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Shared and distinct neural activity during anticipation and outcome of win and loss: A meta-analysis of the monetary incentive delay task

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Abstract

Reward and punishment motivate decision making and behavioral changes. Numerous studies have examined regional activities during anticipation and outcome of win and loss in the monetary incentive delay task (MIDT). However, the great majority of studies reported findings of anticipation or outcome and of win or loss alone. It remains unclear how the neural correlates share and differentiate amongst these processes. We conducted an Activation Likelihood Estimation meta-analysis of 81 studies of the MIDT (5,864 subjects), including 24 published since the most recent meta-analysis, to identify and, with conjunction and subtraction, contrast regional responses to win anticipation, loss anticipation, win outcome, and loss outcome. Win and loss anticipation engaged a shared network of bilateral anterior insula (AI), striatum, thalamus, supplementary motor area (SMA), and precentral gyrus. Win and loss outcomes did not share regional activities. Win and loss outcome each engaged higher activity in medial orbitofrontal cortex (mOFC) and dorsal anterior cingulate cortex. Bilateral striatum and right occipital cortex responded to both anticipation and outcome of win, and right AI to both phases of loss. Win anticipation vs. outcome engaged higher activity in bilateral AI, striatum, SMA and precentral gyrus and right thalamus, and lower activity in bilateral mOFC and posterior cingulate cortex as well as right inferior frontal and angular gyri. Loss anticipation relative to outcome involved higher activity in bilateral striatum and left AI. These findings collectively suggest shared and distinct regional responses during monetary wins and losses. Delineating the neural correlates

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Declaration of Competing Interest

None.

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of these component processes may facilitate empirical research of motivated behaviors and dysfunctional approach and avoidance in psychopathology.

Keywords

Meta-analysis; Monetary incentive delay task (MIDT); Reward; Punishment; fMRI

1. Introduction

Reward- and punishment-driven decision making is fundamental to adaptive behaviors (Jean-Richard-Dit-Bressel et al., 2018; O'Doherty et al., 2017). Dysfunctional reward seeking and/or punishment avoidance have been implicated in many neuropsychiatric disorders (Whitton et al., 2015). For instance, patients with depression showed lower sensitivity to rewards, impaired reward learning, and higher sensitivity to negative feedbacks (Admon and Pizzagalli, 2015; Eshel and Roiser, 2010). In contrast, antisocial personality disorder is characterized by elevated reward seeking and blunted punishment avoidance (Raine, 2018). Investigators have developed a variety of behavioral paradigms, including passive exposure to valenced stimuli, instrumental learning and reward-related decision-making (Richards et al., 2013), as well as the monetary incentive delay task (MIDT) to study the neural bases of reward/punishment processing in health and illness.

As one of the most widely used paradigms, the MIDT allows investigations to distinguish between win and loss as well as between phases of anticipation and consummation/outcome (Balodis and Potenza, 2015; Knutson et al., 2001). For example, as compared to the control group, patients with major depressive disorder showed lower activation in the ventral striatum during the win vs. neutral outcomes in the MIDT (Carl et al., 2016). Adults with attention-deficit/hyperactivity disorder vs. healthy subjects showed lower activation in the ventral striatum during anticipation of win vs. neutral outcomes, but elevated activation in the orbitofrontal cortex (OFC) in response to win vs. neutral outcomes (Strohle et al., 2008). In healthy individuals, the striatum and thalamus showed higher activation during anticipation of win vs. neutral outcomes (Dhingra et al., 2020; Dhingra et al., 2021; Knutson et al., 2001). The medial OFC (mOFC), on the other hand, showed higher responses to win vs. neutral outcomes (Knutson et al., 2001; Treadway et al., 2013). Anticipation of loss vs. neutral outcomes engaged the ventral striatum, lateral thalamus, supplementary motor cortex, and insula (Bjork et al., 2010; Wu et al., 2014). Loss vs. neutral outcomes involved higher activations in the insula, inferior, middle, and superior frontal gyri, and superior parietal lobule (Maresh et al., 2014; Murray et al., 2020). Thus, previous studies have suggested potentially shared and distinct responses to the anticipation and outcome of wins and losses in the MIDT. Systematic reviews and meta-analyses of the studies can help in identifying the shared and distinct correlates.

A few meta-analyses of the MIDT have been published to investigate regional activations associated with win and loss processing. These meta-analyses have largely focused on the anticipation phase, likely because the great majority of fMRI studies reported solely the peak coordinates of win and loss anticipation in whole-brain analyses. An earlier meta-

analysis demonstrated higher activation in the nucleus accumbens during win relative to loss anticipation and in the anterior insula during both win and loss (vs. nil) anticipation (Knutson and Greer, 2008). A more recent meta-analysis of 35 whole-brain (445 subjects) and 13 region-of-interest (ROI; 254 subjects) studies highlighted shared response to loss anticipation and outcome (Dugre et al., 2018). Specifically, bilateral striatum, anterior insula, anterior cingulate cortex (ACC), and amygdala showed higher likelihood of activation during both loss anticipation and outcome. Oldham et al. (2018) identified regional responses to anticipation of wins (49 studies; 1,082 participants) and losses (32 studies; 681 participants), as well as to outcome of wins (22 studies; 691 participants). Specifically, the striatum, insula, amygdala, and thalamus showed higher activation when participants anticipated wins or losses (vs. nil), and the mOFC were recruited only during win outcomes. Notably, none of the meta-analyses have systematically distinguished the shared or distinct correlates of valence and processing stage, namely win anticipation, loss anticipation, win outcome, and loss outcome. Distinguishing win and loss processing is clearly instrumental as the regional activities dictate opposing actions. Distinguishing anticipation and outcome phases of regional activities is also critical, with each reflecting the propensity to act and feedback about the action. These distinct component processes are fundamental to psychological models of adaptive learning.

To address this gap in research, we took advantage of a total of 24 additional studies published since the most recent and comprehensive meta-analysis of the MIDT (Oldham et al., 2018). We performed Activation Likelihood Estimation to investigate the shared and distinct neural correlates underlying anticipation and outcome phases of win and loss processing and employed conjunction and subtraction analyses to identify regional activities that may overlap or differ between events of different valences and/or processing stages. We also performed the seed-based d-mapping to investigate the potential influences of confounding factors, including age, sex ratio, duration of anticipation, win/loss magnitude, and motion exclusion criteria in data preprocessing.

2. Methods

2.1. Literature search

Following the guidelines of “Preferred reporting items for systematic reviews and meta-analyses (PRISMA)”, we searched the literature on PubMed for imaging studies of MIDT with the key words “Monetary Incentive Delay Task” and “fMRI” and “NOT Review” and “NOT Meta-analysis”. We identified 338 studies on March 8, 2022. We also searched on Google Scholar and PsycNet (https://psycnet.apa.org/) using the same key words but found no new studies. A flow-chart for the procedure to arrive at the final sample for meta-analysis is shown in Fig. 1. Only non-duplicate articles in English language (n = 330) were chosen for data mining if they included the following contrasts: anticipation of win vs. neutral (“win anticipation” hereafter), anticipation of loss vs. neutral (“loss anticipation”), win vs. neutral outcome (“win outcome”), or loss vs. neutral outcome (“loss outcome”). Patient studies were included if they contained data of healthy individuals. Likewise, medication or behavioral treatment studies were included if data of pre-treatment scans in healthy controls were available.

Studies (n = 35) were removed based on the exclusion criteria, including life-time diagnosis of schizophrenia, depressive disorder, bipolar or manic disorder, psychotic episodes, obsessive-compulsive disorder, or post-traumatic stress disorder; treatment for mental disorders in the past 12 months, or use of psychotropic medication; history of or current neurological disorders, major medical conditions, substance use, or brain trauma. We did not include studies (n = 63) that used ROI analyses, because the ALE algorithm assumes that the activation foci are obtained through a whole-brain analysis (Muller et al., 2018). One hundred and fifty-one studies were excluded because the coordinates of none of the four contrasts were reported. If rewards with different magnitudes (e.g., $1 and $5) were included in the MIDT, the coordinates for the contrasts with the rewards combined (if available) or with the highest reward were used. A final pool of 81 studies of healthy volunteers were included in the current meta-analysis. A complete list of the studies is shown in Supplementary Table S1, where we described the sample size, sex ratio, age, contrast availability, as well as scan and task parameters, including multi-band, duration of anticipation, win/loss magnitude, average success rate, and availability of whole-brain statistical maps. Among the 81 studies, 79, 42, 38, and 14 reported peak coordinates (foci) of win anticipation, loss anticipation, win outcome, and loss outcome, respectively. We converted all foci that were reported in Talairach space to MNI space using the Lancaster transformation (Lancaster et al., 2007).

2.2. Activation likelihood estimation (ALE)

We used the GingerALE software package (version 3.0.2, http://brainmap.org/ale/) to perform the ALE meta-analyses on coordinates in MNI space (Eickhoff et al., 2012; Eickhoff et al., 2009; Turkeltaub et al., 2012). The non-additive algorithm was used to reduce the bias of any single experiment (Turkeltaub et al., 2012). The ALE meta-analysis followed four main steps: computation of ALE scores, establishing a null distribution for statistical testing, thresholding, and cluster statistics, as described in detail in the GingerALE Manual (http://brainmap.org/ale/manual.pdf).

We performed the ALE single dataset analysis of each contrast - win anticipation, loss anticipation, win outcome, and loss outcome, using a cluster-forming threshold of voxel-level $p < 0.001$, uncorrected. Briefly, the non-additive ALE method was used to create a modelled activation (MA) map for each experiment (Turkeltaub et al., 2012) and a statistical whole-brain map was produced by combining all MA maps, where each voxel has an ALE value indicating its probability of activation. The resulting supra-threshold clusters were compared to a null distribution of cluster sizes established by 1,000 permutations of the data, at a family-wise error(FWE) corrected threshold of $p < 0.05$. We also performed ALE conjunction and subtraction analyses each to identify regional activities shared between contrasts and distinct to individual contrasts. The conjunction was created using the voxel-wise minimum value of the input ALE images as calculated in the single dataset analysis and the results were evaluated with a cluster-forming threshold of $p < 0.001$ uncorrected and a cluster-level threshold of $p < 0.05$ FWE corrected. The subtraction analysis was performed by repeating the following procedure for 5,000 times (Eickhoff et al., 2011): 1) GingerALE created simulated data by pooling the foci datasets and randomly dividing them into two groups of the same size as the original data set; 2) an ALE score was calculated at

each voxel for each group; and 3) the difference between ALE scores was computed. The ALE values were collated across 5,000 permutations to yield an empirical null distribution for statistical inference. A *p*-value was assigned to each voxel based on how many times the difference in the null distribution exceeded the actual group difference. We applied a threshold of $p < 0.001$ uncorrected with a minimum cluster size of 100 mm^3 to identify differences between any two contrasts, with a *Z*-score indicating the size of the differences at each voxel.

Prior evidence suggests differences between adults and non-adults in neural activation during reward and punishment processing; however, the findings are not consistent (Silverman et al., 2015). In order to examine whether the two age groups involved similar regional activities during win and loss processing, we also performed ALE meta-analyses (single dataset, conjunction, and subtraction) for win anticipation, loss anticipation, win outcome, and loss outcome based on studies of adults and of non-adults separately. Further, in the typical MIDT, an automated adaptive timing algorithm is used to adjust target speed for neutral and incentive trials to maintain a success rate of approximately 66% throughout the experiment. However, some studies maintained a success rate ≥ 66% and others < 66% to meet specific research aims. An earlier study found that certainty about winning and losing may impact the regional processes (Cooper and Knutson, 2008). Thus, to determine whether the meta-analytic findings were influenced by the uncertainty, we grouped studies by the success rate and performed single ALE analyses separately for those with a rate ≥ 66% and < 66%, followed by conjunction and subtraction analyses. We evaluated these results with the same threshold as describe above.

2.3. Evaluation of publication bias

We performed a “Fail-Safe N (FSN)” analysis to evaluate potential publication bias (Acar et al., 2018). We used the *R* program to generate a list of null studies with no statistically significant activation, all with the number of peaks and sample size equal to those of individual studies included in the original meta-analysis. The coordinates of these peaks were randomly drawn from the mask used by the ALE algorithm. For each single dataset analysis (i.e., win anticipation, loss anticipation, win outcome, and loss outcome), we computed the minimum numbers of null studies required in the FSN analysis $-5k+10$ with k denoting the number of studies included in the original meta-analysis (Rosenthal, 1979). Specifically, at least 380, 200, 180, and 80 null studies were required for win anticipation, loss anticipation, win outcome, and loss outcome, respectively. We combined the original and these null studies and repeated the ALE meta-analyses. If the ALE findings remain significant, it means that results are sufficiently robust and are supported by at least the desired minimum of contributing studies. If adding a minimum of null studies alters the significant results of original ALE analyses, this indicates that meta-analytic results may not be robust when bias due to missing (noise) studies in the meta-analysis is present.

2.4. Seed-based d-mapping (SDM) analyses

Variability across studies in age, sex ratio, duration of anticipation, win/loss magnitude, and motion exclusion criteria in data preprocessing may confound the results. We performed meta-regressions using the SDM approach to examine whether and how these factors may

influence the findings. SDM uses reported peak coordinates to recreate, albeit to a limited extent, the original maps of each study (Radua and Mataix-Cols, 2009; Radua et al., 2010). A standard random-effect variance weighted meta-analysis for each voxel is then executed. To ensure that the confounding factors were not biasing the results, we ran the SDM meta-analyses both without and with the covariates included.

Specifically, the data were pre-processed, and the coordinates of cluster peaks were selected according to SDM inclusion criteria for each study. The lower and upper bounds of possible effect size images were estimated. The most likely effect size and its standard error were estimated, with imputations by adding noise to these estimations within the bounds. Each imputed dataset was meta-analyzed and the imputed meta-analyzed datasets were combined following Rubin's rules. Finally, subject images were recreated for a standard permutation test, in which the process was repeated for 1,000 times with each set of permuted images and the maximum statistic of the final image was saved; the distribution of these maxima was used to correct for FWE in multiple comparisons. Linear models were then estimated to explore the potential effects of covariates of interest. Subsequently, the meta-analytic mean was calculated. If any covariate showed significant effect in the linear models, the meta-analytic means would be re-calculated with the specific covariate(s) included. Correction for FWE was attained by running a subject-base permutation test for 1,000 times to achieve a distribution of the maximum statistic. This distribution was then used to threshold the meta-analysis images obtained in the mean calculations, resulting in a corrected p-value map. We applied a voxel-wise threshold of $p < 0.001$ FWE-corrected with a minimum cluster size of 100 voxels, with an *SDM*-Z scores indicating the size of activation at each voxel.

We assessed the heterogeneity of the findings, with higher values of I^2 statistic indicating greater heterogeneity. For each contrast we also evaluated publication bias with the Egger's tests for asymmetry in the funnel plots of the peak activation of the largest cluster (Egger et al., 1997). Specifically, we tested for small-study effect and excess significance. The former examined whether there was asymmetry in the funnel plot (i.e., larger effect size in smaller studies), suggesting that smaller studies were published only if large effect sizes were found. The latter examined whether the number of studies with statistically significant results was larger than expected, which could indicate that studies were only published if they found statistically significant results. Both heterogeneity and publication bias analyses were performed for the meta-analytic findings from the analyses without and with covariates.

3. Results

3.1. Single dataset analyses

The results of ALE analyses of individual contrasts are shown in Fig. 2. We found higher activation likelihood during win anticipation in bilateral midbrain regions (including red nucleus and superior colliculus), middle frontal gyri (MFG), supplementary motor area (SMA), anterior insula (AI), precentral gyri, occipital cortex (OC), thalamus, amygdala, and striatum (Fig. 2A). Loss anticipation showed greater activation likelihood in bilateral SMA, AI, precentral gyri, thalamus, and striatum, and right amygdala (Fig. 2B). Win outcome revealed clusters in bilateral mOFC, rostral anterior cingulate cortex (rACC), posterior

cingulate cortex (PCC), striatum, and OC, left superior frontal gyrus, and right inferior frontal gyrus (Fig. 2C). Loss outcome showed a large cluster in the AI extending to lateral posterior OFC, and temporal pole in the right hemisphere, and bilateral superior colliculus and dorsal ACC (Fig. 2D). The clusters are summarized in Supplementary Table S2.

The publication bias was evaluated for individual contrasts, with additional null studies included in the ALE analyses. The ALE maps evaluated at the same threshold (Supplementary Figure S1) showed similar but fewer clusters in comparison with the original meta-analyses except that there were no significant findings for win outcome. The clusters are summarized in Supplementary Table S5. The findings indicated that the results for win anticipation, loss anticipation, and loss outcome were robust whereas the results for win outcome were subject to publication bias.

3.2. Conjunction and subtraction analyses

As shown in Fig. 3A, win and loss anticipation shared activities in bilateral striatum, AI, precentral gyri, SMA, and thalamus. No clusters shared activities significantly between win and loss outcome. Win anticipation and outcome in conjunction showed clusters in bilateral striatum and right OC (Fig. 3C). Loss anticipation and outcome in conjunction involved a small cluster of activity in the right AI extending to lateral OFC (Fig. 3D). The clusters identified in conjunction analyses are summarized in Supplementary Table S3.

Win and loss anticipation showed no significant differences in activity. Win relative to loss outcome showed higher activation likelihood in bilateral mOFC (Fig. 4B). Loss relative to win outcome revealed no significant differences. Win anticipation vs. outcome showed higher activity in bilateral AI (but predominantly right AI), striatum, SMA, and precentral gyri, and right thalamus. Win outcome vs. anticipation, on the contrary, activated bilateral mOFC and PCC, as well as right inferior frontal and angular gyri (Fig. 4C). Loss anticipation relative to outcome involved bilateral striatum, and left AI, while loss outcome vs. anticipation showed no significant differences (Fig. 4D). The clusters identified in subtraction analyses are summarized in Supplementary Table S4.

3.3. Post-hoc ALE analyses

We performed post-hoc ALE analyses to investigate the age effects on the meta-analytic findings. Most studies included in the current meta-analysis are of adults (n = 66). Ten studies recruited subjects < 18 years and five recruited a mixed sample. Note that two of these five studies reported group results of adolescents and adults separately whereas the other three studies did not show results by age group. Overall, as compared to the findings with adult and non-adult studies combined, meta-analysis with adult studies only showed similar clusters (Supplementary Figures S2a, S3a, and S4; and Tables S6a), whereas non-adult studies showed key structures, including the striatum, AI, and ACC, but broadly much fewer and smaller clusters (Supplementary Figures S2b and S3b; and Tables S6b), which may result from the small number of studies included in each dataset/contrast.

In addition, we examined whether the meta-analytic results depended on the success rate over the MIDT experiment. Of the 81 studies included in meta-analyses, 50 showed higher average success rate (≥ 66%), 17 showed lower rate (< 66%), and 14 did not report success

rate. Overall, as compared to the findings with all studies combined, the findings with studies of higher success rate showed similar clusters (Supplementary Figures S5a, S6a, and S7a; and Tables S7a), and the studies of lower success rate showed the striatum, AI, and thalamus, but broadly much fewer and smaller clusters (Supplementary Figures S5b, S6b, and S7b; and Tables S7b), which again may result from the small number of studies.

3.4. SDM analyses

We performed SDM in meta-regressions of potential confounding factors, including age, sex ratio, duration of anticipation, win/loss magnitude, and motion exclusion criteria in data preprocessing. Without covariates, the meta-analytic findings of SDM (Supplementary Figure S8a and Table S8b) are largely comparable with ALE findings. Meta-regressions showed significant win/loss magnitude effects on win and loss anticipation; age, win/loss magnitude, anticipation duration, and motion criterion effects on win outcome; and sex ratio effects on loss outcome (Supplementary Table S8a). Therefore, we included these confounding factors as covariates for each contrast in post-hoc SDM analyses. The results remained largely unaltered (Supplementary Figure S8b and Table S8b).

For the findings of meta-analyses without covariates, the I^2 statistics showed small heterogeneity for win anticipation (4.67%), loss anticipation (5.66%), win outcome (0.28%), and loss outcome (1.05%). The funnel plots are shown in Supplementary Figure 9a. The results did not show asymmetry for win anticipation, win outcome, or loss outcome. Neither tests for small-study effect (bias ≤ 0.36; p's ≥ 0.173) or for excess of significance were significant (p's ≥ 0.890) for these contrasts, indicating no publication bias. For loss anticipation, the funnel plots showed some asymmetry, and the test for excess of significance was not significant, whereas the test for small-study effect was significant (bias = 1.08; p = 0.035), indicating that the findings may be biased since smaller studies were published with larger effect sizes.

We also tested heterogeneity and publication bias for the findings of meta-analyses with covariates. The I^2 statistics showed small heterogeneity for win anticipation (9.53%), loss anticipation (3.47%), win outcome (0.28%), and loss outcome (0.06%). The funnel plots did not show asymmetry for any contrast (Supplementary Figure 9b). Neither the tests for small-study effect (bias ≤ 0.25; p's ≥ 0.258) nor the tests for excess of significance were significant (p's ≥ 0.786).

4. Discussion

To our knowledge, this is the first sufficiently powered meta-analysis of whole-brain MIDT studies to investigate regional brain responses to the anticipatory and consummatory phases of win and loss processing. The processes engaged both shared and distinct neural correlates, in line with previous findings (Dugre et al., 2018; Knutson and Greer, 2008; Liu et al., 2011; Oldham et al., 2018). With a larger number of studies included for meta-analysis, we observed regional activities, particularly those related to loss outcome, that were not reported previously (see Table 1 for comparisons). Further, with conjunction and subtraction analyses, we identified regional activities that were significantly different between valences and across processing stages. Specifically, win and loss anticipation both

engaged the fronto-striatal-thalamic networks; in contrast, win and loss outcomes shared no regional activities. The mOFC and dACC play specific roles each in processing win and loss outcome. Win anticipation and outcome both engaged bilateral ventral striatum (VS) and the right-hemispheric OC, whereas loss anticipation and outcome both involved higher activity in the right lateral OFC and AI. Win anticipation vs. outcome involved higher activity in their shared fronto-striatal-thalamic network and lower activity in mOFC, PCC, and right AG, regions of the default mode network. Notably, win anticipation vs. outcome involved higher activity in bilateral but predominantly right AI, whereas loss anticipation vs. outcome involved higher left AI activity. In the below, we provided an overview of the regional activities with reference to previous studies (Section 4.1), discussed the shared (4.2) and distinct (4.3) correlates as well as potential effects of confounding factors (4.4).

4.1. Neural correlates of win/loss anticipation and outcome

We replicated the findings for win and loss anticipation in the most recently published meta-analysis of MIDT (Oldham et al., 2018), showing activations across a wide swath of brain regions, including the amygdala, midbrain, striatum, AI, thalamus, SMA, precentral gyrus, and OC. Moreover, we observed activation of other frontal cortical regions, including the MFG for win anticipation. Encompassing behavioral tasks that included the MIDT, a recent meta-analysis also showed activation of MFG and SMA during win anticipation (Jauhar et al., 2021). Although the roles of the MFG in win/loss processing have not been investigated systematically, prior studies implicated the MFG in motivated behaviors (Bahlmann et al., 2015). The MFG was activated in reward (high > low) × cognitive load (high > low) interaction during goal-directed behaviors (Pochon et al., 2002; Taylor et al., 2004). Moreover, individual approach and avoidance traits were associated with activation of left- and right- lateralized MFG, respectively, during Stroop conflicts (Spielberg et al., 2011). Here, we observed bilateral MFG activation during win anticipation only; thus, the behavioral contexts that support functional lateralization of the MFG remains to be clarified.

We observed that the rACC, inferior and superior frontal gyri, angular gyrus, and OC, in addition to the striatum, amygdala, mOFC, and PCC as demonstrated by Oldham et al. (2018), showed higher likelihood of activation for win vs. nil outcome. For loss vs. nil outcome, we found activation in the temporal pole, lateral posterior OFC, AI, dACC, and superior colliculus, predominantly in the right hemisphere. The latter findings contrasted with bilateral putamen and globus pallidum reported in Dugre et al. (2018), which included both whole-brain and ROI studies and employed effect-size SDM, instead of ALE, for meta-analysis. Notably, we identified mOFC and lateral OFC each during win and loss outcome, consistent with previous evidence that reward and punishment are represented medially and laterally, respectively, in the OFC during reversal learning (O'Doherty et al., 2001).

4.2. Shared neural correlates during win and loss processing

We found that both VS and dorsal striatum (DS) contribute substantially to win and loss anticipation as well as to win outcome, in accord with Oldham et al. (2018). Previous studies suggested functional heterogeneity within striatal subregions, with the VS involved in encoding both positive and negative stimuli and the DS in associative and motor aspects

of decision-making (Burton et al., 2015). Studies in rats also showed elevated neuronal activities in the VS and DS each in association with the expectation of larger rewards and behavioral responses to retrieve the reward (Burton et al., 2014; Roesch et al., 2009). During Pavlovian conditioning, the VS was critical in learning motivationally salient stimuli, independent of valence, to bias action selection (Jensen et al., 2007). Therefore, the VS may encode salience during the anticipatory period and modulate motivational processes in the DS to initiate the pursuit of reward or to avoid loss (Burton et al., 2015; Oldham et al., 2018). The findings here and of previous studies that the striatum responds to anticipation of wins and losses may reflect the fact that avoiding monetary loss is equivalent to winning in the MIDT. Studies that distinguish reward and punishment (e.g., with electric shocks) categorically may be needed to differentiate striatal responses to anticipation of positive and negative outcomes.

Previous meta-analysis identified the VS and left amygdala as common correlates during win anticipation and outcome at a threshold of $p < 0.005$ (Oldham et al., 2018). Our conjunction analyses did not show the left amygdala at $p < 0.001$ but did at $p < 0.005$ (results not shown). Our findings further showed a higher likelihood of activation of right OC in the conjunction of win anticipation and outcome. In addition to processing visual information (Op de Beeck and Baker, 2010), the OC is involved in encoding emotional salience and motivation (Geday et al., 2003; Sabatinelli et al., 2011), as during reward conditioning (Kirsch et al., 2003) and passive exposure to pictures of food vs. objects (Schur et al., 2009). The OC also showed higher activation during decision-making under risky and uncertain but not certain conditions, suggesting its broad engagement in behavioral responses to saliency (Blankenstein et al., 2017; Guo et al., 2013).

With conjunction analysis, we showed shared responses of the right AI (rAI) to loss anticipation and outcome. The rAI showed stronger activation during risky vs. safe choices in decision making and its activity during risky choices was significantly correlated with the likelihood of selecting a safe response after punishment and with higher individual scores of harm avoidance (Paulus et al., 2003). An MIDT study reported rAI activity during anticipation of large (but not small) losses in association with individual traits of negative (but not positive) emotional arousal (Wu et al., 2014). These along with the current findings suggest an outsized role of the rAI in loss processing and behavioral avoidance.

4.3. Distinct neural correlates of win and loss processing

The mOFC play important roles in motivational and emotional regulation (Rempel-Clower, 2007; Rudebeck and Rich, 2018). Here, we demonstrated higher likelihood of activation of the mOFC in response to win but not loss outcome. The differences in regional activities were confirmed by the subtraction analysis of win > loss outcome, broadly in line with mOFC response to reward but not punishment across multiple behavioral tasks (O'Doherty et al., 2001; Rolls, 2019; Rolls et al., 2020). Subtraction analysis also showed that the mOFC was more likely to be activated during win outcome vs. anticipation, as reported earlier by Oldham et al (2018). This is consistent with the finding from behaving monkeys that mOFC neurons rapidly encoded the value of a selected action and continued to signal the outcome until after its delivery in a two-option gambling task (Strait et al., 2014). As

discussed earlier, medial and lateral OFC respond to rewarding and punishing outcomes, respectively. Although the subtraction analysis failed to reveal lateral OFC activity in loss vs. win outcome, investigators should revisit this issue as studies of MIDT accrue in the literature.

We showed higher likelihood of activation of the dACC to loss outcome but not anticipation, although subtraction analysis did not substantiate the differences. The dACC has been implicated in integrating and learning the risk of an action to optimize decision-making (Bush et al., 2002; Kennerley et al., 2006; Rushworth et al., 2004). The dACC showed higher activation during decisions to quit vs. to chase losses (Campbell-Meiklejohn et al., 2008), suggesting dACC's role in processing negative outcomes for behavioral adjustment. Prior studies also demonstrated co-activation of the rAI and dACC during the anticipation of an electric shock (Chua et al., 1999). More broadly, both rAI and dACC showed higher activation to social exclusion vs. inclusion in the Cyberball task (Moor et al., 2012). Here, with the rAI responding to both loss anticipation and outcome and the dACC only to loss outcome, future work may investigate how rAI and dACC dynamically interact in loss processing for behavioral control.

The thalamus showed higher likelihood of activation during the anticipatory period only, regardless of valence, although the phase specificity was confirmed for win but not loss with the subtraction analyses of anticipation vs. outcome. Oldham et al. (2018) too observed thalamic activity during win anticipation vs. outcome. Also in support were findings that rodent thalamic neurons elevated firing as reward values increased during the delay period, peaking before the delivery of reward, suggesting reward anticipation and prediction (Komura et al., 2001). These findings are nonetheless surprising given the role of the thalamus in processing and relaying sensory inputs to the cortex (Sherman and Guillery, 2006) and in salience detection (Matsumoto et al., 2001), irrespective of valence (Kirouac, 2015). Neurons in the thalamus of mice encoded the saliency of both appetitive or aversive outcomes, and the inhibition of these thalamic responses suppressed appetitive or aversive associative learning and extinction (Zhu et al., 2018). In dynamic causal modeling of the MIDT data, an earlier work proposed a functional circuit of incentive processing where anticipation of win or loss generated "alerting" signals in the thalamus that integrate with interoceptive information conveyed by the AI to shape action selection in the striatum (Cho et al., 2013). It was also proposed that the thalamus receives inputs from the striatum and in turn projects to the PFC, thereby linking reward signals to "higher-order" cognitive functions (Rademacher et al., 2010). In other studies, neuronal responses in the thalamus, global pallidus, and ACC were parametrically modulated by reward levels only whereas parametric responses to both reward and punishment were observed in bilateral insula, caudate head, and OFC (Elliott et al., 2000). Thus, the thalamus shows higher likelihood of activation during anticipation and the differences between anticipation and outcome activities are most evident during reward processing. Future research may address the effective connectivity within the thalamic-striatal-insular/frontal networks for both win and loss processing, to better understand how the regional activities and connectivities support motivated behavior, including those involved in drug seeking (Li et al., 2022; Naqvi and Bechara, 2009).

We observed activation of the SMA for both win and loss anticipation, consistent with a role of this medial frontal region in behavioral selection based on stimulus-reward associations and representation of risky decisions involving a potential loss (Bickel et al., 2009; Hartstra et al., 2010). The SMA encodes reward expectancy, as demonstrated with neuronal recordings in monkeys (Campos et al., 2005; Lee, 2004). The SMA did not appear to be engaged in the outcome phase of either win or loss processing, although this difference was confirmed in win anticipation vs. outcome but not in loss anticipation vs. outcome. These findings broadly support the role of the SMA in action preparation rather than feedback evaluation after actions. In this role, the SMA may partake in integrating contextual memory, including the outcomes of previous choices, with ongoing behavioral contingencies (Nachev et al., 2008). Moreover, win anticipation vs. outcome involved higher activity in their shared fronto-striatal-thalamic network and lower activity in mOFC, PCC, and right AG, consistent with opposing patterns of activity of the executive control and default mode networks (DMN; Raichle, 2015). These findings should also be considered along with DMN regional reactivity to motivationally salient stimuli (Breiter et al., 2001; Dohmatob et al., 2020; Mohanty et al., 2008; Pearson et al., 2011; Rogers et al., 2004). In monkeys, neurons in the PCC showed transient phasic increases in firing during the detection of salient environmental changes (Hayden et al., 2009), such as the delivery of a reward (McCoy et al., 2003). In humans, the PCC responds to motivational salience of the target in guiding shifts of spatial attention (Dohmatob et al., 2020). Indeed, here we also observed higher mOFC, PCC, and right AG activity during win outcome vs. nil (Fig. 2), which appeared to drive the difference in these DMN regional activities between win anticipation and outcome.

A few findings suggest functional lateralization of the AI. First, whereas both win and loss anticipation engaged bilateral AI, loss outcome engaged the right AI only and win outcome engaged neither right nor left AI. As a result, win anticipation vs. outcome involved higher activity in bilateral but predominantly right AI, whereas loss anticipation vs. outcome involved higher left AI activity. In earlier reviews Craig and colleagues suggested that the right and left AI responds to aversive and to positive and affiliative emotions, respectively (Craig, 2009; Craig, 2005). For instance, in healthy individuals, pleasant vs. unpleasant music (Koelsch et al., 2006) as well as anticipation of (Simmons et al., 2004) and exposure to (Straube and Miltner, 2011) emotionally aversive vs. neutral pictures activated the right but not left AI. However, these findings contrast with other reports associating greater responses of the left AI with visually aversive vs. neutral stimuli and higher negative valence ratings of the stimuli (Caria et al., 2010) as well as meta-analysis linking predominantly right and left insula activity each to approach/positive emotion and withdrawal/negative emotion-related behaviors (Wager et al., 2003). The latter reports appeared to be consistent with our finding that win anticipation vs. outcome involved higher activity in bilateral but predominantly right AI, whereas loss anticipation vs. outcome involved higher left AI activity. Together, these observations along with studies showing sensitivity of the AI to uncertainty (Fan et al., 2014; Wu et al., 2021) suggest the potential importance in considering the processing phase of anticipation and consummation in elucidating functional lateralization of the AI.

4.4. Potential effects of confounding factors

We grouped studies by age (68 adult vs. 12 non-adult studies) and performed post-hoc subgroup ALE analyses for each contrast. Although the meta-analyses of non-adult studies (n<15) were likely under-powered, we observed activation of the striatum and insula, in accord with recent meta-analytic findings that adolescents vs. adults showed higher likelihood for activation in the insula, striatum, amygdala, ACC, and OFC during reward processing (Silverman et al., 2015). The findings support the roles of the striatum and insula in win and loss processing regardless of age. As the reward circuits "mature" before self-regulation circuits during this developmental period (Casey, 2015; Casey et al., 2008; Chen et al., 2020), it would be of instrumental importance to investigate how win and loss processes and their neural mechanisms evolve from adolescence to adulthood. We also performed subgroup ALE analyses on studies with average success rate ≥ 66% and < 66%, respectively. The findings look similar but the clusters for studies with rate < 66% were fewer and smaller, most likely due to the limited number of studies.

An advantage with SDM is that we can perform meta-regressions to explore the linear effects of confounding factors on meta-analytic findings. We observed that the putamen was involved in all processes except for loss outcome, where its activity appeared to be accounted for by win/loss magnitude, in accord with striatal neuronal encoding of expectation of reward magnitudes (Cromwell and Schultz, 2003). Besides the magnitude-related effect, we also showed an age-related effect on the activation of right putamen during win outcome, although this appeared at odds with our previous findings associating age with higher prefrontal cortical, but not striatal, responses to the outcome of dollar win vs. neutral (Dhingra et al., 2020). In the latter study, we revealed an age-related constriction in sensitivity to win/loss magnitude – age incurs lower neural responses to anticipation of higher monetary gain and higher responses to smaller loss, suggesting an interaction of age and win/loss magnitude processing. The current findings add to the literature by highlighting the potential roles of the right putamen in the interplay of age and reward magnitude processing.

SDM findings for loss anticipation may be biased by the small-study effect. The potential publication bias was no longer observed with loss magnitude included as a covariate, suggesting that the factors confounding the meta-analytic findings may also affect the estimation of publication bias. Further, we showed that the results for win outcome were subject to publication bias in ALE but not SDM analyses, suggesting the need of more nuanced approach to assessing publication bias in meta-analyses using different methodologies.

4.5. Limitations of the study, other considerations, and conclusions

A few limitations should be acknowledged. Firstly, the studies reporting the contrasts of loss events are fewer in number than those reporting win events, which may have impacted the statistical power of ALE analyses. With more MIDT studies to investigate the neural mechanism of loss processing, meta-analyses are to follow up on the roles of shared and distinct regional response to wins and losses. Secondly, an earlier meta-analysis distinguished VS sensitivity to reward magnitudes during both prediction and consumption

and mOFC sensitivity only during consumption (Diekhof et al., 2012). Very few MIDT studies reported coordinates for the contrasts of different magnitudes; thus, we were not able to verify these differences. Thirdly, studies of relatively small sample sizes are limited in showing the true effects (Button et al., 2013), which in turn may impact meta-analytic findings (Pereira and Ioannidis, 2011). An additional challenge for ALE and SDM is that no routines are available for correction of multiple testing, either with the same samples evaluated for multiple contrasts or same contrasts included in multiple meta-analyses. Finally, both ALE and SDM are limited by the inclusion of reported peak coordinates but not spatial extent of the clusters in the analyses (Radua et al., 2012). With more and more studies to upload the statistical parametric maps in publication, investigators would be able to employ the effect size maps (i.e., effect-size SDM or 'ES-SDM') for more exhaustive and accurate meta-analyses.

In conclusion, we demonstrated both shared and non-shared neural correlates of anticipatory and consummatory win and loss processing. The findings highlighted that while win and loss outcomes shared no regional activities, win and loss anticipation both engaged the fronto-striatal-thalamic network; the mOFC and dACC play distinct roles each in processing win and loss outcome; and win anticipation vs. outcome engaged bilateral but predominantly right AI, whereas loss anticipation vs. outcome involved higher left AI activity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

No data was used for the research described in the article.

References

Acar F, Seurinck R, Eickhoff SB, Moerkerke B, 2018. Assessing robustness against potential publication bias in activation likelihood estimation (ALE) meta-analyses for fMRI. PLoS One 13, e0208177. [PubMed: 30500854]

Admon R, Pizzagalli DA, 2015. Dysfunctional reward processing in depression. Curr. Opin. Psychol 4, 114–118. [PubMed: 26258159]

Bahlmann J, Aarts E, D'Esposito M, 2015. Influence of motivation on control hierarchy in the human frontal cortex. J. Neurosci 35, 3207–3217. [PubMed: 25698755]

Balodis IM, Potenza MN, 2015. Anticipatory reward processing in addicted populations: a focus on the monetary incentive delay task. Biol. Psychiatry 77, 434–444. [PubMed: 25481621]

Bickel WK, Pitcock JA, Yi R, Angtuaco EJ, 2009. Congruence of BOLD response across intertemporal choice conditions: fictive and real money gains and losses. J. Neurosci 29, 8839–8846. [PubMed: 19587291]

Bjork JM, Smith AR, Chen G, Hommer DW, 2010. Adolescents, adults and rewards: comparing motivational neurocircuitry recruitment using fMRI. PLoS One 5, e11440. [PubMed: 20625430]

Blankenstein NE, Peper JS, Crone EA, van Duijvenvoorde ACK, 2017. Neural mechanisms underlying risk and ambiguity attitudes. J. Cogn. Neurosci 29, 1845–1859. [PubMed: 28686139]

Breiter HC, 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. [PubMed: 11395019]

Burton AC, Bissonette GB, Lichtenberg NT, Kashtelyan V, Roesch MR, 2014. Ventral striatum lesions enhance stimulus and response encoding in dorsal striatum. Biol. Psychiatry 75, 132–139. [PubMed: 23790313]

Burton AC, Nakamura K, Roesch MR, 2015. From ventral-medial to dorsal-lateral striatum: neural correlates of reward-guided decision-making. Neurobiol. Learn. Mem 117, 51–59. [PubMed: 24858182]

Bush G, Vogt BA, Holmes J, Dale AM, Greve D, Jenike MA, Rosen BR, 2002. Dorsal anterior cingulate cortex: a role in reward-based decision making. Proc. Natl. Acad Sci. U. S. A 99, 523–528. [PubMed: 11756669]

Button KS, Ioannidis JP, Mokrysz C, Nosek BA, Flint J, Robinson ES, Munafo MR, 2013. Power failure: why small sample size undermines the reliability of neuroscience. Nat. Rev. Neurosci 14, 365–376. [PubMed: 23571845]

Campbell-Meiklejohn DK, Woolrich MW, Passingham RE, Rogers RD, 2008. Knowing when to stop: the brain mechanisms of chasing losses. Biol. Psychiatry 63, 293–300. [PubMed: 17662257]

Campos M, Breznen B, Bernheim K, Andersen RA, 2005. Supplementary motor area encodes reward expectancy in eye-movement tasks. J. Neurophysiol 94, 1325–1335. [PubMed: 15843484]

Caria A, Sitaram R, Veit R, Begliomini C, Birbaumer N, 2010. Volitional control of anterior insula activity modulates the response to aversive stimuli. A real-time functional magnetic resonance imaging study. Biol. Psychiatry 68, 425–432. [PubMed: 20570245]

Carl H, Walsh E, Eisenlohr-Moul T, Minkel J, Crowther A, Moore T, Gibbs D, Petty C, Bizzell J, Dichter GS, Smoski MJ, 2016. Sustained anterior cingulate cortex activation during reward processing predicts response to psychotherapy in major depressive disorder. J. Affect. Disord 203, 204–212. [PubMed: 27295377]

Casey BJ, 2015. Beyond simple models of self-control to circuit-based accounts of adolescent behavior. Annu. Rev. Psychol 66, 295–319. [PubMed: 25089362]

Casey BJ, Getz S, Galvan A, 2008. The adolescent brain. Dev. Rev 28, 62–77. [PubMed: 18688292]

Chen Y, Chen C, Wu T, Qiu B, Zhang W, Fan J, 2020. Accessing the development and heritability of the capacity of cognitive control. Neuropsychologia 139, 107361. [PubMed: 31987849]

Cho YT, Fromm S, Guyer AE, Detloff A, Pine DS, Fudge JL, Ernst M, 2013. Nucleus accumbens, thalamus and insula connectivity during incentive anticipation in typical adults and adolescents. Neuroimage 66, 508–521. [PubMed: 23069809]

Chua P, Krams M, Toni I, Passingham R, Dolan R, 1999. A functional anatomy of anticipatory anxiety. Neuroimage 9, 563–571. [PubMed: 10334900]

Cooper JC, Knutson B, 2008. Valence and salience contribute to nucleus accumbens activation. Neuroimage 39, 538–547. [PubMed: 17904386]

Craig A, 2009. How do you feel–now? The anterior insula and human awareness. Nat. Rev. Neurosci 10.

Craig AD, 2005. Forebrain emotional asymmetry: a neuroanatomical basis? Trends Cogn. Sci 9, 566–571. [PubMed: 16275155]

Cromwell HC, Schultz W, 2003. Effects of expectations for different reward magnitudes on neuronal activity in primate striatum. J. Neurophysiol 89, 2823–2838. [PubMed: 12611937]

Dhingra I, Zhang S, Zhornitsky S, Le TM, Wang W, Chao HH, Levy I, Li CR, 2020. The effects of age on reward magnitude processing in the monetary incentive delay task. Neuroimage 207, 116368. [PubMed: 31743790]

Dhingra I, Zhang S, Zhornitsky S, Wang W, Le TM, Li CR, 2021. Sex differences in neural responses to reward and the influences of individual reward and punishment sensitivity. BMC Neurosci. 22, 12. [PubMed: 33639845]

Diekhof EK, Kaps L, Falkai P, Gruber O, 2012. 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. Neuropsychologia 50, 1252–1266. [PubMed: 22366111]

Dohmatob E, Dumas G, Bzdok D, 2020. Dark control: the default mode network as a reinforcement learning agent. Hum. Brain Mapp 41, 3318–3341. [PubMed: 32500968]

Dugre JR, Dumais A, Bitar N, Potvin S, 2018. Loss anticipation and outcome during the monetary incentive delay Task: a neuroimaging systematic review and meta-analysis. PeerJ 6, e4749. [PubMed: 29761060]

Egger M, Smith GD, Schneider M, Minder C, 1997. Bias in meta-analysis detected by a simple, graphical test. Bmj 315, 629–634. [PubMed: 9310563]

Eickhoff SB, Bzdok D, Laird AR, Kurth F, Fox PT, 2012. Activation likelihood estimation meta-analysis revisited. Neuroimage 59, 2349–2361. [PubMed: 21963913]

Eickhoff SB, Bzdok D, Laird AR, Roski C, Caspers S, Zilles K, Fox PT, 2011. Co-activation patterns distinguish cortical modules, their connectivity and functional differentiation. Neuroimage 57, 938–949. [PubMed: 21609770]

Eickhoff SB, Laird AR, Grefkes C, Wang LE, Zilles K, Fox PT, 2009. Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: a random-effects approach based on empirical estimates of spatial uncertainty. Hum. Brain Mapp 30, 2907–2926. [PubMed: 19172646]

Elliott R, Friston KJ, Dolan RJ, 2000. Dissociable neural responses in human reward systems. J. Neurosci 20, 6159–6165. [PubMed: 10934265]

Eshel N, Roiser JP, 2010. Reward and punishment processing in depression. Biol. Psychiatry 68, 118–124. [PubMed: 20303067]

Fan J, Van Dam NT, Gu X, Liu X, Wang H, Tang CY, Hof PR, 2014. Quantitative characterization of functional anatomical contributions to cognitive control under uncertainty. J. Cognit. Neurosci 26, 1490–1506. [PubMed: 24392900]

Geday J, Gjedde A, Boldsen A-S, Kupers R, 2003. Emotional valence modulates activity in the posterior fusiform gyrus and inferior medial prefrontal cortex in social perception. Neuroimage 18, 675–684. [PubMed: 12667845]

Guo Z, Chen J, Liu S, Li Y, Sun B, Gao Z, 2013. Brain areas activated by uncertain reward-based decision-making in healthy volunteers. Neural Regen. Res 8, 3344–3352. [PubMed: 25206656]

Hartstra E, Oldenburg JF, Van Leijenhorst L, Rombouts SA, Crone EA, 2010. Brain regions involved in the learning and application of reward rules in a two-deck gambling task. Neuropsychologia 48, 1438–1446. [PubMed: 20105435]

Hayden BY, Smith DV, Platt ML, 2009. Electrophysiological correlates of default–mode processing in macaque posterior cingulate cortex. Proc. Natl. Acad. Sci. U. S. A 106, 5948–5953. [PubMed: 19293382]

Jauhar S, Fortea L, Solanes A, Albajes-Eizagirre A, McKenna PJ, Radua J, 2021. Brain activations associated with anticipation and delivery of monetary reward: a systematic review and meta-analysis of fMRI studies. PLoS One 16, e0255292. [PubMed: 34351957]

Jean-Richard-Dit-Bressel P, Killcross S, McNally GP, 2018. Behavioral and neurobiological mechanisms of punishment: implications for psychiatric disorders. Neuropsychopharmacology 43, 1639–1650. [PubMed: 29703994]

Jensen J, Smith AJ, Willeit M, Crawley AP, Mikulis DJ, Vitcu I, Kapur S, 2007. Separate brain regions code for salience vs. valence during reward prediction in humans. Hum. Brain Mapp 28, 294–302. [PubMed: 16779798]

Kennerley SW, Walton ME, Behrens TE, Buckley MJ, Rushworth MF, 2006. Optimal decision making and the anterior cingulate cortex. Nat. Neurosci 9, 940–947. [PubMed: 16783368]

Kirouac GJ, 2015. Placing the paraventricular nucleus of the thalamus within the brain circuits that control behavior. Neurosci. Biobehav. Rev 56, 315–329. [PubMed: 26255593]

Kirsch P, Schienle A, Stark R, Sammer G, Blecker C, Walter B, Ott U, Burkart J, Vaitl D, 2003. Anticipation of reward in a nonaversive differential conditioning paradigm and the brain reward system. Neuroimage 20, 1086–1095. [PubMed: 14568478]

Knutson B, Fong GW, Adams CM, Varner JL, Hommer D, 2001. Dissociation of reward anticipation and outcome with event-related fMRI. Neuroreport 12, 3683–3687. [PubMed: 11726774]

Knutson B, Greer SM, 2008. Anticipatory affect: neural correlates and consequences for choice. Philos. Trans. R. Soc. Lond. B Biol. Sci 363, 3771–3786. [PubMed: 18829428]

Koelsch S, Fritz T, DY VC, Muller K, Friederici AD, 2006. Investigating emotion with music: an fMRI study. Hum. Brain Mapp 27, 239–250. [PubMed: 16078183]

Komura Y, Tamura R, Uwano T, Nishijo H, Kaga K, Ono T, 2001. Retrospective and prospective coding for predicted reward in the sensory thalamus. Nature 412, 546–549. [PubMed: 11484055]

Lancaster JL, Tordesillas-Gutierrez D, Martinez M, Salinas F, Evans A, Zilles K, Mazziotta JC, Fox PT, 2007. Bias between MNI and Talairach coordinates analyzed using the ICBM-152 brain template. Hum. Brain Mapp 28, 1194–1205. [PubMed: 17266101]

Lee D, 2004. Behavioral context and coherent oscillations in the supplementary motor area. J. Neurosci 24, 4453–4459. [PubMed: 15128859]

Li G, Chen Y, Chaudhary S, Tang X, Li CR, 2022. Loss and frontal striatal reactivities characterize alcohol use severity and rule-breaking behavior in young adult drinkers. Biol. Psychiatry Cogn. Neurosci. Neuroimaging

Liu X, Hairston J, Schrier M, Fan J, 2011. Common and distinct networks underlying reward valence and processing stages: a meta-analysis of functional neuroimaging studies. Neurosci. Biobehav. Rev 35, 1219–1236. [PubMed: 21185861]

Maresh EL, Allen JP, Coan JA, 2014. Increased default mode network activity in socially anxious individuals during reward processing. Biol. Mood Anxiety Disord 4, 1–12. [PubMed: 24447313]

Matsumoto N, Minamimoto T, Graybiel AM, Kimura M, 2001. Neurons in the thalamic CM-Pf complex supply striatal neurons with information about behaviorally significant sensory events. J. Neurophysiol 85, 960–976. [PubMed: 11160526]

McCoy AN, Crowley JC, Haghighian G, Dean HL, Platt ML, 2003. Saccade reward signals in posterior cingulate cortex. Neuron 40, 1031–1040. [PubMed: 14659101]

Mohanty A, Gitelman DR, Small DM, Mesulam MM, 2008. The spatial attention network interacts with limbic and monoaminergic systems to modulate motivation-induced attention shifts. Cereb. Cortex 18, 2604–2613. [PubMed: 18308706]

Moor BG, Guroglu B, Op de Macks ZA, Rombouts SA, Van der Molen MW, Crone EA, 2012. Social exclusion and punishment of excluders: neural correlates and developmental trajectories. Neuroimage 59, 708–717. [PubMed: 21791248]

Muller VI, Cieslik EC, Laird AR, Fox PT, Radua J, Mataix-Cols D, Tench CR, Yarkoni T, Nichols TE, Turkeltaub PE, Wager TD, Eickhoff SB, 2018. Ten simple rules for neuroimaging meta-analysis. Neurosci. Biobehav. Rev 84, 151–161. [PubMed: 29180258]

Murray L, Lopez-Duran NL, Mitchell C, Monk CS, Hyde LW, 2020. Neural mechanisms of reward and loss processing in a low-income sample of at-risk adolescents. Soc. Cogn. Affect. Neurosci 15, 1310–1325. [PubMed: 33216937]

Nachev P, Kennard C, Husain M, 2008. Functional role of the supplementary and pre-supplementary motor areas. Nat. Rev. Neurosci 9, 856–869. [PubMed: 18843271]

Naqvi NH, Bechara A, 2009. The hidden island of addiction: the insula. Trends Neurosci. 32, 56–67. [PubMed: 18986715]

O'Doherty J, Kringelbach ML, Rolls ET, Hornak J, Andrews C, 2001. Abstract reward and punishment representations in the human orbitofrontal cortex. Nat. Neurosci 4, 95–102. [PubMed: 11135651]

O'Doherty JP, Cockburn J, Pauli WM, 2017. Learning, reward, and decision making. Annu. Rev. Psychol 68, 73–100. [PubMed: 27687119]

Oldham S, Murawski C, Fornito A, Youssef G, Yucel M, Lorenzetti V, 2018. The anticipation and outcome phases of reward and loss processing: a neuroimaging meta–analysis of the monetary incentive delay task. Hum. Brain Mapp 39, 3398–3418. [PubMed: 29696725]

Op de Beeck HP, Baker CI, 2010. The neural basis of visual object learning. Trends Cogn. Sci 14, 22–30. [PubMed: 19945336]

Paulus MP, Rogalsky C, Simmons A, Feinstein JS, Stein MB, 2003. Increased activation in the right insula during risk-taking decision making is related to harm avoidance and neuroticism. Neuroimage 19, 1439–1448. [PubMed: 12948701]

Pearson JM, Heilbronner SR, Barack DL, Hayden BY, Platt ML, 2011. Posterior cingulate cortex: adapting behavior to a changing world. Trends Cogn. Sci 15, 143–151. [PubMed: 21420893]

Pereira TV, Ioannidis JP, 2011. Statistically significant meta-analyses of clinical trials have modest credibility and inflated effects. J. Clin. Epidemiol 64, 1060–1069. [PubMed: 21454050]

Pochon JB, Levy R, Fossati P, Lehericy S, Poline JB, Pillon B, Le Bihan D, Dubois B, 2002. The neural system that bridges reward and cognition in humans: an fMRI study. Proc. Natl. Acad. Sci. U. S. A 99, 5669–5674. [PubMed: 11960021]

Rademacher L, Krach S, Kohls G, Irmak A, Grunder G, Spreckelmeyer KN, 2010. Dissociation of neural networks for anticipation and consumption of monetary and social rewards. Neuroimage 49, 3276–3285. [PubMed: 19913621]

Radua J, Mataix-Cols D, 2009. Voxel-wise meta-analysis of grey matter changes in obsessive-compulsive disorder. Br. J. Psychiatry 195, 393–402. [PubMed: 19880927]

Radua J, Mataix-Cols D, Phillips ML, El-Hage W, Kronhaus DM, Cardoner N, Surguladze S, 2012. A new meta-analytic method for neuroimaging studies that combines reported peak coordinates and statistical parametric maps. Eur. Psychiatry 27, 605–611. [PubMed: 21658917]

Radua J, van den Heuvel OA, Surguladze S, Mataix-Cols D, 2010. Meta-analytical comparison of voxel-based morphometry studies in obsessive-compulsive disorder vs other anxiety disorders. Arch. Gen. Psychiatry 67, 701–711. [PubMed: 20603451]

Raichle ME, 2015. The brain's default mode network. Annu. Rev. Neurosci 38, 433–447. [PubMed: 25938726]

Raine A, 2018. Antisocial personality as a neurodevelopmental disorder. Annu. Rev. Clin. Psychol 14, 259–289. [PubMed: 29401045]

Rempel-Clower NL, 2007. Role of orbitofrontal cortex connections in emotion. Ann. N. Y. Acad. Sci 1121, 72–86. [PubMed: 17846152]

Richards JM, Plate RC, Ernst M, 2013. A systematic review of fMRI reward paradigms used in studies of adolescents vs. adults: the impact of task design and implications for understanding neurodevelopment. Neurosci. Biobehav. Rev 37, 976–991. [PubMed: 23518270]

Roesch MR, Singh T, Brown PL, Mullins SE, Schoenbaum G, 2009. Ventral striatal neurons encode the value of the chosen action in rats deciding between differently delayed or sized rewards. J. Neurosci 29, 13365–13376. [PubMed: 19846724]

Rogers RD, Ramnani N, Mackay C, Wilson JL, Jezzard P, Carter CS, Smith SM, 2004. Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. Biol. Psychiatry 55, 594–602. [PubMed: 15013828]

Rolls ET, 2019. The orbitofrontal cortex and emotion in health and disease, including depression. Neuropsychologia 128, 14–43. [PubMed: 28951164]

Rolls ET, Cheng W, Feng J, 2020. The orbitofrontal cortex: reward, emotion and depression. Brain Commun. 2, fcaa196.

Rosenthal R, 1979. The file drawer problem and tolerance for null results. Psychol. Bull 86.

Rudebeck PH, Rich EL, 2018. Orbitofrontal cortex. Curr. Biol 28, R1083–R1088. [PubMed: 30253144]

Rushworth MF, Walton ME, Kennerley SW, Bannerman DM, 2004. Action sets and decisions in the medial frontal cortex. Trends Cogn. Sci 8, 410–417. [PubMed: 15350242]

Sabatinelli D, Fortune EE, Li Q, Siddiqui A, Krafft C, Oliver WT, Beck S, Jeffries J, 2011. Emotional perception: meta-analyses of face and natural scene processing. Neuroimage 54, 2524–2533. [PubMed: 20951215]

Schur EA, Kleinhans NM, Goldberg J, Buchwald D, Schwartz MW, Maravilla K, 2009. Activation in brain energy regulation and reward centers by food cues varies with choice of visual stimulus. Int. J. Obes. (Lond.) 33, 653–661. [PubMed: 19365394]

Sherman SM, Guillery RW, 2006. Exploring the Thalamus and Its Role in Cortical Function. MIT press.

Silverman MH, Jedd K, Luciana M, 2015. Neural networks involved in adolescent reward processing: an activation likelihood estimation meta-analysis of functional neuroimaging studies. Neuroimage 122, 427–439. [PubMed: 26254587]

Simmons A, Matthews SC, Stein MB, Paulus MP, 2004. Anticipation of emotionally aversive visual stimuli activates right insula. Neuroreport 15, 2261–2265. [PubMed: 15371746]

Spielberg JM, Miller GA, Engels AS, Herrington JD, Sutton BP, Banich MT, Heller W, 2011. Trait approach and avoidance motivation: lateralized neural activity associated with executive function. Neuroimage 54, 661–670. [PubMed: 20728552]

Strait CE, Blanchard TC, Hayden BY, 2014. Reward value comparison via mutual inhibition in ventromedial prefrontal cortex. Neuron 82, 1357–1366. [PubMed: 24881835]

Straube T, Miltner WH, 2011. Attention to aversive emotion and specific activation of the right insula and right somatosensory cortex. Neuroimage 54, 2534–2538. [PubMed: 20946962]

Strohle A, Stoy M, Wrase J, Schwarzer S, Schlagenhauf F, Huss M, Hein J, Nedderhut A, Neumann B, Gregor A, Juckel G, Knutson B, Lehmkuhl U, Bauer M, Heinz A, 2008. Reward anticipation and outcomes in adult males with attention-deficit/hyperactivity disorder. Neuroimage 39, 966–972. [PubMed: 17996464]

Taylor SF, Welsh RC, Wager TD, Phan KL, Fitzgerald KD, Gehring WJ, 2004. A functional neuroimaging study of motivation and executive function. Neuroimage 21, 1045–1054. [PubMed: 15006672]

Treadway MT, Buckholtz JW, Zald DH, 2013. Perceived stress predicts altered reward and loss feedback processing in medial prefrontal cortex. Front. Hum. Neurosci 7, 180. [PubMed: 23730277]

Turkeltaub PE, Eickhoff SB, Laird AR, Fox M, Wiener M, Fox P, 2012. Minimizing within-experiment and within-group effects in activation likelihood estimation meta-analyses. Human Brain Mapp. 33, 1–13.

Wager TD, Phan KL, Liberzon I, Taylor SF, 2003. Valence, gender, and lateralization of functional brain anatomy in emotion: a meta-analysis of findings from neuroimaging. Neuroimage 19, 513–531. [PubMed: 12880784]

Whitton AE, Treadway MT, Pizzagalli DA, 2015. Reward processing dysfunction in major depression, bipolar disorder and schizophrenia. Curr. Opin. Psychiatry 28, 7–12. [PubMed: 25415499]

Wu CC, Samanez-Larkin GR, Katovich K, Knutson B, 2014. Affective traits link to reliable neural markers of incentive anticipation. Neuroimage 84, 279–289. [PubMed: 24001457]

Wu T, Schulz KP, Fan J, 2021. Activation of the cognitive control network associated with information uncertainty. Neuroimage 230, 117703. [PubMed: 33385564]

Zhu Y, Nachtrab G, Keyes PC, Allen WE, Luo L, Chen X, 2018. Dynamic salience processing in paraventricular thalamus gates associative learning. Science 362, 423–429. [PubMed: 30361366]

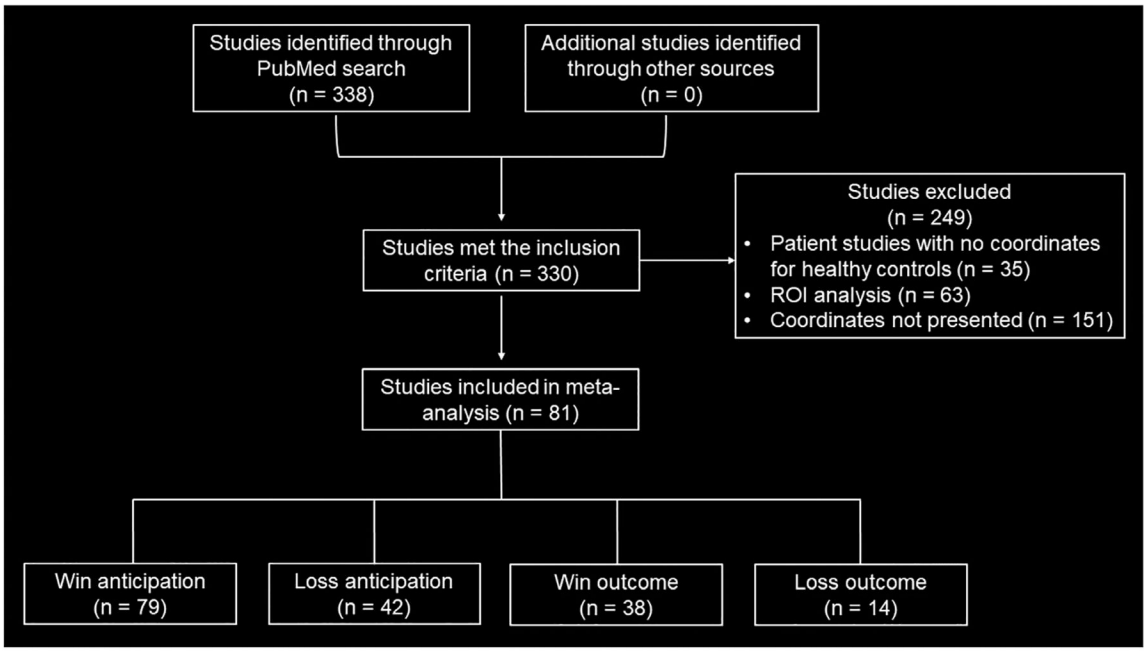

Figure 1.

A flow-chart for the procedure to arrive at the final sample for meta-analysis, following 'Preferred reporting items for systematic reviews and meta-analyses (PRISMA).'

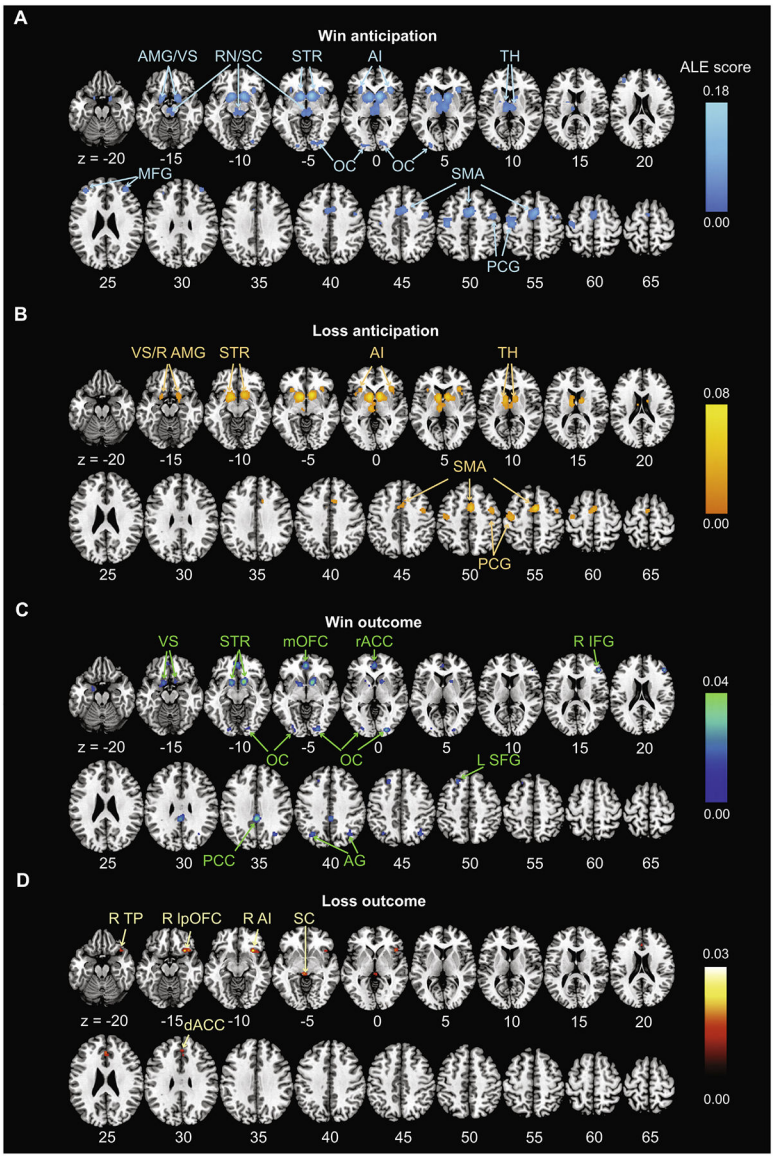

Figure 2.

ALE single dataset analyses. (A) Win anticipation; (B) Loss anticipation; (C) Win outcome; and (D) Loss outcome. *Note:* The results were evaluated with a cluster-forming threshold of $p < 0.001$ uncorrected and a cluster-level threshold of $p < 0.05$ FWE corrected. Color bars represent ALE scores. L: left; R: right; ACC: anterior cingulate cortex; AI: anterior insula; AG: angular gyrus; AMG: amygdala; dACC: dorsal ACC; IFG: inferior frontal gyrus; lpOFC: lateral posterior orbitofrontal cortex; MFG: middle frontal gyrus; mOFC: medial orbitofrontal cortex; OC: occipital cortex; PCC: posterior cingulate cortex; PCG: precentral gyrus; rACC: rostral ACC; RN: red nucleus; SC: superior colliculus; SFG: superior frontal gyrus; SMA: supplementary motor area; STR: striatum; TH: thalamus; TP: temporal pole; VS: ventral striatum.

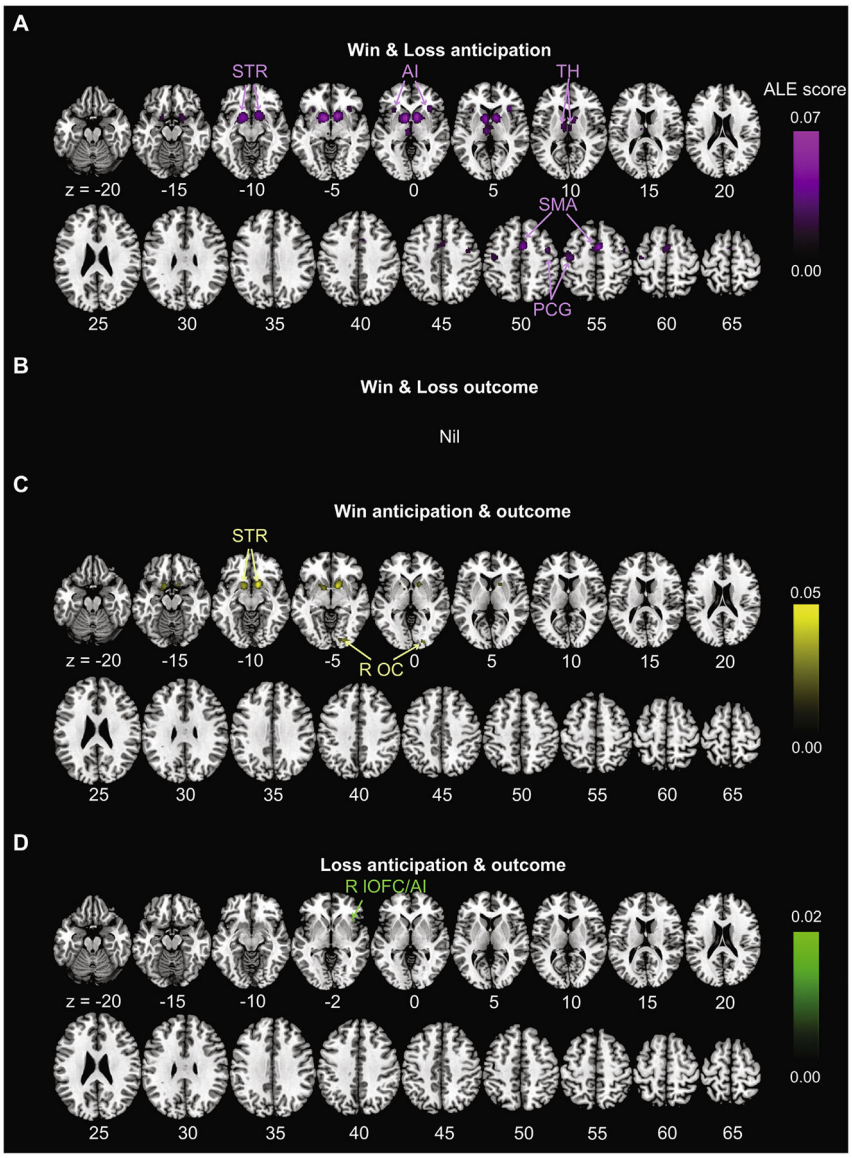

Figure 3.

ALE conjunction analyses: (A) Win and Loss anticipation; (B) Win and Loss outcome; (C) Win anticipation and outcome; and (D) Loss anticipation and outcome. The results were evaluated with a cluster-forming threshold of $p < 0.001$ uncorrected and a cluster-level threshold of $p < 0.05$ FWE corrected. Color bars represent ALE scores. Nil: no significant findings. R: right; AI: anterior insula; OC: occipital cortex; PCG: precentral gyrus; SMA: supplementary motor area; STR: striatum; TH: thalamus.

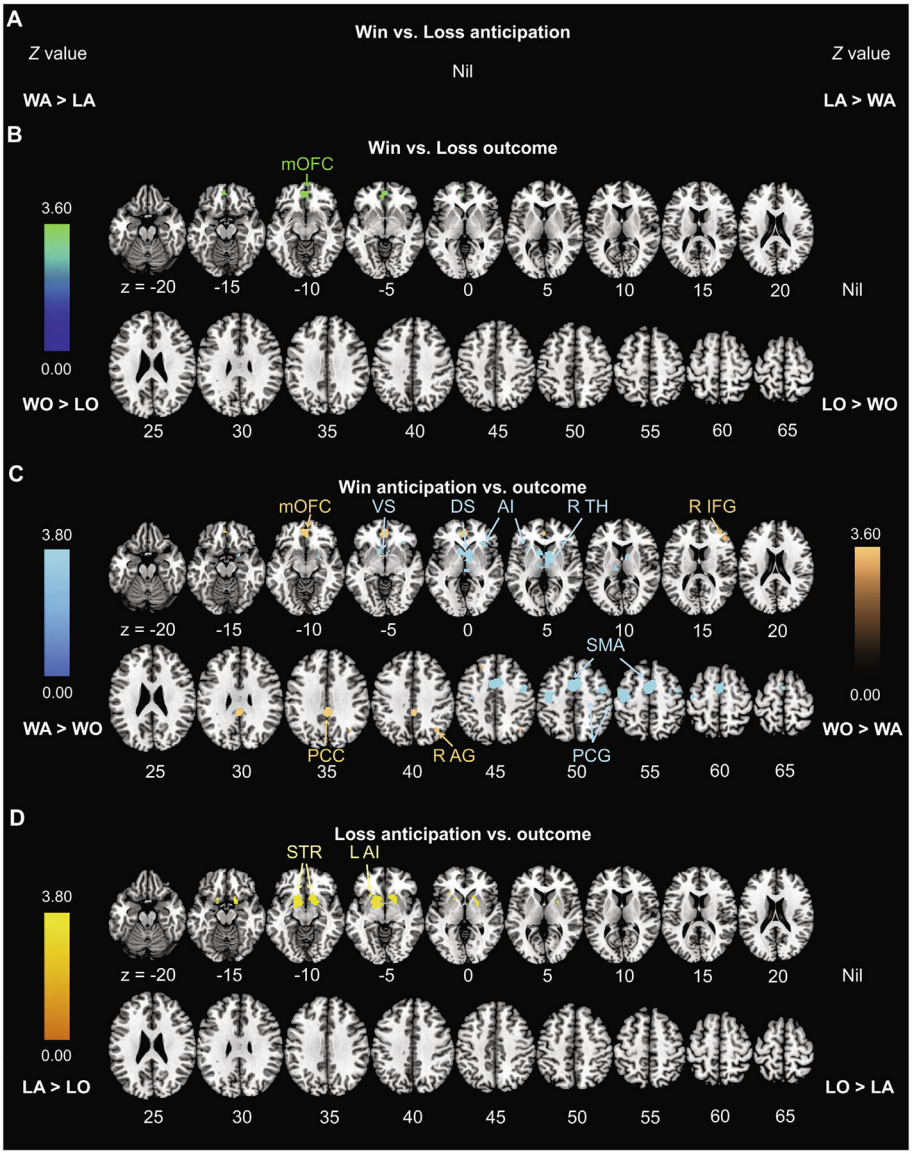

Figure 4.

ALE subtraction analyses: (A) Win vs. Loss anticipation; (B) Win vs. Loss outcome; (C) Win anticipation vs. outcome; and (D) Loss anticipation vs. outcome. *Note:* Subtraction analyses were conducted with a significance level of $p < 0.001$ with a minimal cluster size of 100 mm^3. Color bars represent Z values. No significant findings (Nil) were found for WA > LA, LA > WA, LO > WO, or LO > WA. WA: win anticipation; WO: win outcome; LA: loss anticipation; LO: loss outcome. L: left; R: right; AG: angular gyrus; AI: anterior insula; DS: dorsal striatum; IFG: inferior frontal gyrus; mOFC: medial orbitofrontal cortex; PCC: posterior cingulate cortex; PCG: precentral gyrus; SMA: supplementary motor area; STR: striatum; TH: thalamus; VS: ventral striatum.

Table 1

Comparisons between the current and two previous meta-analyses of MIDT

Meta-analysis	Current	Oldham et al. (2018)	Dugre et al. (2018)
Approach	ALE and SDM	ALE	SDM
Studies included	WB analysis	WB analysis	WB & ROI analysis
Single contrast	WA, LA, WO, LO	WA, LA, WO	LA, LO
Conjunction	Yes	Yes	No
Subtraction	Yes	Yes	No
Exclusive findings			
WA	MFG	Nil	NA
LA	Nil	Midbrain, Cerebellum	ACC, SFG
WO	rACC, IFG, SFG, AG, OC	Nil	NA
LO	TP, lpOFC, AI, dACC, SC	NA	PU, GP

Note: ALE: Activation likelihood estimation; SDM: seed-based d-Mapping; WB: whole-brain; ROI: region-of-interest; NA: not investigated; Nil: investigated but no new significant findings; WA: win anticipation; LA: loss anticipation; WO: win outcome; LO: loss outcome; MFG: middle frontal gyrus; ACC: anterior cingulate gyrus; SFG: superior frontal gyrus; rACC: rostral ACC; IFG: inferior frontal gyrus; AG: angular gyrus; OC: occipital cortex; TP: temporal pole; lpOFC: lateral posterior orbitofrontal cortex; AI: anterior insula; dACC: dorsal ACC; SC: superior colliculus; PU: putamen; GP: globus pallidus.