and outcome processing. Coordinate-based quantitative meta-analysis offers a useful tool to answer these questions by assessing the convergence of existing neuroimaging findings that used different reward tasks (Eickhoff et al., 2009; Laird, McMillan, et al., 2005; Turkeltaub, Eden, Jones, & Zeffiro, 2002). The identification of the specific role of these brain regions in reward anticipation and consumption – independent of the disadvantages of study-specific characteristics (e.g., experimental design, stimulus modality, or data analysis technique) – may thereby further our understanding of the neural mechanisms underlying motivational drive.

2. Materials and methods

We performed a coordinate-based quantitative meta-analysis using the activation likelihood estimation (ALE) method (Eickhoff et al., 2009; Laird, McMillan, et al., 2005; Turkeltaub et al., 2002 available at http://brainmap.org/ale/index.html). This analysis assessed the voxelwise correspondence of neuroimaging results from studies of reward processing. In particular, we wanted to examine the functional role of the vSTR and the medial OFC/VMPFC in the representation of reward magnitude during reward expectation and the consummatory phase. This was done by assessing the spatial concordance and regional overlap of activation in the anticipation and outcome phases of different reward tasks.

2.1. Search criteria

We performed a systematic PubMed search (http://www.ncbi.nlm.nih.gov/pubmed/) for the search terms "reward value" or "reward magnitude". These terms were each combined ("AND") with "fMRI" or "PET" to identify relevant functional neuroimaging studies. We also employed a snow-ball search for additional, potentially relevant articles using the reference lists of the identified articles. The search was restricted to relevant research articles published within the past decade (i.e., the publication date lay between January 2000 and December 2010). Studies were included if they reported functional brain imaging results from the population of healthy adult human subjects. This led to exclusion of neuroimaging studies dealing with pediatric cases, adolescent cases or patients. In addition, results from structural MRI studies and from functional MRI studies that did not report coordinates were also excluded.

2.2. Coordinate selection

In order to identify brain regions that were specifically related to evaluation of reward in general and of reward magnitude in particular, coordinates from the anticipation and outcome phase were included in the database if they reflected reward-related hyperactivations in one of the following comparisons: (1.) reward compared to a neutral control condition (e.g., the contrast of "expectation of reward ($5) versus expectation of no reward ($0)"), (2.) a high reward compared to a lower

[1] However, these active decision paradigms that required the integration of multiple dimensions are not included in the current meta-analysis. The intention of the present study was to focus specifically on the passive evaluation of reward predictors and their magnitude as well as on outcome-related responses that were unconfounded by decision-related brain activation.

Table 1
Studies that assessed reward expectancy (anticipation phase).

Authors	Number of subjects	Number of foci	Reward contingency	Reward type	Contrast type[a]	Results based on ROI analyses
Abler et al. (2009)	15	5[b]	Performance-dependent	Money	2	No
Adcock et al. (2006)	29	17	Performance-dependent	Money	1,3	No
Breiter et al. (2001)	12	8	Gamble	Money	2	No
Carter, Macinnes, Huettel, and Adcock (2009)	20	20	Performance-dependent	Money	1	No
Cohen et al. (2005)	17	14	Performance-dependent	Money	1	No
Croxson, Walton, O'Reilly, Behrens, and Rushworth, (2009)	16	9	Performance-dependent	Money	2	No
Galvan et al. (2005)	12	6[b]	Performance-dependent	Money	2	No
Gottfried et al. (2003)	13	7[b]	Passive	Food-related odor	1	No
Kim et al. (2010)	18	5[b]	Performance-dependent	Money or juice	n.a.	Yes
Kirsch et al. (2003)	27	43	Performance-dependent	Money	1	No
Knutson, Adams, et al. (2001)	18	22	Performance-dependent	Money	1,2	No
Knutson, Fong, et al. (2001)	9	13	Performance-dependent	Money	1	No
Knutson et al. (2003)	12	10	Performance-dependent	Money	1	No
Knutson et al. (2005)	14	17	Performance-dependent	Money	1,3	No
Koeneke et al. (2008)	19	20	Gamble	Chocolate bars	1	No
O'Doherty et al. (2002)	8	12	Passive	Glucose solution	1,3	No
Pochon et al. (2002)	6	11	Performance-dependent	Money	1	No
Rademacher et al. (2010)	28	26	Performance-dependent	Money or happy faces	1	No
Rolls et al. (2008)	13	2[b]	Gamble	Money	n.a.	Yes
Schott et al. (2007)	18	2	Performance-dependent	Money	1	No
Smith et al. (2009)	25	10	Gamble	Money	2	No
Spreckelmeyer et al. (2009)	32	17[b]	Performance-dependent	Money	1,2	No
Tobler et al. (2007)	16	4[b]	Performance-dependent	Money	2	No
Yacubian et al. (2006)	42	6	Gamble	Money	n.a.	Yes

[a] Reported contrast type: 1 = [reward versus no reward]; 2 = [high versus low reward]; 3 = [reward versus loss]; n.a. = studies that reported only results from ROI analyses were not included in the separate analyses for the different contrast types.
[b] Study contributed coordinates from relevant brain-behavior correlation (e.g., correlation with anticipated magnitude of upcoming reward).

amount of reward (e.g., "receipt of $5 versus $1"), or (3.) reward compared to a loss (e.g., "receipt of $1 versus loss of $1"). In addition, we also included coordinates from relevant brain-behavior correlations that may reflect actual magnitude evaluation (e.g., the positive correlation between the reported pleasure to eat chocolate and reward-related brain activation; see Small, Zatorre, Dagher, Evans, & Jones-Gotman, 2001). This was done, since some studies exclusively reported correlative data (these studies are explicitly marked in Tables 1 and 2). Importantly, if a study provided data from both brain-behavior correlations (or parametrical contrasts) and from classical subtraction analyses (t-contrasts), we included data from only one of these analyses in our meta-analysis. We thereby preferred the analysis (correlation or contrast) that most specifically tested for the representation of reward magnitude (i.e., "more versus less of a certain reward"). This was done, because we wanted to avoid a potential bias in the subsequent meta-analytic results caused by redundancy in our data. For example, with regard to the study by Xue et al. (2009) we decided to include the 5 coordinates from the parametrical contrast that specifically tested for brain activation paralleling the increase of the magnitude of rewards presented during the outcome phase. These coordinates were included in the meta-analysis of all studies (Table 4) and in the meta-analysis that was restricted to coordinates from the magnitude comparison (Table 6). The remaining 3 coordinates from the direct comparison of "win > loss" were only included in the specific meta-analysis of "reward versus loss" (Table 6), but not in the meta-analysis of all studies (Table 4).

Moreover, we deliberately decided against inclusion of coordinates from contrasts of the actual decision phase. This was done because we wanted to isolate the neural correlates of passive reward expectancy and reward reception from the processes of (1.) mere motor decision-making and (2.) any higher-order cognitive operations necessary to make an informed decision. For example, studies that used a BDM auction procedure to determine "subjective reward value" (e.g., Hare, O'Doherty, Camerer, Schultz, & Rangel, 2008) were not included in the present analyses, because these studies assessed brain activation during active decision making (e.g., during monetary bids for food items that reflected the willingness-to-pay) and not during passive outcome processing. Similarly, coordinates from studies and/or individual subtraction contrasts examining changes in reward-related brain activation in the context of decisions involving risk-taking, delay discounting, probability discounting or effort discounting were excluded. This was done, because reward valuation in these contexts probably also required higher-order evaluative operations like a weighing of the expected benefit (e.g., the expected reward magnitude) and the actual decision costs (e.g., the temporal delay or the probability of an available reward) (Peters & Büchel, 2010), which were not of primary interest here. For the same reason we also excluded coordinates from individual contrasts that assessed the representation of different degrees of reward probability during anticipation (e.g., "high versus low probability of expected reward") or that explicitly assessed "expected value" as the product of "expected reward probability x predicted reward magnitude". However, if the respective studies that assessed "expected value" also included contrasts that assessed the main effect of reward magnitude, activation foci from these contrasts were included in the present meta-analysis (see for example Knutson, Taylor, Kaufman, Peterson, & Glover, 2005). Finally, coordinates from studies that exclusively assessed activation related to the "error in reward prediction" without considering different reward magnitudes were also not part of the current database.

2.3. ALE meta-analysis of hyperactivations during reward expectancy and receipt

ALE maps were created according to the procedure described by Turkeltaub et al. (2002) and Laird, McMillan, et al. (2005), using the algorithm revised by Eickhoff et al. (2009) and Turkeltaub et al. (2012), which is implemented in GingerALE 2.1. By using an estimation of the intersubject and interlaboratory variability the revised algorithm assesses above-chance clustering between experiments and is used to model the spatial uncertainty of each coordinate. It also includes a weighting of each study by the number of included subjects. The identified coordinates can then be modeled with a three-dimensional Gaussian distribution and the concordance across experiments can be quantitatively examined. By calculating the above-chance clustering between experiments the meta-analytic results allow random-effects inference and can thus be generalized to the entire population of studies analyzed (Eickhoff et al., 2009). Importantly, the modifications implemented in GingerALE 2.1 further minimize the within-experiment and within-group effects. This means that effects merely caused by the number or spatial proximity of foci reported in an experiment or simply by the fact that some studies report multiple contrasts in one experiment are reduced, which optimizes the degree to which ALE values represent regional concordance of findings across independent reports (Turkeltaub et al., 2012). All ALE meta-analyses were performed in MNI reference space using version 2.1. Coordinates published in Talairach reference space were converted to MNI space using the Lancaster transformation (tal2icbm; Lancaster et al., 2007). ALE maps were thresholded at a false discovery rate of $p < 0.05$, corrected (Laird, Fox, et al., 2005), with a minimal clustersize of 200 mm^3. Images were displayed on the Colin T1-template (http://brainmap.org/ale/index.html) using Mango (multi-image analysis GUI, Research Imaging Center San Antonio, http://ric.uthscsa.edu/mango/).

ALE meta-analyses were performed for each of the two phases independently. Studies that only reported coordinates from a priori defined regions of interest (ROIs) located in the core reward system were excluded from the analyses. For studies that reported results from both ROI and whole-brain analyses, only coordinates from the latter analyses were included (see also Tables 1 and 2). This was done in order to eliminate a potential bias in our meta-analytic data that may have driven the results in favor of the vSTR and the mOFC/VMPFC. In addition, we also performed three independent meta-analyses for each phase that included only coordinates from one of the three contrast categories described in Section 2.2. Through this procedure we wanted to ascertain whether the vSTR and mOFC also specifically represented

Table 2
Studies that assessed processing of reward receipt (outcome phase).

Authors	Number of subjects	Number of foci	Reward contingency	Reward type	Contrast type[a]	Results based on ROI analyses
Aharon et al. (2001)	6	11	Passive	Attractive female faces	n.a.	No
Akitsuki et al. (2003)	36	12	Gamble	Money	2,3	No
Bray and O'Doherty (2007)	25	6	Passive	Attractive faces	n.a.	No
Breiter et al. (2001)	12	4	Gamble	Money	n.a.	Yes[c]
Christakou, Brammer, Giampietro, and Rubia (2009)	19	10	Performance-dependent	Money	3	No
Cloutier, Heatherton, Whalen, and Kelley (2008)	48	19[b]	Passive	Attractive faces	2	No
Cohen et al. (2005)	17	25	Performance-dependent	Money	1	No
Cox, Andrade, and Johnsrude (2005)	22	28	Gamble	Money	3	No
De Araujo, Kringelbach, Rolls, and McGlone (2003)	11	2	Passive	Water	2	No
De Greck et al. (2008)	15	20	Gamble	Positive feedback	3	No
Delgado et al. (2000)	9	17	Gamble	Money	n.a.	Yes
Delgado et al. (2003) (E1)	18	24	Gamble	Money	2,3	No
Delgado et al. (2003) (E2)	10	3				
Elliott et al. (2000)	9	7[b]	Gamble	Money	2	No
Elliott, Newman, Longe, and Deakin (2003)	12	11	Performance-dependent	Money	1	No
Elliott, Newman, Longe, and Deakin (2004)	12	4	Performance-dependent	Money	2	No
Fujiwara et al. (2009)	17	18	Performance-dependent	Money	n.a.	No
Grabenhorst and Rolls (2009)	12	3[b]	Passive	Food-related odors	n.a.	Yes
Grabenhorst et al. (2010)	14	8[b]	Passive	High- & low-fat drinks	n.a.	Yes
Huettel, Stowe, Gordon, Warner, and Platt (2006)	12	18	Performance-dependent	Money	1	No
Kampe et al. (2001)	16	2[b]	Passive	Attractive faces	n.a.	Yes
Killgore et al. (2003)	13	25	Passive	Photographs of food	1,2	No
Kim, Shimojo, and O'Doherty (2006)	16	1	Performance-dependent	Money	1	No
Kim et al. (2010)	18	7[b]	Performance-dependent	Money or juice	n.a.	Yes
Knutson, Fong, et al. (2001)	9	10	Performance-dependent	Money	1,2	No
Knutson et al. (2003)	12	4	Performance-dependent	Money	1	No
Koeneke et al. (2008)	19	38	Gamble	Chocolate bars	1	No
Kringelbach, O'Doherty, Rolls, and Andrews (2003)	9	1	Passive	Tasty drinks	2	No
Nieuwenhuis et al. (2005)	14	10	Gamble	Money	2	No
O'Doherty, Kringelbach, Rolls, Hornak, and Andrews (2001)	9	2	Performance-dependent	Money	1,2	No
O'Doherty et al. (2002)	8	2	Passive	Glucose solution	1	No
O'Doherty, Winston, et al. (2003)	25	5	Passive	Attractive faces	n.a.	Yes
O'Doherty, Critchley, Deichmann, and Dolan (2003) (E1)	15	7	Performance-dependent	Money	3	No
O'Doherty, Critchley, et al. (2003) (E2)	15	4	Passive			
Rademacher et al. (2010)	28	22	Performance-dependent	Money or happy faces	1	No
Rogers et al. (2004)	14	12	Gamble	Money	3	No
Rothemund et al. (2007)	13	1	Passive	Photographs of food	n.a.	Yes
Schienle et al. (2009)	19	12	Passive	Photographs of food	1	No
Sescousse, Redouté, and Dreher (2010)	18	45[b]	Performance-dependent	Money or erotic stimuli	1,2	No
Small et al. (2001)	9	18[b]	Passive	Chocolate	2	No
Smith et al. (2010)	23	44[b]	Passive	Money or attractive faces	2,3	No
Schott et al. (2007)	18	1	Performance-dependent	Money	1	No
Van den Bos, McClure, Harris, Fiske, and Cohen (2007)	19	5	Performance-dependent	Juice	3	No
Winston, O'Doherty, Kilner, Perrett, and Dolan (2007)	26	6[b]	Passive	Attractive faces	2	No
Yacubian et al. (2006)	42	4	Gamble	Money	n.a.	Yes
Xue et al. (2009)	13	8[b]	Gamble	Money	2,3	No
Zalla et al. (2000)	10	4	Performance-dependent	Positive feedback	2,3	No

[a] Reported contrast type: 1 = [reward versus no reward]; 2 = [high versus low reward]; 3 = [reward versus loss]; n.a. = studies that reported only results from ROI analyses were not included in the separate analyses for the different contrast types.
[b] Study contributed coordinates from relevant brain-behavior correlation (e.g., correlation with perceived pleasantness).
[c] In the study by Breiter et al. (2001) only part of the reported coordinates were derived from a whole-brain analysis. For the outcome phase none of these coordinates lay within the mask used by GingerALE.

reward magnitude in the second contrast type of "large versus small (potential) gains" and whether the identified regions were comparable to those identified in the other contrast types.

Finally, to examine the regional overlap of ALE maps from the anticipation and the outcome phase, respectively, a formal two-way conjunction analysis was performed by multiplying binarized versions of the thresholded ALE maps with imcalc as implemented in SPM5 (i.e., a test against the conjunction null at $p < 0.05$, FDR-corrected). Significant differences between the two phases were further determined by comparison of the two data sets (i.e., a subtraction). For this purpose we used the thresholded NIfTI images from dataset A (i.e., "anticipation", at $p < 0.05$), dataset B (i.e., "outcome", at $p < 0.05$), and pooled dataset A + B (i.e., "anticipation and outcome", at $p < 0.05$). Regional differences between the anticipation and outcome phase were tested by performing the ALE meta-analysis separately for each phase and computing the voxel-wise difference between the resultant ALE maps. In a second step, the pooled data were used and were randomly divided into two groups of the same size as the original two data sets of experiments, which reflected the contrasted ALE analyses. For these two randomly assembled groups ALE-scores were calculated and the difference between these scores was recorded for each voxel. Repeating this process over 5000 permutations yielded a null-distribution for differences in ALE-scores. The observed differences in ALE scores were then compared against this permutation distribution producing a p-value at each voxel. p-values were thresholded at 0.05 and only significant clusters with a minimal size of 200 mm^3 are reported (for similar procedures please see Eickhoff et al., 2011 and Friebel, Eickhoff, & Lotze, 2011).

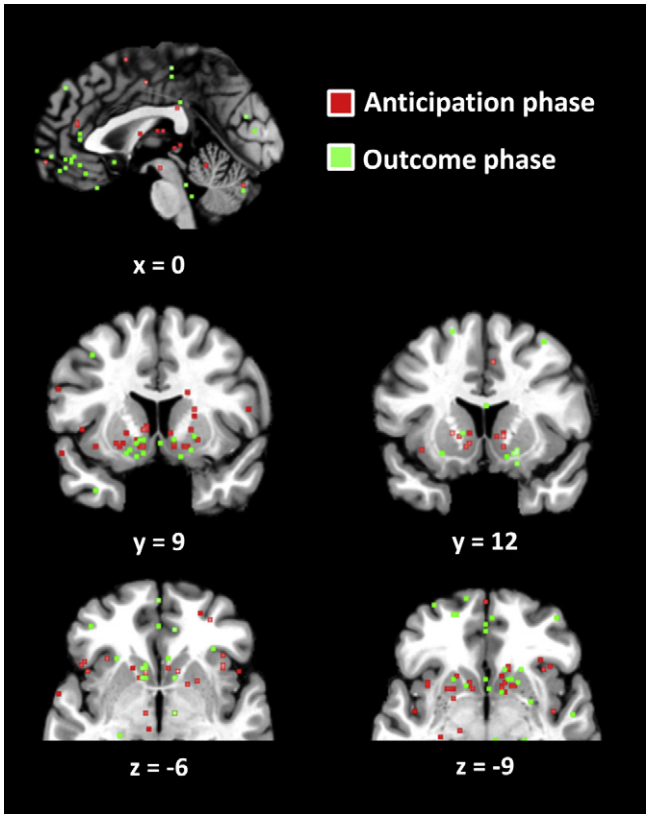

Fig. 1. Regional distribution of individual activation foci from studies of the anticipation and outcome phase displayed on coronal and axial slices of the Colin Template in MNI reference space.

3. Results

A systematic search of the PubMed database and application of the inclusion and exclusion criteria yielded a total of 24 relevant research articles (326 coordinates) for the anticipation phase and 46 relevant neuroimaging studies (549 coordinates) that reported reward-related hyperactivations from relevant contrasts during the outcome phase (see Tables 1 and 2). After exclusion of all coordinates that were derived from ROI analyses, 21 studies (307 coordinates) from the anticipation phase and 35 Studies (461 coordinates) from the outcome phase remained in the sample. Of these, seven studies assessed reward valuation in both the anticipation and the outcome phase (Cohen et al., 2005; Knutson, Fong, et al., 2001, Knutson et al., 2003; Koeneke et al., 2008; O'Doherty et al., 2002; Rademacher et al., 2010; Schott et al., 2007).

3.1. Commonalities in the vSTR during reward anticipation and reward receipt

Visual inspection of the identified coordinates from individual studies on coronal sections of the Colin T1-template (Colin27_T1_seg_MNI.nii; available at http://brainmap.org/ale/index.html) already revealed a regional clustering of activation foci in the vSTR in both phases (Fig. 1). The two separate phase-specific ALE meta-analyses supported this observation (Tables 3 and 4). The region with the highest concordance in each of the two phases was thereby located in the bilateral vSTR. In the meta-analysis of the anticipation phase the huge striatal cluster comprised additional sub-maxima in adjacent brain regions like the right caudate nucleus and the thalamus (Table 3), while in the outcome phase additional sub-maxima were detected in the right head of caudate nucleus, and in the left amygdala (Table 4). Despite these variations in exact cluster location and cluster extent between phases, the vSTR nevertheless was the only brain region that exhibited a significant overlap between phases in the conjunction analysis (Fig. 2). Finally, the separate meta-analyses for the three different contrast types also confirmed this regional concordance across phases (Tables 5 and 6). They showed that the vSTR may also process reward magnitude in particular as well as reward compared to loss during both reward anticipation and receipt (see Figs. 3 and 4).

3.2. Regional differences in the mOFC/VMPFC in the comparison of the outcome and anticipation phase

A regional clustering of activation foci in the medial OFC and in the adjacent VMPFC in the outcome phase, but not during reward expectancy, was already evident from visual inspection of the plot of the identified coordinates on an axial section of the Colin template (see Fig. 1). ALE meta-analyses further confirmed this finding by showing that only during the outcome phase a cluster of regional concordance could be observed in the mOFC/VMPFC (Table 4; see Fig. 2). This cluster was completely absent in the meta-analysis of coordinates from the anticipation phase even when lowering the cluster threshold to 0, and the apparent phase-selectivity was further confirmed by the direct comparison between phases (Table 8; see Fig. 2). Importantly, in order to rule out that the phase-selectivity of activation of the mOFC/VMPFC was simply an artifact of differences in image acquisition techniques used by different studies (e.g., it may be possible that studies assessing reward anticipation used an imaging sequence that was optimized for the ventral striatum, but not necessarily for the mOFC/VMPFC), we also performed two additional meta-analyses that were restricted to coordinates from the seven studies that examined brain activation in both phases (see above). These studies yielded a total of 96 activation foci for the anticipation phase and 102 coordinates for the outcome phase, which was sufficient to perform reliable ALE meta-analyses. These analyses also supported the phase-selectivity of the mOFC/VMPFC finding no evidence of concordant medial orbitofrontal activation in the anticipation phase, but only in the outcome phase (MNI-coordinates for the outcome phase: 2 58 −14; ALE-value = 0.014; Clustersize = 360 mm^3). However, one limitation of the current GingerALE algorithm is that it currently does not adequately deal with the within-experiment variance inherent to data from single studies that provide coordinates from different contrasts (like in our case the seven studies that provided data from both the anticipation and outcome phase, which were subsequently compared for regional disparities). As Turkeltaub et al. (2012) point out, ALE values represent regional concordance of findings across independent reports, and coordinates from the same study, but from different contrasts (or in our study from different phases), therefore may be treated as if coming from independent samples. Based on this consideration, we reran the subtraction analysis of all anticipation and outcome data (i.e., "outcome > anticipation phase") without the seven studies that reported coordinates from both the anticipation and the outcome phase. This subtraction confirmed the initial finding of a phase selectivity of the VMPFC/mOFC during the outcome phase (MNI-coordinates: −1 38 −13/0 40 −4; *Z*-value = 3.54/2.85; Clustersize = 784 mm^3), which makes us confident that an inclusion of those seven studies did not affect the overall results.

Finally, the separate meta-analyses of coordinates from the three different contrast types supported our initial finding of a phase-specific role of the mOFC/VMPFC in the graded processing of reward magnitude beyond the main effect of reward (Table 6; see also second and third column in Fig. 4). The location of the clusters was thereby similar to the ones observed in the analyses of all coordinates (i.e., the main effect of reward) reported in

Table 3
ALE meta-analysis of reward-related hyperactivations during the anticipation phase (without results from ROI analyses).

Region	MNI-coordinates	Extrema value	Clustersize (mm^3)	Number of foci inside cluster	Number of studies inside cluster
L/R vSTR[a]	**−10 10 −2**	**0.070**	**17,480**	**86**	**17**[b]
	12 14 −4	**0.073**			
R caudate nucleus	20 8 10	0.027			
R thalamus	2 −16 12	0.040			
L/R anterior insula	−46 16 −6	0.019	280	3	2
	38 20 −8	0.028	1672	9	6
	30 32 −2	0.025			
L/R ACC	2 28 30	0.024	1248	8	6
L middle occipital cortex	−22 −90 10	0.030	776	4	1
L VTA	−4 −16 −14	0.019	712	6	3
	−8 −14 −4	0.016			
L/R pre-SMA	2 4 48	0.025	672	5	4

This meta-analysis contained coordinates from 21 studies with a total of 307 foci within the mask ($p < 0.05$, corrected; clustersize > 200 mm^3).

[a] Cluster maxima in the vSTR are located in the Nacc and in the ventral caudate nucleus.

[b] i.e., Breiter et al. (2001), Knutson, Adams, et al. (2001), Knutson, Fong, et al. (2001), Knutson et al. (2003, 2005), Gottfried et al. (2003), Kirsch et al. (2003), Cohen et al. (2005), Galvan et al. (2005), Adcock et al. (2006), Schott et al. (2007), Tobler et al. (2007), Abler et al. (2009), Carter et al. (2009), Croxson et al. (2009), Spreckelmeyer et al. (2009), Rademacher et al. (2010).

Table 4, but the clusters were somewhat smaller and comprised less sub-maxima. However, a direct comparison of the meta-analysis of this subset of coordinates from the anticipation and outcome phase using the subtraction analysis implemented in GingerALE 2.1 did not directly support the phase selectivity of the magnitude-related activation in the mOFC/VMPFC in contrasts comparing activation related to "high versus low reward". Only when also including the relevant coordinates from studies, which employed ROI analyses and thus may bias the meta-analysis in favor of the medial OFC (i.e., Aharon et al., 2001; Bray & O'Doherty, 2007; Breiter et al., 2001; Delgado, Nystrom, Fissell, Noll, & Fiez, 2000; Fujiwara, Tobler, Taira, Iijima, & Tsutsui, 2009; Grabenhorst & Rolls, 2009; Grabenhorst et al., 2010; Kampe, Frith, Dolan, & Frith, 2001; Kim et al., 2010; O'Doherty, Winston, et al., 2003; Rothemund et al., 2007; Yacubian et al., 2006), a significant difference in the subtraction of "outcome > anticipation phase" could be detected for the contrast type assessing reward magnitude (MNI-coordinates: 7 47 −12; *Z*-Value = 3.04; Clustersize = 616 mm^3).

3.3. Regional concordance outside of the core reward network in the outcome and anticipation phases

The two phase-specific meta-analyses of all coordinates also identified additional brain regions of concordance that are listed in Tables 3–4 for completeness. In the anticipation phase these comprised brain regions that may reflect an increased dopaminergic response (ventral tegmental area (VTA)), heightened attention and arousal (anterior insula, thalamus and anterior cingulate cortex (ACC)) as well as task-preparatory brain activation (pre-supplementary motor area (pre-SMA)) during anticipation (see Tables 3 and 5). Notably, the ACC, the thalamus and the right anterior insula also showed a phase-selective response during the reward anticipation (see Table 7) suggesting that these brain regions represent cognitive operations specific to the situation, in which subjects waited for a reward. Further, in the outcome phase apart from the mOFC/VMPFC and vSTR several other regions specialized for reward

Table 4
ALE meta-analysis of reward-related hyperactivations during the outcome phase (without results from ROI analyses).

Region	MNI-coordinates	Extrema value	Clustersize (mm^3)	Number of foci inside cluster	Number of studies inside cluster
L/R vSTR[a]	**−10 12 −6**	**0.038**	**10,056**	**50**	**21**[b]
	16 12 −12	**0.043**			
R head of caudate nucleus	18 22 2	0.019			
L amygdala	−20 −2 −16	0.024			
mOFC/VMPFC	**0 46 −10**	**0.039**	**5424**	**28**	**13**[c]
	−10 42 −24	**0.020**	**424**	**4**	**3**[e]
Anterior MPFC/VMPFC	**−16 40 −18**	**0.017**			
	−2 64 −2	**0.043**			
	10 64 0	**0.022**			
Pregenual ACC/VMPFC	**0 38 8**	**0.027**	**816**	**4**	**3**[d]
R amygdala	26 0 −26	0.019	456	5	5
	28 0 −12	0.018			
L middle frontal gyrus/superior frontal sulcus	−22 26 52	0.026	1320	8	4
	−26 32 44	0.025			
R H-shaped orbital gyrus	28 26 −20	0.026	528	4	2
R middle occipital cortex/inferior occipital cortex	40 −82 8	0.022	360	3	2
R PCC	4 −50 22	0.019	296	4	4

This meta-analysis contained coordinates from 35 studies with a total of 461 foci within the mask ($p < 0.05$, corrected; clustersize > 200 mm^3).

[a] Cluster maxima in the vSTR are located in the Nacc and in the putamen.

[b] i.e., Elliott et al. (2000), Knutson, Fong, et al. (2001), Small et al. (2001), Akitsuki et al. (2003), De Araujo et al. (2003), Delgado et al. (2003, 1&2), Killgore et al. (2003), O'Doherty, Critchley, et al. (2003), Rogers et al. (2004), Cohen et al. (2005), Cox et al. (2005), Nieuwenhuis et al. (2005), Van den Bos et al. (2007), De Greck et al. (2008), Schienle et al. (2009), Xue et al. (2009), Cloutier et al. (2008), Rademacher et al. (2010), Sescousse et al. (2010), Smith et al. (2010).

[c] i.e., Knutson, Fong, et al. (2001), Knutson et al. (2003), Akitsuki et al. (2003), Killgore et al. (2003), 'Doherty, Critchley, et al. (2003), Cox et al. (2005), Huettel et al. (2006), Koeneke et al. (2008), Schienle et al. (2009), Xue et al. (2009), Rademacher et al. (2010), Sescousse et al. (2010), Smith et al. (2010).

[d] i.e., Cloutier et al. (2008), Schienle et al. (2009), Rademacher et al. (2010).

[e] i.e., Cohen et al. (2005), Cox et al. (2005), Cloutier et al. (2008).

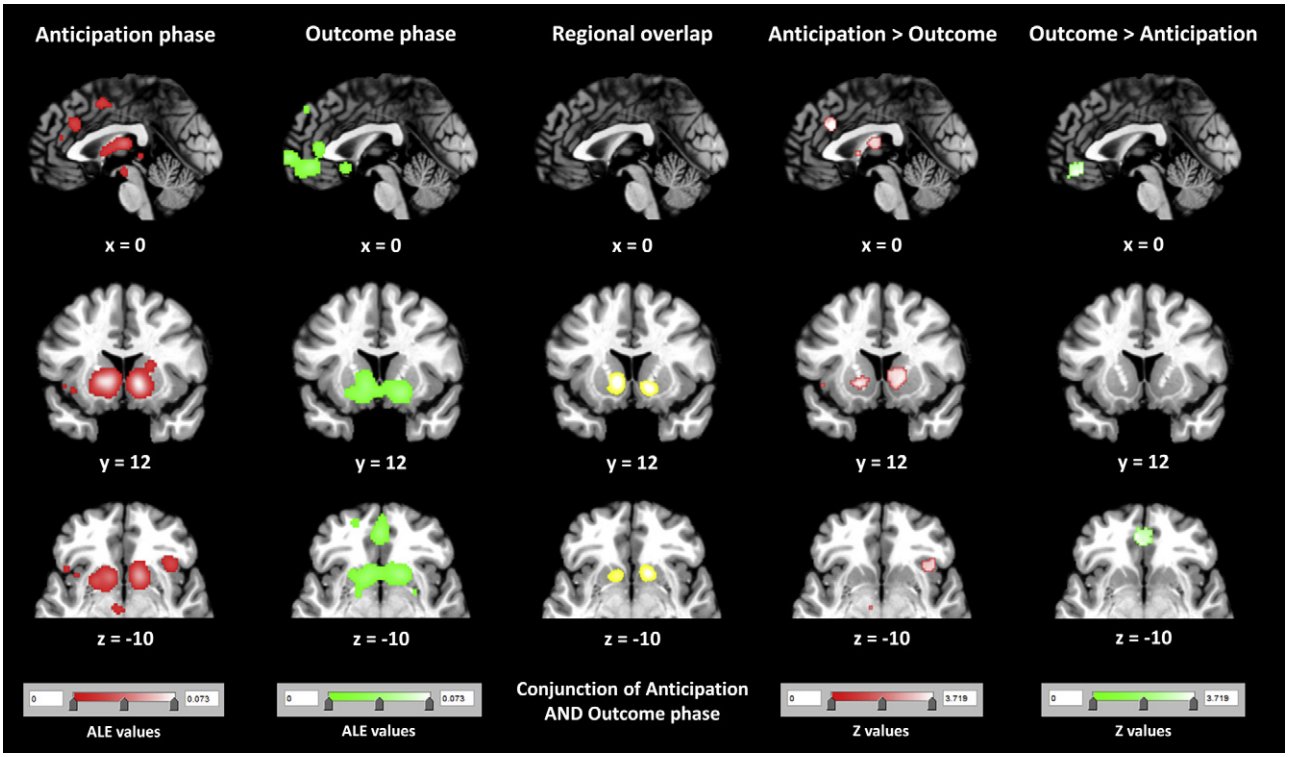

Fig. 2. Results of the ALE meta-analyses of all studies reporting reward-related activation during the anticipation and the outcome phase. Meta-analytic maps are displayed on slices of the Colin template in MNI reference space. The first and second columns display the results of the two separate meta-analyses of the anticipation and outcome phase, respectively. Scales below horizontal slices display ALE-values within significant clusters. The third column displays the result of the two-way conjunction of meta-analytic results from the anticipation and outcome phase (at $p < 0.05$, corrected). The fourth and fifth columns display the results of the meta-analytic subtraction analyses. Scales displays *Z*-values within significant clusters.

processing and higher-order cognitive operations were concordantly activated (e.g., the amygdala bilaterally, right lateral OFC, posterior cingulate cortex (PCC) and lateral prefrontal cortex; see Table 4), but these regions showed no significant phase-selectivity (Table 8). Nevertheless, compared to the clusters in the vSTR and mOFC/VMPFC all other clusters reported in Tables 3 and 4 were quite small and appeared less consistently across studies, which was reflected by reduced ALE values and

Table 5
ALE meta-analysis of reward-related hyperactivations in different contrasts during the anticipation phase (without results from ROI analyses).

Region	MNI-coordinates	Extrema value	Clustersize (mm^3)	Number of foci inside cluster	Number of studies inside cluster
1.) Convergent anticipation-related activation in the contrast [anticipation of reward versus no reward][a]					
L/R vSTR (nucleus accumbens, ventral nucleus caudatus and putamen)	**−10 10 −2**	**0.051**	**15,768**	**66**	**12**
	12 12 −4	**0.059**			
L/R thalamus	0 −16 12	0.028			
R SMA/preSMA	2 4 48	0.023	1816	14	8
	6 16 42	0.013			
R ACC	2 30 32	0.019			
R anterior insula	38 20 −8	0.027	1240	6	5
	32 32 0	0.016	208	2	2
L/R VTA	4 −18 −14	0.016	768	6	5
L thalamus	−8 −14 −4	0.016	256	2	1
2.) Convergent anticipation-related activation in the contrast [anticipation high reward versus low reward][b]					
L/R vSTR (nucleus accumbens, ventral nucleus caudatus and putamen)	**−10 6 2**	**0.023**	**2880**	**10**	**7**
	10 16 −8	**0.012**	**664**	**4**	**4**
L/R middle occipital cortex	−22 −90 10	0.018	576	2	1
	26 −90 16	0.013	344	2	1
R ACC	2 26 26	0.012	312	2	1
3.) Convergent anticipation-related activation in the contrast [anticipation of reward versus loss][c]					
R vSTR (nucleus accumbens, ventral nucleus caudatus and putamen)	**12 12 −8**	**0.010**	**768**	**3**	**2**

[a] This meta-analysis contained coordinates from 15 studies with a total of 221 foci within the mask ($p < 0.05$, corrected; clustersize > 200 mm^3).
[b] This meta-analysis contained coordinates from 8 studies with a total of 68 foci within the mask ($p < 0.05$, corrected; clustersize > 200 mm^3).
[c] This meta-analysis contained coordinates from 3 studies with a total of 18 foci within the mask ($p < 0.05$, corrected; clustersize > 200 mm^3).

Table 6
ALE meta-analysis of reward-related hyperactivations in different contrasts during the outcome phase (without results from ROI analyses).

Region	MNI-coordinates	Extrema value	Clustersize (mm^3)	Number of foci inside cluster	Number of studies inside cluster
1.) Convergent outcome-related activation in the contrast [receipt of reward versus no reward][a]					
L/R amygdala	−20 −2 −18	0.022	1584	6	5
	26 0 −26	0.018	760	3	3
L/R H-shaped orbital sulcus	−28 32 −14	0.014	352	2	2
	28 26 −20	0.026	1536	4	7
Pregenual ACC/VMPFC	**0 38 8**	**0.025**	**1216**	**5**	**3**
L hippocampus	−32 −12 −20	0.015	776	3	3
L fusiform gyrus	−42 −40 −22	0.018	616	3	3
L/R anterior MPFC/mOFC/VMPFC	**−8 62 −2**	**0.016**	**512**	**3**	**3**
	2 56 −16	**0.016**	**592**	**3**	**3**
R vSTR (nucleus accumbens)	**14 12 −12**	**0.015**	**456**	**3**	**2**
R PCC	4 −50 26	0.014	440	3	3
L medial superior frontal gyrus	−2 60 28	0.012	352	3	3
L lingual gyrus	−20 −72 −4	0.014	240	2	2
L angular gyrus	−48 −62 28	0.013	240	2	2
2.) Convergent outcome-related activation in the contrast [receipt of high reward versus low reward][b]					
L/R anterior MPFC/VMPFC	**0 66 −2**	**0.017**	**1776**	**9**	**4**
	2 50 −8	**0.014**			
	12 60 0	**0.010**			
L/R vSTR (nucleus accumbens, ventral caudate nucleus and putamen)	**−10 8 −12**	**0.015**	**1432**	**7**	**5**
	−14 14 0	**0.012**			
	20 12 −12	**0.015**	**1008**	**6**	**5**
	8 20 −6	**0.012**			
	10 16 −12	**0.012**			
R middle occipital cortex/superior occipital cortex	38 −82 12	0.014	720	4	3
	36 −84 16	0.014			
L VTA	−6 −22 10	0.017	656	3	3
L frontopolar cortex	−20 54 −10	0.018	616	3	2
R thalamus	12 −14 −4	0.013	592	4	3
R mOFC/VMPFC	**10 48 −24**	**0.016**	**456**	**2**	**2**
R putamen	28 −4 2	0.012	336	2	2
L middle occipital cortex	−16 −90 22	0.013	256	2	2
R pregenual ACC/VMPFC	**4 38 2**	**0.011**	**200**	**2**	**2**
L precuneus	−16 −64 52	0.010	200	3	2
	−12 −64 58	0.010			
3.) Convergent outcome-related activation in the contrast [receipt of reward versus loss][c]					
L/R vSTR (nucleus accumbens, ventral putamen)	**−16 10 −14**	**0.024**	**4560**	**18**	**8**
	−8 16 −8	**0.022**			
	16 14 −10	**0.018**			
L superior frontal sulcus/middle frontal gyrus	−26 32 44	0.023	1976	9	3
	−22 26 52	0.021			
L/R mOFC/VMPFC	**0 44 −8**	**0.031**	**1408**	**6**	**3**
L/R anterior MPFC/VMPFC	**−2 64 −2**	**0.020**	**552**	**3**	**2**
	10 64 2	**0.014**	**280**	**2**	**2**
R putamen	28 0 −12	0.016	288	2	2

[a] This meta-analysis contained coordinates from 14 studies with a total of 175 foci within the mask ($p < 0.05$, corrected; clustersize > 200 mm^3).
[b] This meta-analysis contained coordinates from 17 studies with a total of 147 foci within the mask ($p < 0.05$, corrected; clustersize > 200 mm^3).
[c] This meta-analysis contained coordinates from 11 studies with a total of 135 foci within the mask ($p < 0.05$, corrected; clustersize > 200 mm^3).

smaller numbers of activation foci located inside the clusters. Since the main focus of the present article was on the role of the vSTR and the mOFC/VMPFC in the representation of reward magnitude, these remaining brain regions will not be further discussed here.

4. Discussion

In this study we used coordinate-based ALE meta-analysis to determine the individual roles of the vSTR and the mOFC/VMPFC in the passive representation of reward in general and of reward

Table 7
Subtraction analysis of "anticipation versus outcome phase" (without results from ROI analyses).

Region	MNI-coordinates	*Z* value	Clustersize (mm^3)	Number of foci inside cluster	Number of studies inside cluster
L/R caudate nucleus	**3 6 0**	**3.72**	**5296**	**34**	**13**
	6 7 2	**3.54**			
L/R thalamus	−3 −9 12	3.24			
	2 −11 14	3.35			
L/R ACC	−6 24 30	3.24	1200	7	5
	3 28 29	3.72			
R anterior insula	38 17 −6	3.72	832	4	4

This meta-analysis contained coordinates from 56 studies (21 studies from the anticipation versus 35 studies from the outcome phase) with a total of 768 foci (307 foci versus 461 foci) within the mask ($p < 0.05$, corrected; clustersize > 200 mm^3).

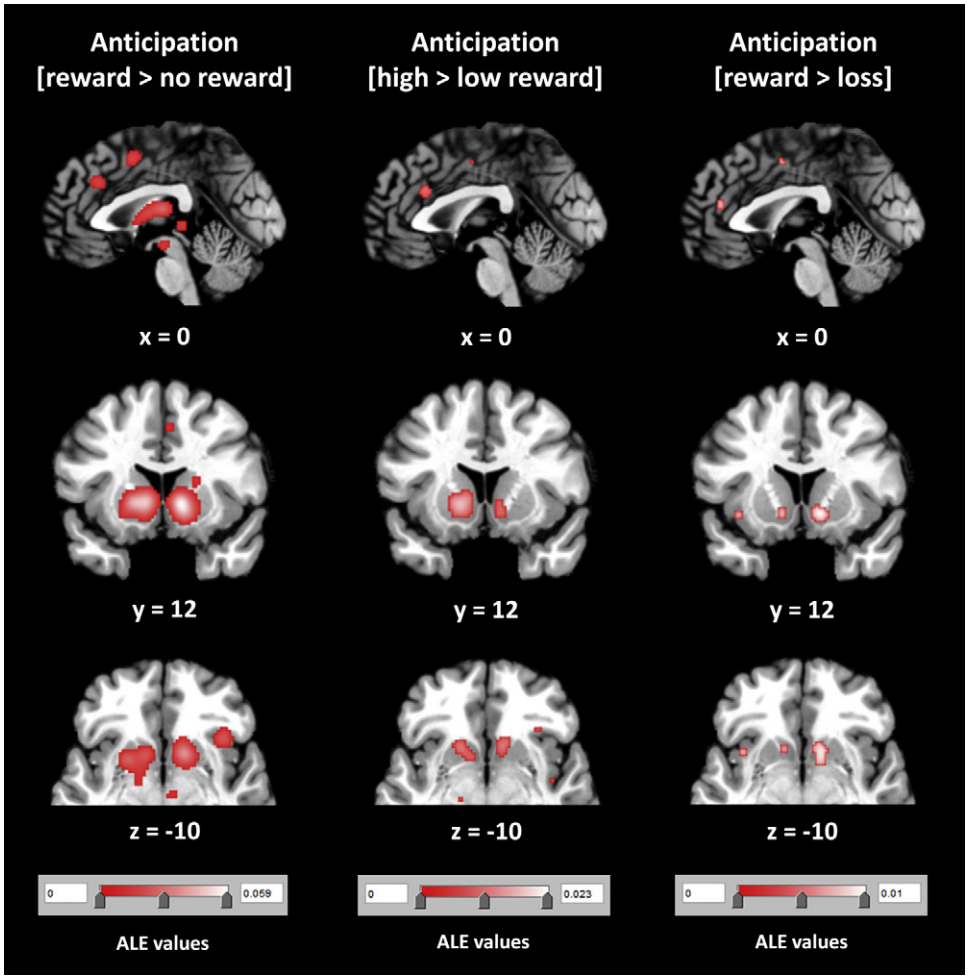

Fig. 3. Results of the three refined ALE meta-analyses of the anticipation phase that were restricted to studies reporting activation only in the comparison of (1.) reward versus neutral stimuli (221 coordinates from 15 studies), (2.) high versus low amount of reward (68 coordinates from 8 studies), (3.) reward versus loss (18 coordinates from 3 studies). Meta-analytic maps are displayed on slices of the Colin Template in MNI reference space. Scales below horizontal slices display ALE-values within significant clusters.

magnitude in particular. Specifically, we wanted to assess commonalities and differences in regional brain activation during the passive anticipation and consumption of rewards. A systematic search of the existing neuroimaging literature yielded a total of 875 relevant coordinates of which 768 coordinates remained in the sample after excluding results from ROI analyses. Two independent meta-analyses of coordinates from the anticipation and outcome phase, respectively, revealed a phase-independent role for the vSTR, and an apparent phase-specific function for the mOFC/VMPFC, the latter being restricted to reward receipt (Tables 3 and 4; see also Fig. 2). This phase-specificity of the medial orbitofrontal cluster was also confirmed by two additional meta-analyses that used only coordinates from studies that assessed brain activation in both phases. Through this procedure it was possible to rule out that differences in image acquisition techniques used by studies assessing either anticipatory or outcome-related processing may have mainly driven this meta-analytic result. Finally, a more refined meta-analysis of a subset of coordinates that were restricted to different types of contrasts comparing (1.) reward versus neutral stimuli, (2.) different quantities of reward, and (3.) reward versus loss, further extended these findings by showing that the human vSTR and the mOFC/VMPFC may not only be sensitive to reward per se, but may in fact also represent (objective) gradations of reward magnitude as well as the difference between reward and loss (Tables 5 and 6; Figs. 3 and 4). In sum, these meta-analytic data may help to reconcile the heterogeneity of previous neuroimaging findings by overcoming differences in study-specific characteristics (e.g., experimental design, imaging parameters or reward modality). Our findings thereby underscore the assumption that the human vSTR and the mOFC/VMPFC

Table 8
Subtraction analysis of "outcome versus anticipation phase" (without results from ROI analyses).

Region	MNI-coordinates	*Z* Value	Clustersize (mm^3)	Number of foci inside cluster	Number of studies inside cluster
L/R mOFC/VMPFC	**−2 43 −14**	**3.72**	**1328**	**7**	**4**

This meta-analysis contained coordinates from 56 studies (35 studies from the outcome versus 21 studies from the anticipation phase) with a total of 768 foci (461 foci versus 307 foci) within the mask ($p < 0.05$, corrected; clustersize > 200 mm^3).

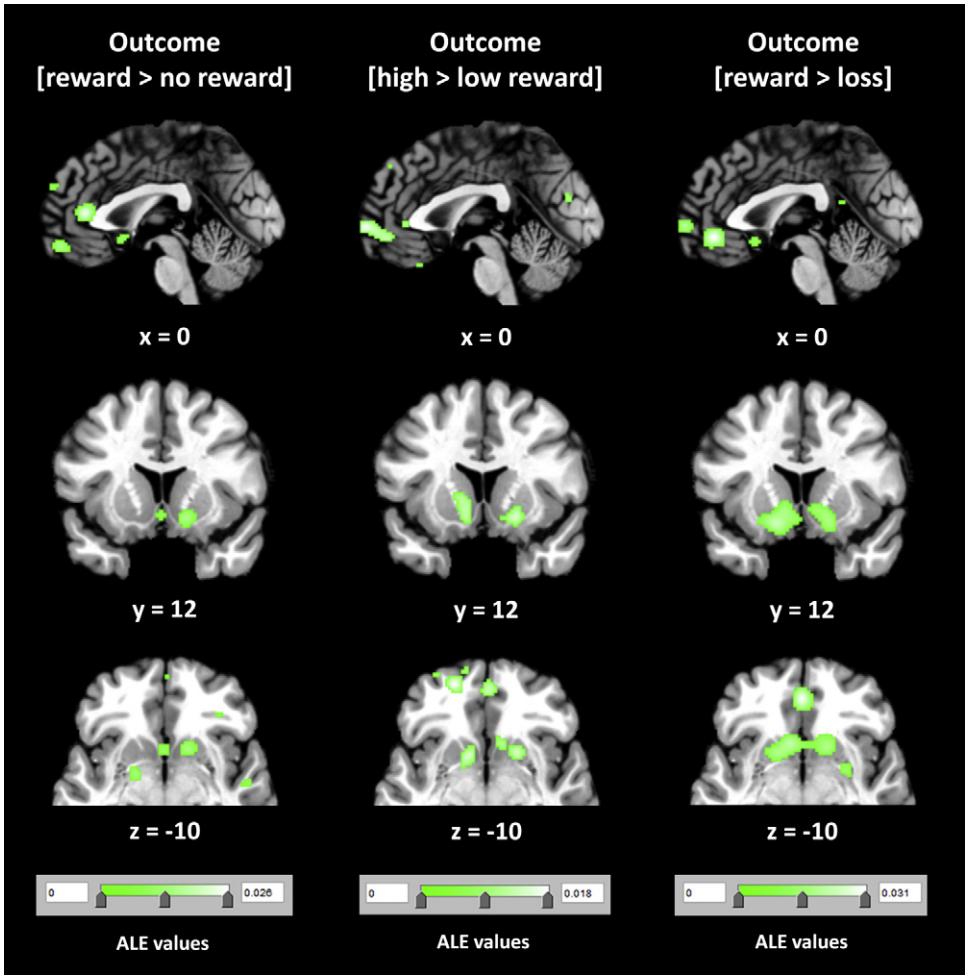

Fig. 4. Results of the three refined ALE meta-analyses of the outcome phase that were restricted to studies reporting activation only in the comparison of (1.) reward versus neutral stimuli (175 coordinates from 14 studies), (2.) high versus low amount of reward (147 coordinates from 17 studies), (3.) reward versus loss (135 coordinates from 11 studies). Meta-analytic maps are displayed on slices of the Colin Template in MNI reference space. Scales below horizontal slices display ALE-values within significant clusters.

may subserve somewhat different roles in the processing of reward magnitude during passive reward anticipation and its consumption.

4.1. Concordant regional activation in the vSTR during reward anticipation and consumption

The present meta-analytic finding of a consistent ventral striatal activation during passive reward anticipation is in line with both the general role of this brain region in reward prediction (e.g., Adcock, Thangavel, Whitfield-Gabrieli, Knutson, & Gabrieli, 2006; Kirsch et al., 2003; Knutson, Fong, et al., 2001; Knutson et al., 2003, 2005; Schott et al., 2007), as well as with its specific role in the representation of expected reward magnitude (Abler et al., 2009; Breiter et al., 2001; Cromwell & Schultz, 2003; Knutson, Adams, et al., 2001; Knutson et al., 2005; Yacubian et al., 2007). Converging evidence already suggests that after successful acquisition of a stimulus-reward contingency, the response of the vSTR shifts from the rewarding event itself to its predictor representing the expected magnitude of the future reward (Cromwell & Schultz, 2003; McClure, York, & Montague, 2004; O'Doherty, Dayan, Friston, Critchley, & Dolan, 2003; O'Doherty, 2004; Schultz, Tremblay, & Hollerman, 2000). These predictions are then used to guide subsequent behavior letting organisms preferentially seek out certain locations or initiate motor actions that promise higher amounts of reward in the future (Cromwell & Schultz, 2003). The ventral striatal clusters in the refined meta-analysis of the expectancy phase (see Fig. 3) coincided nicely with the striatal subregion (i.e., the posterior ventromedial striatum) that had been identified as representing "expected reward magnitude" in a large cohort of 98 human subjects (Yacubian et al., 2007). Yacubian et al. (2007) demonstrated that this part of the vSTR showed a consistent response preference for reward magnitude, even at the single subject level, while reward probability was associated with more lateral-anterior peaks in individual subjects. In terms of its anatomical connectivity, the ventromedial striatum is ideally located for using information on expected reward magnitude to guide adaptive action preparation and reward-related learning. The primate vSTR receives both focal and diffuse projections from different prefrontal subregions and itself projects to the ventral pallidum and the midbrain, which makes it one "hot spot" of plasticity for integrating reward value, predictability, and salience (Haber, Kim, Mailly, & Calzavara, 2006; see also Draganski et al., 2008; Haber & Knutson, 2009; Haber & McFarland, 1999; Haber & McFarland, 2000; Lehéricy et al., 2004). Given the fact, that the present meta-analysis of the anticipatory period did not include coordinates from the actual "decision phase" (i.e., the phase, in which choices between different reward options were made and the associated motor responses were executed), our data further support the idea that the vSTR indeed coded the forthcoming magnitude of a reward rather than the

associated motor response or the actual decision. This assumption would also conform with the observation made by prior neuroimaging studies that directly compared brain activation elicited during the decision phase with that observed during the subsequent delay when subjects waited for the reward (e.g., Ernst et al., 2004), or which used an experimental design that allowed a statistical dissociation of the different phases (e.g., Knutson, Adams, et al., 2001).

Apart from confirming the functional role of the human vSTR in reward prediction, the present meta-analyses provided additional evidence for a consistent involvement of the vSTR in the processing of reward outcome in general (Table 4; Fig. 2), and of reward magnitude in particular (Table 6; Fig. 4). A straightforward explanation for these findings may be provided by the nature of the experimental design. Accordingly, in most of the included studies the reward outcome was to some degree uncertain and therefore reward occurred rather unpredictably. For example, in the study by Smith et al. (2010) subjects viewed a random sequence of rewarding stimuli (i.e., pictures of human faces with varying levels of attractiveness or of money bills with varying value), which made it impossible to predict the nature of an upcoming picture. Moreover, Cohen et al. (2005) and Elliott et al. (2000) used gambling tasks with varying degrees of uncertainty, and subjects had to guess which option was to offer a higher amount of reward or any reward at all. For this reason, subject could never be sure whether to receive a reward in the subsequent outcome phase. It has already been demonstrated that when uncertainty is maximal (i.e., a 50% chance to gain a reward), then activation in the vSTR can be observed during the delay to reward (Dreher, Kohn, & Berman, 2006) and at the time of the unpredictable receipt of reward (e.g., Berns et al., 2001; Yacubian et al., 2006). This means that in a situation of uncertainty, in which a reliable predictor is absent, the ventral striatal signal is also closely tied to the occurrence of the unpredictable reward (McClure et al., 2004). In that way, the present meta-analytic data further support the prediction error theory of ventral striatum activity (McClure, Berns, Montague, 2003; McClure, Daw, Montague, 2003). This theory posits that in an unpredictable sequence or during uncertain gambles subjects are unable to predict when the next reward is coming and what it will be like. For this reason, in an uncertain context each unpredictable reward delivery represents more than the subject would expect, which should trigger a positive signal in the vSTR known as the "positive error of reward prediction" (McClure et al., 2004; Schultz, Dayan, & Montague, 1997; Schultz et al., 2000; please also see Niv & Schoenbaum, 2008 for a critical review of the prediction error theory). Although coordinates from contrasts that exclusively assessed the "error of reward prediction" without considering magnitude variations were excluded from the present database, our meta-analytic result thus nevertheless showed that many of the remaining neuroimaging studies obviously incorporated an uncertainty component that probably drove the ventral striatal response in the outcome phase. Interestingly, the present data further showed that the supposedly uncertainty-driven consummatory response in the vSTR also consistently scaled with the magnitude of received reward across studies (Table 6; Fig. 4). In that way, our findings may also conform with the view that the ventral striatal signal is probably triggered by interaction with down-stream dopaminergic cells of the midbrain that are not only sensitive to unexpected reward, but may also code the magnitude of this reward (Pagnoni, Zink, Montague, & Berns, 2002; Schultz, 2002; Tobler, Fiorillo, & Schultz, 2005). Finally, it is important to note that recent evidence from research in rodents further demonstrated that the vSTR, but not the OFC, is similarly involved in learning from both changes in reward value and from alterations of reward identity (McDannald, Lucantonio, Burke, Niv, & Schoenbaum, 2011). This suggests that the vSTR may also generate error signals representing differences in reward identity, which is currently not taken into account by model-free temporal difference learning algorithms. Therefore, as suggested by McDannald et al. (2011), current temporal difference learning models for the vSTR need to be extended to incorporate information beyond general reward value when conceptualizing reward expectancies and the resultant reward prediction errors. Nevertheless, from the present meta-analytic results we can only infer that the human vSTR may be consistently implicated in reward prediction in general and also specifically in the representation of (uncertain) reward magnitude.

4.2. Concordant regional activation in the mOFC/VMPFC during reward consumption

Activity in the mOFC/VMPFC consistently reflected reward magnitude at the time of consumption, but, in contrast to the vSTR, mOFC/VMPFC activity did not differ as a function of reward magnitude during passive reward anticipation. This was demonstrated by the results of (1.) the general meta-analysis (Fig. 2), (2.) the refined meta-analysis of studies comparing different reward magnitudes (Fig. 4), and (3.) the results of the subtraction analysis (Fig. 2). These findings thus strongly support the important function of mOFC/VMPFC in the evaluation of reward magnitude during its consumption (i.e., the representation of "outcome value", see Peters & Büchel, 2010), while a consistent role for this medial frontal brain region in passive reward prediction could not be confirmed by the present meta-analyses. As already indicated above, the medial OFC is anatomically linked to the ventral striatum as well as to several other structures of the reward system including the amygdala, the thalamus and the hypothalamus (Cavada, Compañy, Tejedor, Cruz-Rizzolo, & Reinoso-Suárez, 2000; Öngür & Price, 2000). In that way, the observation of a consistent involvement of the mOFC/VMPFC in outcome processing may support the view that this brain region monitors internal need states and integrates them with incoming sensory information to determine the magnitude of the experienced outcome (Kringelbach & Rolls, 2004; Kringelbach, 2005; Rolls, 2004; see also Peters & Büchel, 2010). This also means that one may typically expect to find magnitude-related activation in the mOFC/VMPFC when a factual reward is present, which explains why most reward prediction studies failed to observe increased activation in the mOFC/VMPFC during passive reward anticipation. In fact, only four of the initially identified 24 studies of the anticipation phase found increased activation in the mOFC proper or in the adjacent VMPFC (i.e., Kim et al., 2010; Koeneke et al., 2008; Rolls et al., 2008; Smith et al., 2009). Of these, two studies (i.e., Kim et al., 2010; Rolls et al., 2008) were not included in the present meta-analysis, because the exclusively reported coordinates from ROI analyses. Nevertheless, the particular studies that reported medial orbitofrontal activation had in common, that the employed tasks were not very demanding and that the anticipatory period was either considerably long (particularly in the studies by Koeneke et al., 2008 and Rolls et al., 2008, with an anticipatory interval of 10 s and 12 s, respectively), or that the expected outcome was already highly certain (Kim et al., 2010; see also Tobler et al., 2007 for additional evidence on the relation between medial orbitofrontal activation and reward certainty). One may therefore speculate that the observed anticipatory medial orbitofrontal activation in these particular studies most likely reflected a kind of "stimulus-substitution" (Pavlov, 1927), meaning that in these studies anticipatory cues could have already triggered a simulation of the unconditioned reaction normally elicited by the reward itself. Crude forms of mental simulation are often habitually engaged during passive anticipation or during phases of rest, when one has already a good idea of what is going to happen next (i.e., "proactive processing"; Bar, 2009; Moulton & Kosslyn, 2009). A recent neuroimaging study showed that factual sensory input is not always

necessary to drive reward-related activation in the mOFC/VMPFC. In this study, mental imagery of rewarding events activated the same medial orbitofrontal region as the actual receipt of a monetary reward (Bray et al., 2010). Other studies demonstrated that the value-related response in the mOFC/VMPFC can even override incoming sensory information leading to a more positive evaluation of environmental stimuli, which was independent of factual sensory input (Diekhof, Kipshagen, et al., 2011; Grabenhorst, Rolls, & Bilderbeck, 2008; Plassmann, O'Doherty, Shiv, & Rangel, 2008; see also Diekhof, Geier, et al., 2011). Finally, there is also evidence that medial parts of the OFC may respond to hypothetical forms of reward (e.g., the simulated outcome of an unchosen gamble that is regretted; Coricelli et al., 2005; see also Abe & Lee, 2011). Based on these considerations and the results from the present meta-analysis, one may speculate that the mOFC/VMPFC plays an important role in both actually experienced and mentally simulated evaluation of reward magnitude (of which the latter can also happen during anticipation, but only seldom does). Peters and Büchel (2010) already discussed this possibility in their recent review article, and argued that more abstract forms of reward evaluation (i.e., the constructs of "goal value" and "decision value") more heavily rely on mental simulation than the straightforward construct of "outcome value" (i.e., the value of a physical reward determined upon its passive receipt and consumption). For instance, studies like the one by Plassmann et al. (2007), which was not included in the present meta-analysis because it assessed reward-related activation during active decisions in a BDM auction, found that activity in the mOFC/VMPFC reflected predicted reward value. When one compares rewards from different modalities [like in the in a BDM auction] or weighs expected benefits with anticipated costs (like weighing expected reward magnitude with the temporal delay to the reward), the capacity of mental simulation of a potential value supposedly is a necessary prerequisite to derive at a conclusive decision (Peters & Büchel, 2010). We would extend this deduction by suggesting that rather passive forms of anticipatory reward processing should also recruit the mOFC/VMPFC if subjects are given time to think during the delay or if the predicted outcome is already highly certain during anticipation. The studies that assessed passive reward anticipation, but failed to find increased activation in the mOFC/VMPFC during the anticipation of different reward magnitudes often used experimental designs with shorter delays and/or uncertain reward (e.g., the MID-task by Knutson, Westdorp, Kaiser, & Hommer (2000), in which the individual response speed determined the reward outcome, which resulted in a factual reward in only 60% of trials). This may have precluded a consistent mental simulation of reward magnitude during the anticipatory period. Finally, it is also possible that these anticipatory cues themselves did not function as strong conditioned reinforcers and thus did not activate the mOFC/VMPFC. A large proportion of previous studies used secondary reinforcers as outcomes (money), and if primary reinforcers were used, they were only provided in relatively small amounts like gushes of juice (see also Table 2). Consequently it is highly likely that these outcomes represented conditioned reinforcers, which might have triggered some kind of decision-related simulations (e.g., upon receipt of a small amount of juice, participants might have considered purchasing a bottle of the juice later that day, or upon receipt of money, they might have deliberated what they will subsequently buy with their earnings) and thus eventually activated the mOFC/VMPFC. Of course, future studies have to carefully test these assumptions and further have to examine, whether passive anticipatory or decision-related activation in the mOFC/VMPFC may depend on factors like anticipated reward (un)certainty or the length of delay to reward. From the present results we can only infer that reward outcome and its magnitude, respectively, are consistently represented by the human mOFC/VMPFC.

4.3. Limitations of the present meta-analytic findings

There are several critical points and limitations that need to be taken into account when interpreting the present meta-analytic findings. First of all, the absence of any concordant orbitofrontal activity (also not in lateral and caudal subregions of the OFC) in the anticipation phase to some extent conflicts with previous results from single neuron and ensemble recordings in non-human primates (e.g., Roesch & Olson, 2007) and rats (e.g., Miyazaki, Miyazaki, & Matsumoto, 2004; van Duuren, Lankelma, & Pennartz, 2008), which demonstrated a quite consistent involvement of the OFC in passive reward expectancy. This was in so far surprising as reward processing is a rather basic process that should be expected to be strongly conserved across species. Therefore the important question arises whether conventional fMRI is an appropriate method to assess the role of the mOFC in humans? The problem of increased signal-dropout, geometric distortion and susceptibility artifacts in cortices near air-filled sinuses is well known when using EPI at higher magnetic field strengths, which led to the development of specific EPI sequences to maximize the signal in the human OFC (see Kringelbach & Rolls, 2004). Given the fact that most of the neuroimaging studies included in the present meta-analyses failed to use optimized acquisition sequences like coronal slicing and given the smaller number of studies that assessed passive reward expectancy in comparison to outcome processing one cannot be sure that a lack of medial orbitofrontal activation during anticipation is not simply a result of these artifacts. In order to resolve this open issue and to minimize the differential influence of susceptibility artifacts on the two phases, we performed additional meta-analyses, which used only the subset of studies that assessed reward activation in both the anticipatory and the outcome phase. These validation analyses confirmed the preferential involvement of the mOFC/VMPFC in outcome processing, which to some extent argues against the possible interference by study-specific susceptibility artifacts. Further, we cannot rule out that other parts of the OFC (e.g., more lateral or caudal parts) may have been involved in passive reward expectancy, but only for certain reward modalities. In fact, information from different reward modalities (e.g., taste, smell, vision) initially arrives at anatomically distinct subregions of the OFC (Carmichael & Price, 1995) before it is further projected and integrated by medial orbitofrontal parts to guide behavioral choice (Öngür & Price, 2000). For this reason, it may also be possible that diverse parts of the OFC initially coded the expected value and the anticipated magnitude of upcoming rewards in a modality-specific way (e.g., Rolls, 1997). Since the OFC is a much larger region than the vSTR this could also explain the absence of regional concordance in the OFC in the meta-analysis of the passive anticipation phase. Future studies have to further assess in detail, if the present meta-analytic findings from the anticipatory phase were biased towards the vSTR, because the coding of expected reward magnitude in the OFC is topologically organized according to sensory modality.

Moreover, the present meta-analyses were restricted to a quite homogeneous database of studies that assessed the neural representation of reward magnitude. From this it follows that the identified regions of concordance represented the cognitive process inherent to the passive perception of "more versus less", but not to the active decision for or against a bigger or smaller reward. The present results are therefore not intended to imply that the passive evaluation of reward magnitude and the representation of outcome value is the only function of the vSTR and the mOFC/VMPFC in the context of reward and motivation. In fact, passive magnitude processing may only be one specific aspect of reward valuation. It has been suggested that in particular the mOFC/VMPFC may also participate in higher-order active evaluation processes and decision making allowing humans to way expected decision costs and benefits to guide adaptive, context-appropriate behavior during

reward anticipation (see Peters & Büchel, 2010 for overview). The vSTR and other parts of the OFC may further represent relative reward value that can be flexibly adjusted to the organism's current needs or preferences (e.g., Cromwell, Hassani, & Schultz, 2005; Grabenhorst & Rolls, 2009; Tremblay & Schultz, 1999). One could even imagine that additional regions like the caudate nucleus may contribute in active decision-making that is modulated by anticipated reward magnitude (e.g. Sharot, De Martino, & Dolan, 2009). Future meta-analyses and neuroimaging studies have to further concern themselves with these additional questions.

5. Conclusions

Taken together, the present meta-analytic findings demonstrate the important role of the human vSTR and the mOFC/VMPFC in the representation of reward during its passive prediction and consumption, and highlight the complementary functions of these brain regions that have close anatomical connections. In particular, our data underscore that different reward sizes (i.e., reward magnitude) may be represented by the vSTR during both passive anticipation and receipt of reward, while the mOFC/VMPFC, in the restricted context of passive reward tasks, apparently processes reward magnitude only during reward consumption. A consummatory reward response of the vSTR was found to be most pronounced in studies with maximal reward uncertainty. Conversely, in the mOFC/VMPFC outcome-related activation was independent of reward uncertainty, but rather appeared to depend on the physical presence of reward.

References

Abe, H., & Lee, D. (2011). Distributed coding of actual and hypothetical outcomes in the orbital and dorsolateral prefrontal cortex. *Neuron*, *70*, 731–741.

Abler, B., Herrnberger, B., Grön, G., & Spitzer, M. (2009). From uncertainty to reward: BOLD characteristics differentiate signaling pathways. *BMC Neuroscience*, *10*, 154.

Adcock, R. A., Thangavel, A., Whitfield-Gabrieli, S., Knutson, B., & Gabrieli, J. D. E. (2006). Reward-motivated learning: Mesolimbic activation precedes memory formation. *Neuron*, *50*, 507–517.

Aharon, I., Etcoff, N., Ariely, D., Chabris, C. F., O'Connor, E., & Breiter, H. C. (2001). Beautiful faces have variable reward value: fMRI and behavioral evidence. *Neuron*, *32*, 537–551.

Akitsuki, Y., Sugiura, M., Watanabe, J., Yamashita, K., Sassa, Y., Awata, S., et al. (2003). Context-dependent cortical activation in response to financial reward and penalty: An event-related fMRI study. *Neuroimage*, *19*, 1674–1685.

Bar, M. (2009). The proactive brain: Memory for predictions. *Philosophical Transactions of the Royal Society London B Biological Science*, *364*, 1235–1243.

Berns, G. S., McClure, S. M., Pagnoni, G., & Montague, P. R. (2001). Predictability modulates human brain response to reward. *Journal of Neuroscience*, *21*, 2793–2798.

Bray, S., & O'Doherty, J. (2007). Neural coding of reward-prediction error signals during classical conditioning with attractive faces. *Journal of Neurophysiology*, *97*, 3036–3045.

Bray, S., Shimojo, S., & O'Doherty, J. P. (2010). Human medial orbitofrontal cortex is recruited during experience of imagined and real rewards. *Journal of Neurophysiology*, *103*, 2506–2512.

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.

Carmichael, S. T., & Price, J. L. (1995). Limbic connections of the orbital and medial prefrontal cortex in macaque monkeys. *Journal of Comparative Neurology*, *363*, 615–641.

Carter, R. M., Macinnes, J. J., Huettel, S. A., & Adcock, R. A. (2009). Activation in the VTA and nucleus accumbens increases in anticipation of both gains and losses. *Frontiers in Behavioral Neuroscience*, *3*, 21.

Cavada, C., Compañy, T., Tejedor, J., Cruz-Rizzolo, R. J., & Reinoso-Suárez, F. (2000). The anatomical connections of the macaque monkey orbitofrontal cortex. A review. *Cerebral Cortex*, *10*, 220–242.

Christakou, A., Brammer, M., Giampietro, V., & Rubia, K. (2009). Right ventromedial and dorsolateral prefrontal cortices mediate adaptive decisions under ambiguity by integrating choice utility and outcome evaluation. *Journal of Neuroscience*, *29*, 11020–11028.

Cloutier, J., Heatherton, T. F., Whalen, P. J., & Kelley, W. M. (2008). Are attractive people rewarding? Sex differences in the neural substrates of facial attractiveness. *Journal of Cognitive Neuroscience*, *20*, 941–951.

Cohen, M. X., Young, J., Baek, J. M., Kessler, C., & Ranganath, C. (2005). Individual differences in extraversion and dopamine genetics predict neural reward responses. *Brain Research. Cognitive Brain Research*, *25*, 851–861.

Collier, G. H. (1982). Determinants of choice. *Nebraska Symposium on Motivation*, *29*, 69–127.

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*, 1255L 62.

Cox, S. M. L., Andrade, A., & Johnsrude, I. S. (2005). Learning to like: A role for human orbitofrontal cortex in conditioned reward. *Journal of Neuroscience*, *25*, 2733–2740.

Cromwell, H. C., & Schultz, W. (2003). Effects of expectations for different reward magnitudes on neuronal activity in primate striatum. *Journal of Neurophysiology*, *89*, 2823–2838.

Cromwell, H. C., Hassani, O. K., & Schultz, W. (2005). Relative reward processing in primate striatum. *Experimental Brain Research*, *162*, 520–525.

Croxson, P. L., Walton, M. E., O'Reilly, J. X., Behrens, T. E. J., & Rushworth, M. F. S. (2009). Effort-based cost-benefit valuation and the human brain. *Journal of Neuroscience*, *29*, 4531–4541.

De Araujo, I. E. T., Kringelbach, M. L., Rolls, E. T., & McGlone, F. (2003). Human cortical responses to water in the mouth, and the effects of thirst. *Journal of Neurophysiology*, *90*, 1865–1876.

De Greck, M., Rotte, M., Paus, R., Moritz, D., Thiemann, R., Proesch, U., et al. (2008). Is our self based on reward? Self-relatedness recruits neural activity in the reward system. *Neuroimage*, *39*, 2066–2075.

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. *Cogn Affect Behav Neurosci.*, *84*, 3072–3077.

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. *Cogn Affect Behav Neurosci.*, *3*, 27–38.

Diekhof, E. K., Kipshagen, H. E., Falkai, P., Dechent, P., Baudewig, J., & Gruber, O. (2011). The power of imagination – How anticipatory mental imagery alters perceptual processing of fearful facial expressions. *Neuroimage*, *54*, 1703–1714.

Diekhof, E. K., Geier, K., Falkai, P., & Gruber, O. (2011). Fear is only as deep as the mind allows. A coordinate-based meta-analysis of neuroimaging studies on the regulation of negative affect. *Neuroimage*, *58*, 275–285.

Draganski, B., Kherif, F., Klöppel, S., Cook, P. A., Alexander, D. C., Parker, G. J., et al. (2008). Evidence for segregated and integrative connectivity patterns in the human basal ganglia. *Journal of Neuroscience*, *28*, 7143–7152.

Dreher, J. C., Kohn, P., & Berman, K. F. (2006). Neural coding of distinct statistical properties of reward information in humans. *Cerebral Cortex*, *16*, 561–573.

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. *Human Brain Mapping*, *30*, 2907–2926.

Eickhoff, S. B., Bzdok, D., Laird, A. R., Roski, C., Caspers, S., Zilles, K., et al. (2011). Co-activation patterns distinguish cortical modules, their connectivity and functional differentiation. *Neuroimage*, *57*, 938–949.

Elliott, R., Friston, K. J., & Dolan, R. J. (2000). Dissociable neural responses in human reward systems. *Journal of Neuroscience*, *20*, 6159–6165.

Elliott, R., Newman, J. L., Longe, O. A., & Deakin, J. F. W. (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.

Elliott, R., Newman, J. L., Longe, O. A., & Deakin, J. F. W. (2004). Instrumental responding for rewards is associated with enhanced neural response in subcortical reward systems. *Neuroimage*, *21*, 984–990.

Ernst, M., Nelson, E. E., McClure, E. B., Monk, C. S., Munson, S., Eshel, N., et al. (2004). Choice selection and reward anticipation: An fMRI study. *Neuropsychologia*, *42*, 1585–1597.

Flaherty, C. F., & Mitchall, C. (1999). Absolute and relative rewarding properties of fructose, glucose and saccharin mixtures as reflected in anticipatory contrast. *Physiology and Behavior*, *66*, 841–853.

Friebel, U., Eickhoff, S. B., & Lotze, M. (2011). Coordinate-based meta-analysis of experimentally induced and chronic persistent neuropathic pain. *Neuroimage*, *58*, 1070–1080.

Fujiwara, J., Tobler, P. N., Taira, M., Iijima, T., & Tsutsui, K. I. (2009). Segregated and integrated coding of reward and punishment in the cingulated cortex. *Journal of Neurophysiology*, *101*, 3284–3293.

Galvan, A., Hare, T. A., Davidson, M., Spicer, J., Glover, G., & Casey, B. J. (2005). The role of ventral frontostriatal circuitry in reward-based learning in humans. *Journal of Neuroscience*, *25*, 8650–8656.

Gottfried, J. A., O'Doherty, J., & Dolan, R. J. (2003). Encoding predictive reward value in human amygdala and orbitofrontal cortex. *Science*, *301*, 1104–1107.

Grabenhorst, F., & Rolls, E. T. (2009). Different representations of relative and absolute subjective value in the human brain. *Neuroimage*, *48*, 258–268.

Grabenhorst, F., & Rolls, E. T. (2011). Value, pleasure and choice in the ventral prefrontal cortex. *Trends in Cognitive Sciences*, *15*, 56–67.

Grabenhorst, F., Rolls, E. T., & Bilderbeck, A. (2008). How cognition modulates affective responses to taste and flavor: Top-down influences on the orbitofrontal and pregenual cingulate cortices. *Cerebral Cortex*, *18*, 1549–1559.

Grabenhorst, F., Rolls, E. T., Parris, B. A., & d'Souza, A. A. (2010). How the brain represents the reward value of fat in the mouth. *Cerebral Cortex*, *20*, 1082–1091.

Haber, S. N., & McFarland, N. R. (1999). The concept of the ventral striatum in nonhuman primates. *Annals of the New York Academy of Sciences*, *877*, 33–48.

Haber, S. N., & Knutson, B. (2009). The reward circuit: Linking primate anatomy and human imaging. *Neuropsychopharmacology*, *35*, 4–26.
Haber, S. N., & McFarland, N. R. (2000). The concept of the ventral striatum in non-human primates. *Annals of the New York Academy of Sciences*, *877*, 33–48.
Haber, S. N., Kim, K. S., Mailly, P., & Calzavara, R. (2006). Reward-related cortical inputs define a large striatal region in primates that interface with associative cortical connections, providing a substrate for incentive-based learning. *Journal of Neuroscience*, *26*, 8368–8376.
Hare, T. A., O'Doherty, J., Camerer, C. F., Schultz, W., & Rangel, A. (2008). Dissociation the role of the orbitofrontal cortex and the striatum in the computation of goal values and prediction errors. *Journal of Neuroscience*, *28*, 5623–5630.
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.
Kable, J. W., & Glimcher, P. W. (2009). The neurobiology of decision: Consensus and controversy. *Neuron*, *63*, 733–745.
Kampe, K. K., Frith, C. D., Dolan, R. J., & Frith, U. (2001). Reward value of attractiveness and gaze. *Nature*, *413*, 589.
Killgore, W. D. S., Young, A. D., Femia, L. A., Bogorodzki, P., Rogowska, J., & Yurgelun-Todd, D. (2003). Cortical and limbic activation during viewing of high- versus low-calorie foods. *Neuroimage*, *19*, 1381–1394.
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.
Kim, H., Shimojo, S., & O'Doherty, J. P. (2010). Overlapping responses for the expectation of juice and money rewards in human ventromedial prefrontal cortex. *Cerebral Cortex*, *21*, 769–776.
Kirsch, P., Schienle, A., Stark, R., Sammer, G., Blecker, C., Walter, B., et al. (2003). Anticipation of reward in a nonaversive differential conditioning paradigm and the brain reward system: An event-related fMRI study. *Neuroimage*, *20*, 1086–1095.
Knutson, B., Westdorp, A., Kaiser, E., & Hommer, D. (2000). FMRI visualization of brain activity during a monetary incentive delay task. *Neuroimage*, *12*, 20–27.
Knutson, B., Adams, C. M., Fong, G. W., & Hommer, D. (2001). Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *Journal of Neuroscience*, *21*, 159–164.
Knutson, B., Fong, G. W., Adams, C. M., Varner, J. L., & Hommer, D. (2001). 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 tracks monetarily rewarding outcomes: Characterization with rapid event-related fMRI. *Neuroimage*, *18*, 263–272.
Knutson, B., Taylor, J., Kaufman, M., Peterson, R., & Glover, G. (2005). Distributed neural representation of expected value. *Journal of Neuroscience*, *25*, 4806–4812.
Koeneke, S., Pedroni, A. F., Dieckmann, A., Bosch, V., & Jäncke, L. (2008). Individual preferences modulate incentive values: Evidence from functional MRI. *Behavior and Brain Function*, *4*, 55.
Kringelbach, M. L. (2005). The human orbitofrontal cortex: Linking reward to hedonic experience. *Nature Reviews Neuroscience*, *6*, 691–702.
Kringelbach, M. L., & Rolls, E. T. (2004). The functional neuroanatomy of the human orbitofrontal cortex: Evidence from neuroimaging and neuropsychology. *Progress in Neurobiology*, *72*, 341–372.
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. *Cerebral Cortex*, *13*, 1064–1071.
Laird, A. R., McMillan, K. M., Lancaster, J. L., Kochunov, P., Turkeltaub, P. E., Pardo, J. V., et al. (2005). A comparison of label-based review and ALE meta-analysis in the Stroop task. *Human Brain Mapping*, *25*, 6–21.
Laird, A. R., Fox, P. M., Price, C. J., Glahn, D. C., Uecker, A. M., Lancaster, J. L., et al. (2005). ALE meta-analysis: Controlling the false discovery rate and performing statistical contrasts. *Human Brain Mapping*, *25*, 155–164.
Lancaster, J. L., Tordesillas-Gutiérrez, D., Martinez, M., Salinas, F., Evans, A., Zilles, K., et al. (2007). Bias between MNI and Talairach coordinates analyzed using the ICBM-152 brain template. *Human Brain Mapping*, *28*, 1194–1205.
Lehéricy, S., Ducros, M., Van de Moortele, P. F., Francois, C., Thivard, L., Poupon, C., et al. (2004). Diffusion tensor fiber tracking shows distinct corticostriatal circuits in humans. *Annuals in Neurology*, *55*, 522–529.
McClure, S. M., Berns, G. S., & Montague, P. R. (2003). Temporal prediction errors in a passive learning task activate human striatum. *Neuron*, *38*, 339–346.
McClure, S. M., Daw, N. D., & Montague, P. R. (2003). A computational substrate for incentive salience. *Trends in Neurosciences*, *26*, 423–428.
McClure, S. M., York, M. K., & Montague, P. R. (2004). The neural substrates of reward processing in humans: The modern role of FMRI. *Neuroscientist*, *10*, 260–268.
McDannald, M. A., Lucantonio, F., Burke, K. A., Niv, Y., & Schoenbaum, G. (2011). Ventral striatum and orbitofrontal cortex are both required for model-based, but not model-free, reinforcement learning. *Journal of Neuroscience*, *31*, 2700–2705.
Miyazaki, K., Miyazaki, K. W., & Matsumoto, G. (2004). Different representation of forthcoming reward in nucleus accumbens and medial prefrontal cortex. *Neuroreport*, *15*, 721–726.
Moulton, S. T., & Kosslyn, S. M. (2009). Imagining predictions: Mental imagery as mental emulation. *Philosophical Transactions of the Royal Society of London B Biological Science*, *364*, 1273–1280.
Nieuwenhuis, S., Heslenfeld, D. J., von Geusau, N. J., Mars, R. B., Holroyd, C. B., & Yeung, N. (2005). Activity in human reward-sensitive brain areas is strongly context dependent. *Neuroimage*, *25*, 1302–1309.
Niv, Y., & Schoenbaum, G. (2008). Dialogues on prediction errors. *Trends in Cognitive Sciences*, *12*, 265–272.
O'Doherty, J. P. (2004). Reward representations and reward-related learning in the human brain: Insights from neuroimaging. *Current Opinion in Neurobiology*, *14*, 769–776.
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.
O'Doherty, J., 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., Winston, J., Critchley, H., Perrett, D., Burt, D. M., & Dolan, R. J. (2003). Beauty in a smile: The role of medial orbitofrontal cortex in facial attractiveness. *Neuropsychologia*, *41*, 147–155.
O'Doherty, J., Dayan, P., Friston, K., Critchley, H., & Dolan, R. (2003). Temporal difference models and reward-related learning in the human brain. *Neuron*, *28*, 329–337.
O'Doherty, J., Critchley, H., Deichmann, R., & Dolan, R. J. (2003). Dissociating valence of outcome from behavioral control in human orbital and ventral prefrontal cortices. *Journal of Neuroscience*, *23*, 7931–7939.
Pagnoni, G., Zink, C. F., Montague, P. R., & Berns, G. S. (2002). Activity in human ventral striatum locked to errors of reward prediction. *Nature Neuroscience*, *5*, 97–98.
Pavlov, I. P. (1927). In G. V. Anrep (Translator, Ed.), *Conditioned reflexes: An investigation of the physiological activity of the cerebral cortex*. London: Oxford University Press.
Pessiglione, M., Schmidt, L., Draganski, B., Kalisch, R., Lau, H., Dolan, R. J., et al. (2007). How the brain translates money into force: A neuroimaging study of subliminal motivation. *Science*, *316*, 904–906.
Peters, J., & Büchel, C. (2010). Neural representations of subjective reward value. *Behavioural Brain Research*, *213*, 135–141.
Plassmann, H., O'Doherty, J., & Rangel, A. (2007). Orbitofrontal cortex encodes willingness to pay in everyday economic transactions. *Journal of Neuroscience*, *27*, 9984–9988.
Plassmann, H., O'Doherty, J., Shiv, B., & Rangel, A. (2008). Marketing actions can modulate neural representations of experienced pleasantness. *Proceedings of the National Academy of Sciences U S A*, *105*, 1050–1054.
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.
Pochon, J. B., Levy, R., Fossati, P., Lehericy, S., Poline, J. B., Pillon, B., et al. (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.
Rademacher, L., Krach, S., Kohls, G., Irmak, A., Gründer, G., & Spreckelmeyer, K. N. (2010). Dissociation of neural networks for anticipation and consumption of monetary and social rewards. *Neuroimage*, *49*, 3276–3285.
Roesch, M. R., & Olson, C. R. (2007). Neuronal activity related to anticipated reward in frontal cortex: Does it represent value or reflect motivation? *Annals of the New York Academy of Sciences*, *1121*, 431–446.
Rogers, R. D., Ramnani, N., Mackay, C., Wilson, J. L., Jezzard, P., Carter, C. S., et al. (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.
Rolls, E. T. (1997). Taste and olfactory processing in the brain and its relation to the control of eating. *Critical Reviews in Neurobiology*, *11*, 263–287.
Rolls, E. T. (2004). The functions of the orbitofrontal cortex. *Brain and Cognition*, *55*, 11–29.
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.
Rothemund, Y., Preuschhof, C., Bohner, G., Bauknecht, H. C., Klingebiel, R., Flor, H., et al. (2007). Differential activation of the dorsal striatum by high-calorie visual food stimuli in obese individuals. *Neuroimage*, *37*, 410–421.
Schienle, A., Schäfer, A., Hermann, A., & Vaitl, D. (2009). Binge-eating disorder: Reward sensitivity and brain activation images of food. *Biological Psychiatry*, *65*, 654–661.
Schott, B. J., Niehaus, L., Wittmann, B. C., Schütze, H., Seidenbecher, C. I., Heinze, H. J., et al. (2007). Ageing and early-stage Parkinson's disease affect separable neural mechanisms of mesolimbic reward processing. *Brain*, *130*, 2412–2424.
Schultz, W. (2002). Getting formal with dopamine and reward. *Neuron*, *36*, 241–263.
Schultz, W. (2006). Behavioral theories and the neurophysiology of reward. *Annual Reviews in Psychology*, *57*, 87–115.
Schultz, W., Dayan, P., & Montague, P. R. (1997). A neural substrate of prediction and reward. *Science*, *275*, 1593–1599.
Schultz, W., Tremblay, L., & Hollerman, J. R. (2000). Reward processing in primate orbitofrontal cortex and basal ganglia. *Cerebral Cortex*, *10*, 272–284.
Sescousse, G., Redouté, J., & Dreher, J. C. (2010). The architecture of reward value coding in the human orbitofrontal cortex. *Journal of Neuroscience*, *30*, 13095–13104.
Sharot, T., De Martino, B., & Dolan, R. J. (2009). How choice reveals and shapes expected hedonic outcome. *Journal of Neuroscience*, *29*, 3760–3765.
Small, D. M., Zatorre, R. J., Dagher, A., Evans, A. C., & Jones-Gotman, M. (2001). Changes in brain activity related to eating chocolate: From pleasure to aversion. *Brain*, *124*, 1720–1733.
Smith, B. W., Mitchell, D. G., Hardin, M. G., Jazbec, S., Fridberg, D., Blair, R. J., et al. (2009). Neural substrates of reward magnitude, probability,

and risk during a wheel of fortune decision-making task. *Neuroimage*, *44*, 600–609.
Smith, D. V., Hayden, B. Y., Truong, T. K., Song, A. W., Platt, M. L., & Huettel, S. A. (2010). Distinct value signals in anterior and posterior ventromedial prefrontal cortex. *Journal of Neuroscience*, *30*, 2490–2495.
Spreckelmeyer, K. N., Krach, S., Kohls, G., Rademacher, L., Irmak, A., Konrad, K., et al. (2009). Anticipation of monetary and social reward differently activates mesolimbic brain structures in men and women. *Scanning*, *4*, 158–165.
Tobler, P. N., Fiorillo, C. D., & Schultz, W. (2005). Adaptive coding of reward value by dopamine neurons. *Science*, *307*, 1642–1645.
Tobler, P. N., O'Doherty, J. P., Dolan, R. J., & Schultz, W. (2006). Human neural learning depends on reward prediction errors in the blocking paradigm. *Journal of Neurophysiology*, *95*, 301–310.
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.
Tremblay, L., & Schultz, W. (1999). Relative reward preference in primate orbitofrontal cortex. *Nature*, *398*, 704–708.
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.
Turkeltaub, P. E., Eickhoff, S. E., Laird, A. R., Fox, M., Wiener, M., & Fox, P. (2012). Minimizing within-experiment and within-group effects in activation likelihood estimation meta-analyses. *Human Brain Mapping*, *33*, 1–13.
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. *Cogn Affect Behav Neurosci.*, *7*, 337–346.
van Duuren, E., Lankelma, J., & Pennartz, C. M. (2008). Population coding of reward magnitude in the orbitofrontal cortex of the rat. *Journal of Neuroscience*, *28*, 8590–8603.
Winston, J. S., O'Doherty, J., Kilner, J. M., Perrett, D. I., & Dolan, R. J. (2007). Brain systems for assessing facial attractiveness. *Neuropsychologia*, *45*, 195–206.
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.
Yacubian, J., Gläscher, J., Schroeder, K., Sommer, T., Braus, D. F., & Büchel, 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.
Yacubian, J., Sommer, T., Schroeder, K., Gläscher, J., Braus, D. F., & Büchel, C. (2007). Subregions of the ventral striatum show preferential coding of reward magnitude and probability. *Neuroimage*, *38*, 557–563.
Zalla, T., Koechlin, E., Pietrini, P., Basso, G., Aquino, P., Sirigu, A., et al. (2000). Differential amygdala responses to winning and losing: A functional magnetic resonance imaging study in humans. *European Journal of Neuroscience*, *12*, 1764–1770.
Öngür, D., & Price, J. L. (2000). The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans. *Cerebral Cortex*, *10*, 206–219.