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Influence of neurobehavioral incentive valence and magnitude on alcohol drinking behavior

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Abstract

The monetary incentive delay (MID) task is a widely used probe for isolating neural circuitry in the human brain associated with incentive motivation. In the present functional magnetic resonance imaging (fMRI) study, 82 young adults, characterized along dimensions of impulsive sensation seeking, completed a MID task. fMRI and behavioral incentive functions were decomposed into incentive valence and magnitude parameters, which were used as predictors in linear regression to determine whether mesolimbic response is associated with problem drinking and recent alcohol use. Alcohol use was best explained by higher fMRI response to anticipation of losses and feedback on high gains in the thalamus. In contrast, problem drinking was best explained by reduced sensitivity to large incentive values in meso-limbic regions in the anticipation phase and increased sensitivity to small incentive values in the dorsal caudate nucleus in the feedback phase. Altered fMRI responses to monetary incentives in mesolimbic circuitry, particularly those alterations associated with problem drinking, may serve as potential early indicators of substance abuse trajectories.

Keywords

monetary incentive delay; fMRI; sensation seeking; impulsivity; problem drinking; alcohol use

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1. Introduction

Alcohol abuse is a major public health concern with devastating physical and mental health consequences [1]. Understanding the neurobehavioral profile of individuals at risk for alcohol abuse has important implications for prevention and early intervention efforts. Individual differences in impulsivity and incentive motivation may be particularly important in alcohol dependence; therefore a deeper understanding of the biological manifestations of these factors may be informative for the design and implementation of substance abuse prevention programs [2]. Using fMRI, the present study characterizes neurobehavioral responses to monetary rewards and losses in people who vary in level of risk for alcohol dependence.

Two motivational states seem particularly important in the transition from alcohol (or other substance) use to dependence: anticipatory and consummatory behaviors. Anticipatory behaviors are often referred to appetitive states of “wanting” whereas consummatory behaviors refer to the “liking” involved when a particular stimulus is delivered or consumed. Wanting and liking may be equally strong motivators during initial drug use, but according to Robinson and Berridge [3] the trajectory to dependence is marked by increased wanting and no change or a subtle decrease in liking. Ostafin et al. [4] also showed that people who had been drinking for longer showed a dissociation in wanting and liking compared to people who had been drinking for fewer years. The present study investigated whether non-alcohol dependent people who report drinking problems show different neural activation profiles (using functional magnetic resonance imaging, fMRI) between the anticipatory and consummatory stages of a monetary incentive delay (MID) task.

Another important consideration in understanding motivational tendencies in people at risk for alcohol dependence is whether anticipatory or consummatory behaviors are driven by positive outcomes or avoidance of negative outcomes. To address this, the present study examined the type of reinforcement contingency on the MID, with positive reinforcement trials associated with anticipation or receipt of monetary gains and avoidance trials associated with anticipation of avoidance or receipt of monetary losses. In other words, the present study determined whether people at risk for alcohol addiction are more sensitive to gains or losses, and we refer to this as incentive valence.

There are also differences in the way that people at risk for substance dependence respond to different magnitudes of reinforcement and punishment. Whereas, for most people, higher magnitude incentives are more motivating than lower magnitude incentives, people at risk for substance dependence (due to sensation seeking personality trait) may be less sensitive to magnitude (i.e., work equally hard to earn small and large drug doses, [5]). Similarly, non-dependent heroin users work equally hard to earn a small dose of morphine as higher doses even though subjective effects were only evident for higher doses [6]. These findings indicate that individual differences in sensitivity to the reinforcing effects of drugs may vary as a function of dose, with greater sensitivity occurring at low doses in individuals at risk for dependence. Consequently, the present study also varied magnitude of monetary gains and losses in order to probe individual differences in sensitivity to reinforcement and punishment magnitude; we refer to this as incentive magnitude.

An important neural substrate for alcohol dependence is the mesolimbic reward system. The monetary incentive delay (MID) task (Figure 1a, [7]) has been used to investigate mesolimbic reward circuitry involvement in risk for alcohol and substance abuse, where risk is indicated by high levels of trait impulsivity, problematic and externalizing behaviors, or positive family history of alcoholism [8–16]. In the MID task, participants can earn or lose money depending on their speed of responding to a briefly presented visual target. Each trial consists of cue, target and feedback phases. The cue phase displays a monetary value that can be won (positive reinforcement trials) or lost (avoidance trials). The target phase consists of a brief presentation of the target, and participants are instructed to respond within the duration of the target display (on the order of 250 ms). If the response time is less than the target duration, the participant earns or avoids losing the money. If the response time exceeds the target duration, the participant does not receive or loses the money. According to the Robinson and Berridge [3] model, behavior during the cue phase would be categorized as anticipatory and during the feedback phase categorized as consummatory.

Whereas some studies report greater mesolimbic sensitivity to gains on the MID task in individuals at risk compared to those not at risk [8, 10–11, 17–19], other findings indicate reduced sensitivity to gains [8, 15, 20–21]. The focus on monetary gains rather than losses is well motivated, but loss sensitivity may also differentiate individuals at risk for substance abuse [11, 20, 22]. Therefore, an understanding of individual differences in incentive motivation should include a comprehensive index of both loss and gain sensitivity, or incentive valence. In addition, isolating sensitivity to incentive magnitude may also reveal differences in mesolimbic response [23], but this has not been explored as extensively as incentive valence. Therefore, the present study focused on both incentive valence (positive reinforcement v. avoidance contingencies during the cue phase; gain v. loss during the feedback phase) and magnitude (large v. small incentives).

MID fMRI responses have traditionally been used to examine individual differences in motivation. However, more recently, MID fMRI responses have also been associated with individual differences in behavioral outcomes such as problematic drinking. Nees et al. [24] reported that personality measures, behavioral measures of risk taking and MID task brain response collectively predicted early onset drinking in adolescence. Weiland et al. [16] showed that functional connectivity of the nucleus accumbens in the anticipation phase of the MID mediated the relationship between sensation seeking and drinking volume in young adults with a family history of alcoholism. However, these studies either focused only on the anticipation phase or did not dissociate anticipation and feedback phases. The two phases invoke different computations [25] and are associated with different neurobiological systems [26]. The outcome phase of the MID reflects consummatory (rather than appetitive) processes and may also be important in differentiating individuals at risk for substance abuse [11, 20, 22]. Moreover, while appetitive and consummatory behaviors may be equally important during initial stages of drug use, these two behaviors may become more dissociated in the transition to dependence [3]. For this reason, it is important to examine both aspects of motivated behavior, as in the present study.

The present study examined whether alcohol drinking behavior in young adults was associated with neurobehavioral MID responses and personality risk for substance abuse.

Using fMRI, incentive magnitude was parametrically manipulated across 5 values (lose \$5, lose \$.5, neither win nor lose, win \$.5, win \$5) to isolate mesolimbic MID response. fMRI response across the 5 incentive values constitutes an fMRI incentive function. The incentive function can be described linearly or fit to a higher-order polynomial function. Fitting the incentive function to a 2nd order polynomial allows decomposing the function into linear and quadratic components (Figure 1b–c). The linear component of the MID incentive function reflects the slope. As shown in Figure 1b, if fMRI response does not vary across the 5 incentive levels, the slope is 0 and the particular brain region is not differentially sensitive to incentive valence. However, if the slope is positive, the region is more sensitive to reinforcement than avoidance contingencies during the cue phase (or gain than loss during the feedback phase); if the slope is negative, the region is more sensitive to avoidance than reinforcement during the cue phase (or loss than gain during the feedback phase). Consequently, the slope parameter of the MID incentive function reflects sensitivity to incentive valence. As shown in Figure 1c, the quadratic component reflects the degree of curvature of the incentive function. If this parameter is 0, then there is no curvature and the incentive function can be described linearly. Curvature of 0 reflects little sensitivity to incentive magnitude. Positive curvature reflects a function with a minimum vertex, yielding a concave function, which reflects a greater response to high magnitudes than to low magnitudes. Negative curvature reflects a function with a maximum vertex, yielding a convex function, which reflects a greater response to low magnitudes than to high magnitudes. In the present study, each individual's fMRI incentive response was fit to a 2nd order polynomial to yield two parameters of interest, slope (reflecting incentive valence) and curvature (reflecting incentive magnitude). Given that mesolimbic reward circuitry is known to be sensitive to both incentive valence and magnitude [23, 27] the overall question was whether mesolimbic hyper- (or hypo-) sensitivity to incentive valence or magnitude in anticipatory or consummatory stages of the MID task was associated with problematic drinking.

2. Methods

2.1 Participants

Eighty-six right-handed, native English-speaking adults (42 males, mean age=21.9 years) with normal or corrected-to-normal vision provided written consent following University of Kentucky Institutional Review Board guidelines. Exclusion criteria were any major medical, neurological, psychiatric conditions or learning disorders, prior closed head injury or concussion, presence of metal in the body, current use of medications affecting the central nervous system, history of substance abuse, daily use of nicotine, and pregnancy. Datasets from four participants (1 male) were excluded due to excessive head motion.

2.2 Procedure

Advertisements distributed throughout the local community directed volunteers to a website, where they provided health and demographic information and completed a Likert-scale variation (item scores of 0 to 4) of the 19-item version of the Impulsivity Sensation Seeking Scale from the Zuckerman-Kuhlman Personality Questionnaire (ZKPQ; [28–30]. Although participants were recruited into separate impulsivity groups based on the ZKPQ (see details

in Appendix A), convergent measures of similar personality dimensions (UPPS Sensation Seeking, SS, and Urgency, URG; [31]) were considered as candidates for continuous predictors for the primary analyses in this study, discussed more below.

Following informed consent, participants completed locally-developed health and personal history questionnaires, a 17-item drug use questionnaire derived from the Addiction Severity Index [32], the self-administered Michigan Alcoholism Screening Test (MAST) [33] and the Edinburgh Handedness Inventory [34]. The MAST is a 24-item questionnaire that asks about drinking habits and problems, such as blackouts, DUI or arrests, adverse effects on relationships and employment and having sought help for drinking problems. Pregnancy and drug use (alcohol, tobacco, cocaine, amphetamines, MTD, MDMA, THC, benzodiazepines, barbiturates, opiates, and PCP) were assessed via breathalyzer (Alcohol Sensor III, Intoximeters, Inc.; piCO Carbon Monoxide Monitor, Bedfont Scientific) and urinalysis (Integrated E-Z Split Key Cup II, Acon Laboratories, San Diego, CA; hCG Assay, Rapid Detect, Inc., Poteau, OK). The drug use questionnaire asked the participant how many of the past 30 days did s/he use coffee or tea, beer, wine, wine coolers, liquor, nicotine (smoked, not smoked, gum or patch), marijuana, inhalants, cocaine, non-prescription narcotics (e.g., opioids), prescription narcotics (e.g., codeine), uppers, downers, relaxants, and hallucinogenic drugs. Participants also completed attention [35] and working memory [36] screening tests. Each participant completed an fMRI session and an electrophysiological recording session on separate days with session order counterbalanced across participants, but only the fMRI session data are reported here. During the fMRI session, participants completed (in fixed order): go/no-go (two 8.5-minute runs), emotional induction (one 10.5-minute run), removal from scanner for old/new recognition study phase (15 minutes), return to scanner for old/new recognition test phase (one 12-minute run), followed by the MID (two 6.5-minute runs). Absence of drug use was verified by urinalysis prior to both sessions.

The MAST was the measure used to characterize drinking problems in the present sample. Scoring of the 24 items followed the procedures in Selzer [33]. Scores ranged from 0 to 13 ($M = 3.63$, $SD = 2.80$). A cutoff score of 12/13 indicates alcohol dependence [37] so this sample would not be characterized as dependent (only 1 participant scored 13, with the next highest score = 10). The total number of drinking days reported on the drug use questionnaire for the alcohol items served as the current measure of alcohol use. Scores ranged from 0 to 40 ($M = 8.8$, $SD = 9.1$). The scores could exceed 30 (number of total days sampled) because each alcohol type was tallied separately then summed.

2.3 MID task design

The task was adapted from Knutson, et al., [7] and Bjork et al., [38] (Figure 1a). Participants could earn or lose money depending on response time to a white rectangle “target” stimulus. Each trial consisted of cue, target and feedback phases. The cue phase displayed the trial incentive condition ($-\$5$, $-\$.5$, 0 , $+\$.5$, $+\$5$) for 1500 ms duration followed by a variable duration (1850 to 6150 ms). The target phase consisted of a white rectangle presented centrally for 250 msec initially. Participants were instructed to respond as quickly as possible when the rectangle appeared. If the response was made during the time that the target was displayed, the participant earned the positive incentive or avoided losing the

negative incentive. If the response was delayed, the participant did not win the positive amount or incurred a loss of the negative amount. Responses during the \$0 incentive trials had no effect on losses or earnings. Responses were made using the index finger of the right or left hand, counterbalanced across participants. After the initial 2 trials, the duration of the target stimulus was adjusted in increments of ± 10 ms (up to a maximum of 360 ms) to keep average accuracy across trials at approximately 67%. Percentage of adjustments across participants ranged from 29% to 90%, (49% average). The feedback phase displayed a blue check mark to indicate timely (i.e., accurate) responses, and notification of gain on positive reinforcement trials, and no loss on avoidance trials, or a red X to indicate delayed (i.e., inaccurate) responses, and notification of no gain on positive reinforcement trials and loss on avoidance trials, with the running total of earnings displayed simultaneously (for 2000 msec). Participants received the amount they earned during the MID task as a component of study compensation.

The three trial phases were separated by intervals of 2, 4 or 6 seconds to allow for deconvolution of the fMRI response associated with the different phases. Trial duration ranged from 9 to 21 sec. Nine repetitions of 5 incentive levels were presented across two runs (23 or 22 trials in a run) to provide a break for participants while in the scanner. The order of the 45 trials was determined using a randomization algorithm (<http://surfer.nmr.mgh.harvard.edu/optseq>), with 362 total brain volumes across both runs.

2.4 fMRI data acquisition and preprocessing

Gradient echo EPI images were acquired with a Siemens 3T Trio MRI system (Erlangen, Germany; TE=27 ms, TR=2000 ms, flip angle=76°, FOV=2.37 × 2.37 cm, interleaved acquisition, 36 axial contiguous 3.7-mm axial slices; 184 volumes in one run, 178 volumes in the other run). A T1-weighted MPRAGE (TE=2.56 ms, TR=1690 ms, TI=1100 ms, FOV=25.6 cm×22.4 cm, flip angle=12° 176 contiguous sagittal 1-mm thick slices) and field map were also collected. E-prime version1 (www.pstnet.com; Psychology Software Tools) running on a Windows computer connected to the MR scanner presented the MID task visually and recorded behavioral responses.

Using FSL (v. 4.1.7, FMRIB, Oxford University, Oxford, UK), preprocessing included motion correction with MCFLIRT, brain extraction using BET, spatial smoothing with a 7-mm FWHM Gaussian kernel and temporal high-pass filtering (cutoff = 100 s).

2.5 Analysis of MID performance

An inverse transformation converted reaction time on each trial to speed in order to meet normality assumptions. Four behavioral measures, $\text{slope}_{\text{speed}}$, $\text{curvature}_{\text{speed}}$, $\text{slope}_{\text{accuracy}}$, $\text{curvature}_{\text{accuracy}}$, were derived by fitting the speed or accuracy incentive functions to a quadratic function to determine the slope and curvature of individual-participant incentive functions. For speed, we used all 45 data points for curve fitting (with each incentive level equally sampled 9 times). However, for accuracy, each individual trial only yielded a correct or incorrect response. Therefore, we averaged the accuracy over all 9 trials for each incentive condition to get average accuracy, then used these 5 data points for curve fitting. Analysis of MID performance by impulsivity groups is provided in Appendix B.

2.6 Voxel-wise analysis of fMRI data

At the individual-participant level, each incentive condition ($-\$5$, $-\$5$, 0 , $+\$5$, $+\$5$) was modeled separately for each trial phase (cue, target, feedback), which yielded 15 explanatory variables (EVs) per task run, each of which included a temporal derivative as an alternative to slice timing correction [39]. The advantage of using temporal derivatives is that differences in image acquisition across slices is addressed by adding a first-order temporal derivative of the hemodynamic response function (HRF) to the general linear model as opposed to using interpolation, which changes the data. A disadvantage of using temporal derivatives is that differences in the latency of the HRF across slices may be blurred. However, the present analysis was not focused on differences in HRF latency. For each participant, parameter estimate maps were registered via the participant's high-resolution T1-weighted anatomical image to the MNI-152 template (12-parameter affine transformation) yielding images with 2mm^3 spatial resolution, then averaged across runs using fixed effects. Two group-level contrasts parametrically examined gain-sensitivity (contrast weights for five incentive levels: $-.75$, $-.25$, 0 , $.25$, $.75$) or magnitude sensitivity (contrast weights: $.1$, $-.1$, -1.8 , $-.1$, 1) using mixed-effects group analyses (FLAME1+2) in the cue and feedback phases separately. Although the target phase was modeled, it was not of primary interest for the main hypotheses of this study. The gain-sensitive and magnitude-sensitive contrast results were combined at the group level using logical “or” (union) in order to isolate regions of interest (ROIs) that were unbiased with respect to gain- or magnitude-sensitivity for the primary analysis (described more below). Note that for the primary analysis, the fMRI signal is used as a predictor in the regression analyses below, rather than used an outcome variable. Therefore, concerns about “double-dipping” [41] do not apply in this analysis.

Although a contrast for loss-sensitivity ($.75$, $.25$, 0 , $-.25$, $-.75$) was also examined, it did not yield any significant clusters. Finally, we did not model fMRI response as a function of reward or loss notification in the voxel-level analysis because the number of trials for each type of notification was low. However, as described in Section 3.4, average accuracy for different incentive levels was correlated with fMRI signal at the ROI level to address this issue.

2.7 Regions-of-interest (ROIs) analysis

Each contrast's statistical map was thresholded at a cluster corrected level of $p=0.0005$ ($Z>3.3$) for the cue phase or $p=.005$ ($Z>2.58$) for the feedback phase, then the gain- and magnitude-sensitive maps for a given task phase (either cue or feedback) were combined using logical “or” via `fslmaths` to yield union statistical maps. The resulting union maps (one for cue and one for feedback) were then masked anatomically to isolate mesolimbic regions of interest, as that was the primary focus of the present study. Anatomical ROIs were defined by the Harvard sub-cortical atlas (left and right nucleus accumbens, left and right putamen, left and right thalamus, left and right caudate) and combined with the union maps using logical “and” via `fslmaths`. Clusters were only considered further if they had a minimum size of 43 voxels. The union of gain- and magnitude-sensitivity yielded 8 clusters for the cue phase and 6 clusters for the feedback phase. These 14 clusters served as ROIs for additional analysis. For each ROI, percent signal change versus baseline were extracted for

each participant and each of the five incentive conditions (using featurquery). For each participant and each ROI, we fit the fMRI incentive function to a quadratic function to determine the slope and curvature of individual-participant incentive functions (Figure 1b–c). As discussed in the introduction, this was motivated by the goal to capture two dimensions of incentive motivation, sensitivity to incentive magnitude, captured by the curvature parameter, and sensitivity to incentive valence, captured by the slope parameter from these quadratic fits. The $slope_{fMRI}$ parameter indicates the slope of the linear component. A positive $slope_{fMRI}$ indicates greater fMRI response to reinforcement than avoidance contingencies during the cue phase (or gain than loss during the feedback phase) and a negative $slope_{fMRI}$ indicates greater fMRI response to avoidance than reinforcement during the cue phase (or loss than gain during the feedback phase). The $curvature_{fMRI}$ parameter indicates the degree of curvature. A $curvature_{fMRI}$ value of 0 indicates no curvature; a positive $curvature_{fMRI}$ value indicates greater concavity and a negative $curvature_{fMRI}$ value indicates greater convexity. A more concave function reflects greater fMRI signal for extreme versus small incentive values but a more convex function reflects greater fMRI signal for small than large values. The $slope_{fMRI}$ and $curvature_{fMRI}$ values were then submitted to linear regression (IBM SPSS Statistics v. 19, Chicago, IL) to determine whether incentive magnitude ($curvature_{fMRI}$) and incentive valence ($slope_{fMRI}$) were associated with alcohol drinking behavior (described below). A secondary analysis examined impulsivity group differences in the $slope_{fMRI}$ and $curvature_{fMRI}$ parameters for cue and feedback phases (Appendix B).

Fitting each participant's incentive function to a 2nd order polynomial reduced the number of parameters needed to describe the incentive functions. A typical approach used in other studies is to use percent signal change from only one of the incentive levels (e.g. high rewards) or various combinations of incentives (such as rewards versus non-rewards) for each participant. However, these approaches may ignore some of the data. In contrast, a quadratic fit describes the incentive functions in just 2 parameters and these 2 parameters capture features of the functions that depend on all 5 values. In our view, this approach is actually more powerful than using, for example, only the high-reward condition which ignores the other 4 incentive values. In addition, isolating the slope and curvature parameters reflects two different aspects of behavior, sensitivity to incentive magnitude or valence. A single incentive level (or combinations / differences across levels) is likely to confound these two aspects of behavior.

2.8 Linear regression analysis

Several variables that could be linked to drinking behavior were measured in the present study, including MID task performance (e.g., $slope_{speed}$ and $curvature_{speed}$), MID task fMRI response (e.g., $slope_{fMRI}$ and $curvature_{fMRI}$ in each ROI), and personality measures (e.g., sensation seeking and urgency). The goal was to determine which of these variables (or which subsets of variables) were most strongly associated with different drinking behavior outcomes (problem drinking or recent alcohol use) using linear regression. The $slope_{fMRI}$ and $curvature_{fMRI}$ variables were central to the hypotheses of the present study because they decomposed MID incentive functions into valence and magnitude dimensions; therefore, these two variables were chosen as predictors. Sensation seeking and Urgency represent

different aspects of impulsive sensation seeking [29] that have been implicated in risk for alcohol use and abuse [42–43] and have been associated with different drinking behaviors [44], as discussed in the Introduction. However, the zero-order correlations of these two personality measures with MAST and ALC scores indicated that only SS showed modest correlations (with MAST: $r=.17$, $p=.12$, $n=82$; with ALC: $r=.29$, $p=.016$, $n=70$) whereas urgency did not ($p's > .38$). Therefore, SS was chosen as a personality predictor. Zero-order correlations also showed that $slope_{speed}$ and $curvature_{speed}$ were strongly associated with $curvature_{fmri}$ from 6 of the ROIs ($p < .05$) and marginally significant with the right caudate body cluster ($p < .069$). Therefore, to avoid multicollinearity issues, performance variables were not included as predictors.

Fourteen regressions were conducted using each of the 14 ROI's (from Tables 1 and 2) $slope_{fmri}$ and $curvature_{fmri}$ parameters and SS as predictors and MAST as the outcome variable. We report the regression results for all models and note which models were significant at both an uncorrected level ($p=.05$) or at a Holm-corrected level [45].

A tertiary analysis explored whether these predictor variables were associated with current alcohol use (ALC; which was the sum of the responses to the four alcohol-related items of the drug-use questionnaire indicating how many days in the past month the participant consumed wine, beer, wine coolers or hard liquor). However, this measure contained responses of 0 from 30 participants which indicated either no drinking days or responses that were not easily coded into number of days. Therefore, 0 values were omitted from the ALC measure before submitting to regression analyses. We also conducted all regressions using high-gain and high-loss fMRI responses instead of $slope_{fmri}$, $curvature_{fmri}$ responses as predictors in order to assess whether valence ($slope_{fmri}$) and magnitude ($curvature_{fmri}$) were more strongly associated with individual differences in MAST or ALC than simply using fMRI signal from high-loss or high-gain conditions.

3. Results

3.1 MID performance

Average accuracy was 65.1%, which is close to the expected value of 66.7%. There were no group differences or interactions in speed or accuracy (see Appendix B for details).

3.2 Voxel-wise results

The gain-sensitive and magnitude-sensitive contrasts for each trial phase are shown in Figure 2 (top). The magnitude-sensitive contrasts revealed extensive group-averaged activation in both the cue and feedback phases, whereas the activation for gain-sensitivity was less extensive. The ROIs resulting from the union of the gain- and magnitude-sensitive contrasts masked by anatomical regions are shown in Figure 2 (bottom).

3.3 Linear regression results with problem drinking (MAST) as the outcome

As shown in Table 3, fMRI response in the majority of the cue and feedback ROIs was associated with MAST scores. (Many of the models were significant at an uncorrected level with others showing a trend toward significance; however, the minimum p-value needed for

Holm-correction was .00625 for models using cue phase ROIs and .0083 for models using feedback ROIs. None of the models was significant at this level). Interestingly, MAST scores were primarily associated with incentive magnitude ($\text{curvature}_{\text{fmri}}$) and less so with valence ($\text{slope}_{\text{fmri}}$). Regression coefficients for the $\text{curvature}_{\text{fmri}}$ parameter were all negative, indicating that higher MAST scores were associated with lower or more negative curvature of the fMRI incentive functions. To illustrate this in a different way, Figure 3 shows curvature of the fMRI incentive functions of three different MAST groups in the ROIs for which the overall model was significant. The three MAST groups were determined using tertiles: high MAST scores (≥ 5 ; $n=38$), intermediate MAST scores (3 to 4; $n=18$) or low MAST scores (0 to 2; $n=26$). Note that the regressions (which were the primary analyses) were based on the entire group of subjects and the graphs in Figure 3 are merely to illustrate the behavior of the slope and curvature properties of the fMRI incentive functions for different ranges of MAST scores.

In the cue phase, the high-MAST group (green) showed an attenuated fMRI response for high-loss or high-gain conditions, compared to the low and intermediate MAST groups, in the caudate, putamen and thalamus (Figure 3a–f). Hence, the high-MAST group was relatively less sensitive to large values (either gains or losses) in the cue phase. MAST scores were also predicted by incentive valence in the right accumbens. As shown in Figure 3g, the high-MAST group showed a more positive slope compared to the other two groups, indicating greater gain-sensitivity.

In the feedback phase, a different picture emerged compared to the cue phase. The high-MAST group showed incentive functions that were markedly different from the other two MAST groups. In the left putamen (Figure 4a), the two lower MAST groups showed greater loss sensitivity and high magnitude sensitivity compared to the high-MAST group, which showed no magnitude or valence sensitivity. In the right caudate (Figure 4b) the two lower MAST groups showed greater loss sensitivity and magnitude sensitivity but the high-MAST group showed gain sensitivity. SS was also associated with MAST scores in some of the models. We also noted that the right caudate cluster was dissociated into clear dorsal and ventral components which mapped onto gain- and magnitude-sensitivity in the original zmaps (Figure 2). Given that the dorsal and ventral striatum are thought to have different roles in the development of addiction [53], we examined incentive functions separately in these two regions (Figure 4c–d). The right ventral caudate generally showed magnitude sensitivity whereas the right dorsal caudate generally showed gain sensitivity (consistent with the original contrasts that isolated this region). However, in each region, the high-MAST group deviated from the other MAST groups by showing gain-sensitivity in the ventral caudate and magnitude sensitivity in the dorsal caudate. Regressions using these regions yielded significant models for both ($p < .004$, $R^2 = .16$ for the right dorsal caudate; $p < .028$, $R^2 = .11$ for the right ventral caudate) but only the right dorsal caudate regression survived Holm correction. In that region, $\text{curvature}_{\text{fmri}}$ was the only significant predictor ($b = -.35$, $p = .002$). In the right ventral caudate, all three predictors were significant (p 's $< .044$; b 's $= .25, -.23, .22$ for $\text{slope}_{\text{fmri}}$, $\text{curvature}_{\text{fmri}}$, SS, respectively).

Results for the regressions conducted with high-gain_{fmri} and high-loss_{fmri} as predictors instead of $\text{slope}_{\text{fmri}}$ and $\text{curvature}_{\text{fmri}}$ variables are in Table 4. These analyses were

conducted to determine whether MAST scores were more strongly associated with measures commonly used in other studies (i.e., fMRI signal in the high incentive conditions) than the derived parameters ($\text{slope}_{\text{fmri}}$ and $\text{curvature}_{\text{fmri}}$) presented here. In general, using high-gain_{fmri} and high-loss_{fmri} as predictors also yielded significant models that had similar levels of explained variance compared to using the derived parameters. (Two of the models, the left caudate and left putamen would pass the minimum threshold for Holm-correction). In some cases, the explained variance was higher using high-gain_{fmri} and high-loss_{fmri} as predictors (left caudate, accumbens and putamen in the cue phase) but in most cases explained variance was lower or equal (left thalamus, right caudate, right accumbens, right putamen, right thalamus in the cue phase; left putamen and right caudate for feedback phase). Interestingly, the high-loss_{fmri} predictor, but not the high-reward_{fmri} predictor, was significantly associated with MAST scores. In addition, SS was a significant predictor of MAST for most of the models. This finding contrasts with the regression results using $\text{curvature}_{\text{fmri}}$ and $\text{slope}_{\text{fmri}}$ as predictors because two variables were needed to explain about the same amount of variance as only the $\text{curvature}_{\text{fmri}}$ variable (Table 3), suggesting that $\text{curvature}_{\text{fmri}}$ more parsimoniously explains individual differences in problem drinking, as measured by the MAST.

The same regression analyses were conducted with only those cases where ALC scores were greater than 0. Results were fundamentally the same except that some models and coefficients that were significant in Table 3 became marginal (see Appendix C).

3.4 Correlations with performance

Many fMRI studies of the MID task examine activation related to reward versus loss notification in the feedback stage. We did not conduct a voxel-wise analysis to separate out reward/loss notification because the number of trials for each type of notification was low (i.e., with overall accuracy constrained to approximately 67%, $n \sim 6$ for loss notification; $n \sim 12$ for reward notification) so this analysis would be underpowered. Nevertheless, we addressed the issue of reward/loss notification in a different way. Higher accuracy in the potential gain conditions indicates more frequent reward notification whereas lower accuracy in the potential loss conditions indicates more frequent loss notification. Therefore, each participant's accuracy for each incentive condition can be correlated with the corresponding fMRI signal for each incentive condition to determine whether the activation was related to reward or loss notification. These correlations help determine whether the fMRI response was related to task performance. We focused these correlations on the two feedback stage regions (left putamen and right caudate) in which the regressions with MAST were significant because the feedback stage is when reward/loss notifications occurred. None of these correlations was significant in any of the feedback stage ROIs.

However, correlations were also conducted between accuracy in the different incentive conditions and the $\text{curvature}_{\text{fmri}}$ and $\text{slope}_{\text{fmri}}$ parameters to determine whether the different shaped incentive functions in Figure 4c–d were related to reward or loss notification. In the right dorsal caudate body higher accuracy in the high-loss condition was associated with positive $\text{curvature}_{\text{fmri}}$, and lower accuracy was associated with more negative curvature ($r = .37$, $p = .001$, $n = 82$). In other words, the pronounced convexity in the right caudate body

(negative curvature symbol in Figure 5a) was associated with higher loss notification and the pronounced concavity was associated with higher loss avoidance for the high loss condition. In contrast, higher accuracy in the small-loss condition was associated with more negative curvature (and lower accuracy was associated with more positive curvature; Figure 5b). Taken together, these correlations indicated that the right dorsal caudate body convexity exhibited in the high MAST group was driven by both higher loss avoidance for small losses and higher loss notification for large losses.

3.5 Linear regression results with recent alcohol use (ALC) as the outcome

Table 5 shows linear regression results with ALC as the outcome variable, only including cases in which ALC scores were greater than 0 ($n=52$; see Appendix C for results that include cases where any numeric response was provided). In contrast to the regressions with MAST as the outcome variable, ALC scores were primarily associated with incentive valence ($\text{slope}_{\text{fmri}}$) and SS. The regression coefficients for the $\text{slope}_{\text{fmri}}$ parameter were all negative, indicating that higher ALC scores were predicted by a lower $\text{slope}_{\text{fmri}}$ value. To visualize this, Figure 6a–b shows the slopes of the fMRI incentive functions according to ALC scores that were low (1 to 4 drinking days), intermediate (5 to 11 drinking days) and high (more than 16 drinking days) in the two cue-phase ROIs associated with significant models in Table 6 (bilateral thalamus). Interestingly, the low-ALC group showed pronounced gain-sensitivity but as number of drinking days increases, the slope of the incentive function becomes flatter, with the high ALC group showing no sensitivity to valence. This flatter slope was largely driven by higher fMRI signal in the high loss condition. For the feedback-phase ROI (left thalamus), incentive magnitude (curvature) was the significant predictor of ALC. As illustrated in Figure 6c, the high-ALC group shows stronger sensitivity to incentive magnitude than the other two groups.

When the regressions were conducted with $\text{high-loss}_{\text{fmri}}$ and $\text{high-gain}_{\text{fmri}}$ as the fMRI predictors (Table 6), the same two models for the cue ROIs (bilateral thalamus) were significant and explained variance was almost identical. The regression coefficients for the $\text{high-loss}_{\text{fmri}}$ variable were all positive, indicating that a higher fMRI response in the high-loss condition was associated with greater ALC scores (as also illustrated clearly in Figure 6). The model for the feedback ROI (left thalamus) was no longer significant. In sum, these regressions indicate that higher ALC scores were most strongly associated with fMRI signal in the high-loss condition, primarily in the cue phase.

4. Discussion

The present study demonstrates that neurobehavioral response on the MID task and sensation seeking personality trait are associated with individual differences in drinking behavior, similar to other findings [8, 16, 24]. One novel contribution of the present study, however, was in isolating the influence of incentive valence (positive reinforcement v. avoidance contingencies during the cue phase; gain v. loss during the feedback phase) from the influence of incentive magnitude (low and high incentives) by modeling fMRI response to gains and losses as a quadratic function, rather than using percent signal change (or their difference score) between different incentive conditions, the analytic approach most

commonly used in previous studies. Interestingly, incentive magnitude (curvature of the quadratic fit) explained individual differences in problem drinking whereas incentive valence (slope of the quadratic fit) explained individual differences in recent alcohol use, as summarized in Figure 7.

High sensation seeking was associated more with higher problem drinking than with higher recent use, and fMRI responses during cue (Appetitive behavior) and feedback (Consummatory behavior) trial phases were differentially associated with problem drinking and recent use. Specifically, reduced appetitive fMRI response in mesolimbic regions (downward red arrow in Figure 7a) was associated with problem drinking whereas increased appetitive fMRI response (upward red arrow in 7b) was associated with recent use. Decreased consummatory fMRI response in the ventral striatum (left putamen and right ventral caudate) was associated with problem drinking but increased consummatory response in the thalamus was associated with recent use (blue arrows in Figure 6). In addition, increased consummatory response in the right dorsal caudate was associated with problem drinking but not with recent use. Taken together, these findings suggest that two different aspects of alcohol drinking behavior are dissociated from each other with respect to neurobehavioral signatures of incentive motivation. Specifically, problem drinking is associated with reduced consummatory and appetitive mesolimbic system response for high incentives, but increased consummatory response to small incentive values. In contrast, recent alcohol use is associated with increased appetitive mesolimbic system response to avoidance contingencies and increased consummatory mesolimbic response to high gains. Because problem drinking as measured by the MAST reflects some behaviors that are associated with DSM-IV criteria for alcohol abuse or dependence [37, 46], people who scored higher on the MAST might be considered at higher risk for abuse.

Some prior findings have reported enhanced mesolimbic reward system responses during the cue phase in individuals who are high in impulsivity/disinhibition, sensation seeking or approach personality [10–11] or who show problematic externalizing behaviors [8]. These findings are consistent with the opponent process framework of motivation [47–48] which predicts hypersensitivity to reward anticipation or outcome on the MID task [47]. This hypersensitivity to reward is consistent with the Robinson and Berridge [3] perspective that transition to dependence is associated with increased “wanting” (Appetitive cue phase) but no change or a subtle decrease in “liking” (Consummatory feedback phase). The present study demonstrated a dissociation between the cue and feedback phases in that high-risk drinkers showed a completely opposite response in the Consummatory phase (in the right dorsal caudate nucleus) than in the Appetitive phase (green incentive functions in Figure 3a–f versus Figure 4d). This finding is consistent with the idea that liking and wanting may become dissociated in the transition to dependence. However, the direction of the effects is not necessarily consistent with the idea of increased wanting and decreased liking given that the high-risk drinkers showed an attenuated appetitive response in mesolimbic regions but a more pronounced consummatory response in the right dorsal caudate compared to low-risk drinkers.

Findings from the present study are more consistent with the reward deficiency syndrome [49] and allostatic [50] hypotheses of motivation which suggest that individuals with, or at

risk for, substance dependence have a deficit in recruiting dopaminergic motivational circuitry in response to non-drug rewards. The present study showed that attenuated anticipatory and consummatory responses to high incentive values (downward arrows in Figure 7) emerged in individuals with more problematic drinking. Indeed, Schneider et al. [15] showed that increased risk-taking bias in young adults and adolescents was associated with attenuated ventral striatum activation for large reward cues versus baseline and that this attenuation was even more pronounced in a sub-group of participants that showed signs of nicotine dependence or alcohol abuse according to well accepted self-report scales. An attenuated reward response has also been observed in detoxified alcoholics [51–52] and in individuals with a positive family history for alcoholism ([8, 20]; but see [18]).

Another aspect of the present findings that was consistent with the reward deficiency syndrome framework was the dissociation of problem drinking and recent alcohol use based on the dorsal striatum response. Sensitivity to incentive magnitude in the dorsal striatum during feedback was associated with problem drinking but not with recent use. In addition, magnitude sensitivity in the dorsal caudate nucleus was significantly associated with problem drinking and explained more variance than magnitude sensitivity in the ventral caudate. Increased engagement of the caudate nucleus and dorsal striatum has been linked to the transition from recreational to compulsive drug seeking by reinforcing stimulus-response habit learning [53]. In the present study, the shape of the right dorsal caudate incentive function that was associated with individuals who reported more drinking problems was also associated with higher loss notification for high losses and higher loss avoidance for small losses. This profile suggests altered sensitivity to magnitude of reinforcement, with decreased sensitivity to receipt of high losses and increased sensitivity to avoidance of small losses. Decreased sensitivity to magnitude of reinforcement has also been demonstrated in self-administration studies in humans. People at risk for substance dependence (due to sensation seeking personality trait) work equally hard to earn small and large drug doses, whereas people not at risk will show greater motivation for the large than small dose [5]. Similarly, non-dependent heroin users work equally hard to earn a small dose of morphine as higher doses even though subjective effects were only evident for higher doses [6]. The changes in sensitivity related to incentive magnitude in the right dorsal caudate in the present study, then, may reflect neuroadaptations that are linked to risk for alcohol abuse or substance dependence [54]. Although speculative, the decreased sensitivity to magnitude of reinforcement may be driven by increased compulsive drug seeking behaviors that are engaged regardless of incentive magnitude.

Heightened sensitivity to small incentives in the right dorsal caudate may reflect greater salience of small incentives or coding the relative value of the incentive conditions. Zink et al. [55] reported that behaviorally relevant but non-rewarding stimuli can activate the caudate nucleus which is consistent with the present finding of higher dorsal caudate response to small incentives in problem drinking. In addition, Nieuwenhuis et al [56] reported that the left caudate (and other regions) showed the greatest response to a monetary incentive that was the best possible outcome for a given range of values; that is, when a neutral condition (no loss) was in the context of only losses, it was the best outcome and yielded the strongest caudate response that was comparable to responses in the highest gain condition amongst a range of gain incentive conditions. In the present study, caudate

response was enhanced for feedback on small gains (Figure 4d) but reduced for feedback on large losses (Figure 4a and c) and this pattern was most pronounced for people who reported drinking problems. Therefore, it is possible that the relative salience of low-gain feedback increases, while the salience of high-loss feedback decreases in association with problem drinking. This altered consummatory incentive processing may be an early indicator of problem drinking.

The present study also examined whether sensation seeking was associated with problematic drinking and recent alcohol use. Prior literature has shown that impulsivity in the form of urgency is more commonly related to alcohol problems whereas sensation seeking is more commonly related to alcohol use and consumption [57–61]. One goal of this study was to determine whether mesolimbic system response in combination with impulsive personality measures could contribute to the assessment of substance abuse vulnerability. Urgency was not strongly associated with alcohol use in the present study (and was not used in the regressions for this reason). However, sensation seeking was more strongly associated with problem drinking than with recent use. Nees et al. [24] reported that personality variables were more closely associated with early onset drinking than were MID brain responses, but that study used only adolescents, who are reported to have reduced appetitive ventral striatal activation on the MID compared to young adults [17, 38]. Also, the greater contribution of MID fMRI response in the present study may be due to modeling incentive magnitude across all valence levels versus only contrasting high versus low gains. MID tasks that incorporate both losses and gains may better differentiate at risk or substance-dependent samples from controls [62]. Interestingly, in the present study, modeling incentive magnitude more parsimoniously explained drinking problems compared to modeling high-gains and high-losses, which also explained drinking problems, but sensation seeking was needed to explain the same amount of variance as incentive magnitude alone in some of the models. Therefore, mesolimbic MID response does appear to explain variation in problem drinking. Mesolimbic MID response also explained some of the variance in alcohol use, primarily in terms of loss anticipation (incentive functions in Figure 6).

The present study had some limitations that should be considered in the interpretation of the results. The MID task is fairly demanding and requires vigilance and sustained attention to perform. Although participants had a break half-way through the task, the task was administered after several other fMRI tasks, at the end of the testing session. Participants in this study were neurotypical and reported no psychiatric conditions, behavioral problems or learning disability, but half of the participants scored high on impulsivity personality measures. Consequently, some of the participants may not have been able to maintain adequate levels of attention to perform at optimal levels, although no group differences in task performance were observed. Another concern was that the measure used for recent alcohol use was not a standardized measure. Some of the participants' responses were not easily coded and some participants reported no alcohol use in the past 30 days, which led to omission of some data from the analysis of recent alcohol use. Nevertheless, the fundamental dissociations between problematic and recent drinking outlined in Figure 7 persisted when only the subset of participants who reported some drinking were included in the regression analyses (Appendix C). Another limitation was that most of the regression models did not survive correction for multiple tests; therefore, replication of the present

findings would be needed. Finally, participants were not selected based on problematic drinking or recent alcohol use. Although we referred to individuals with high MAST scores as a “high-risk” group, we did not measure a constellation of other risk factors, such as externalizing behaviors or familial risk, as examined in other studies [8, 19, 63]. Nevertheless, risk status was determined by the MAST, and some participants in the high-risk group reported adverse effects of drinking on relationships and employment, DUI and alcohol-related hospitalizations. Therefore, while the high-risk group did not meet the cutoff for alcohol dependence [37, 46], they did report significant problems associated with alcohol.

4.1 Conclusions

The present findings suggest that individuals who report problematic drinking but who are not alcohol dependent may show neuroadaptations of mesolimbic reward circuitry during a MID task that are consistent with findings in individuals who are alcohol dependent or at risk due to family history or externalizing behaviors. Problem drinking and recent use were associated with altered response during both appetitive and consummatory processing during the MID task. Neuroadaptations related to problem drinking included mesolimbic hypo-responsiveness to reinforcement magnitude during the cue phase, hyper-responsiveness to small gains and hypo-responsiveness to large losses during feedback. This profile reflects altered sensitivity to incentive magnitude in people who report problem drinking, possibly driven by tendencies to respond to reinforcers regardless of incentive value. Additional research is required to determine whether this neurosensitivity is predictive or a consequence of alcohol use, and whether sensitivity to the specific dimensions of magnitude and valence can be used to differentially inform vulnerability to alcohol use or the emergence of problems associated with alcohol use.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Monetary incentive delay (MID) fMRI response was measured in non-dependent drinkers
- Impulsive sensation seeking predicted drinking problems
- MID fMRI response to incentive magnitude predicted drinking problems
- MID fMRI response to incentive valence predicted alcohol use
- Altered fMRI MID response in problem drinking may be a precursor to dependence

Figure 1.

(a) Monetary Incentive Delay task used in the present study. Participants could earn or lose money depending on speed of responding to a target stimulus (white rectangle). Each trial consisted of cue, target and feedback phases. The cue phase displayed a monetary value that could be won or lost. The target phase consisted of a simple stimulus presented briefly, and participants were instructed to respond within the duration of the target display (on the order of 250 ms). If the response time was less than the target duration a checkmark appeared on the feedback screen and the participant earned or avoided losing money. If the response time exceeded the target duration, an X appeared on the feedback screen and the participant did not win or incurred a loss of money. Across trials, the target display duration was adjusted to maintain trial accuracy at 67% (b) The $\text{slope}_{\text{fMRI}}$ parameter indicates the slope of the linear component of a quadratic function fit to the fMRI signal in the different incentive conditions. A positive $\text{slope}_{\text{fMRI}}$ indicates greater fMRI response to positive incentive values and a negative $\text{slope}_{\text{fMRI}}$ indicates greater fMRI response to negative incentive values. (c) The $\text{curvature}_{\text{fMRI}}$ parameter indicates the degree of curvature of the quadratic function. A $\text{curvature}_{\text{fMRI}}$ value of 0 indicates no curvature; a positive $\text{curvature}_{\text{fMRI}}$ value indicates greater concavity and a negative $\text{curvature}_{\text{fMRI}}$ value indicates greater convexity. In other

words, a more concave function would reflect greater fMRI signal for the extreme compared to small incentive values but a more convex function would reflect a greater fMRI signal for small values.

Figure 2.

Activation maps isolated by the gain-sensitive contrast (red-yellow) and magnitude-sensitive contrast (blue-purple) for cue and feedback phases of the MID. The gain- and magnitude-sensitive activation maps were then combined using logical “or” and masked by anatomical regions.

Figure 3.

(a-f) Curvature of incentive functions in cue-phase ROIs that were associated MAST scores.
 (g) Slope of incentive functions in cue-phase ROIs that were associated MAST scores. Each line represents the average incentive function for each MAST group.

Figure 4.

(a–b) Curvature of incentive functions in feedback-phase ROIs that were associated MAST scores. (c) Curvature of incentive function in the right ventral caudate ROI. (d) Curvature of incentive function in right dorsal caudate ROI. Each line represents the average incentive function for each MAST group.

Figure 5.

(a) Correlation between accuracy in the high loss condition and curvature_{fmri} in the right dorsal caudate. (b) Correlation between accuracy in the small loss condition and curvature_{fmri} in the right dorsal caudate body. The trendlines reflect the correlation for the whole sample, but the different MAST groups are color coded separately.

Figure 6.

(a–c) Slope of incentive functions in ROIs that were associated with ALC scores. Each line represents the average incentive function for each ALC group.

Figure 7.

Summary of results illustrating the significant variables that explained variance in problem drinking (left) and recent alcohol use (right) in the present study: sensation seeking (green arrows), appetitive fMRI response (i.e., responses in the cue phase; red arrows), consummatory fMRI response (i.e., response in the outcome phase; blue arrows). Direction of each arrow indicates the direction of the association with higher problem drinking or higher recent alcohol use.

Table 1

Union of Gain-sensitive and Magnitude-Sensitive Regions in the Cue Phase

Region	Size (voxels)	Max MNI		
		x	y	z
Left Caudate	1126	-13	7	10
Left accumbens	416	-10	12	-7
Left Putamen	1541	-25	0	0
Left Thalamus	1792	-11	-20	6
Right Caudate	1328	14	8	11
Right accumbens	424	10	13	-6
Right Putamen	1949	26	1	0
Right Thalamus	1843	12	-19	6

Table 2

Union of Gain-sensitive and Magnitude-Sensitive Regions in the Feedback Phase

Region	Size (voxels)	Max MNI		
		x	y	z
Left Caudate	448	-13	7	10
Left Putamen	1654	-25	0	0
Left Thalamus	1697	-11	-20	6
Right Caudate	553	14	8	11
Right Putamen	1612	26	1	0
Right Thalamus	1709	12	-19	6

Table 3

Results of Linear Regression Analysis with MAST as Outcome Variable and curvature_{fMRI} and slope_{fMRI} as fMRI predictors, and Sensation Seeking (SS) as the personality predictor

Region	Model F(3, 81)	p	R ²	Predictor	b	p
<i>Regions from Cue Phase</i>						
L caudate	3.82	.013*	.13	curvature _{fMRI}	-.31	.005
L accumbens	2.33	.081	.08	curvature _{fMRI}	-.22	.049
L putamen	3.89	.012*	.13	curvature _{fMRI}	-.30	.008
L thalamus	3.55	.018*	.12	curvature _{fMRI}	-.30	.006
R caudate	4.00	.011*	.13	curvature _{fMRI}	-.31	.005
R accumbens	3.02	.035*	.10	slope _{fMRI}	.23	.037
R putamen	3.21	.027*	.11	curvature _{fMRI}	-.27	.013
R thalamus	3.48	.020*	.12	curvature _{fMRI}	-.30	.007
<i>Region from Feedback Phase</i>						
L caudate	2.04	.116	.07	none		
L putamen	3.26	.026*	.12	curvature _{fMRI}	-.28	.019
				slope _{fMRI}	.23	.047
				SS	.25	.026
L thalamus	1.93	.131	.07	SS	.23	.048
R caudate	3.53	.019*	.12	curvature _{fMRI}	-.31	.009
				SS	.22	.047
R putamen	2.54	.062	.09	SS	.23	.040
R thalamus	1.80	.154	.07	none		

Note: Curvature_{fMRI} refers to the coefficient for the quadratic fit of the fMRI incentive function. SS, UPPS Sensation Seeking. b, standardized parameter estimate.

* model is significant at $p < .05$;

** model is significant at Holm corrected level (.00625 $< p < .05$ for cue phase models; .0083 $< p < .05$ for feedback phase models).

Table 4
Results of Linear Regression Analysis with MAST as Outcome Variable and high-loss_{fMRI} and high-reward_{fMRI} as fMRI predictors, and Sensation Seeking (SS) as the personality predictor

Region	Model F(3, 81)	p	R ²	Predictor	b	p
<i>Regions from Cue Phase</i>						
L caudate	4.48	.006**	.15	high-loss _{fMRI}	-.24	.038
				SS	.22	.038
L accumbens	3.89	.012*	.13	high-loss _{fMRI}	-.26	.024
L putamen	5.04	.003**	.16	high-loss _{fMRI}	-.29	.023
				SS	.22	.041
L thalamus	3.10	.031*	.11	SS	.22	.049
R caudate	3.55	.018*	.12	high-loss _{fMRI}	-.24	.005
R accumbens	2.61	.058	.09	high-loss _{fMRI}	-.28	.027
R putamen	3.22	.027*	.11	none		
R thalamus	3.04	.034*	.11	SS	.22	.049
<i>Region from Feedback Phase</i>						
L caudate	2.57	.061	.09	high-loss _{fMRI}	-.23	.045
				SS	.23	.039
L putamen	3.13	.030*	.11	high-loss _{fMRI}	-.28	.017
				SS	.24	.032
L thalamus	2.18	.097	.08	SS	.23	.048
R caudate	3.06	.033*	.11	high-loss _{fMRI}	-.26	.020
				SS	.23	.041
R putamen	2.53	.064	.09	high-loss _{fMRI}	-.25	.030
				SS	.23	.040
R thalamus	1.89	.137	.07	none		

Note: High reward refers to the fMRI signal in the high-gain condition. High-loss refers to the fMRI signal in the high-loss condition. b, standardized parameter estimate.
* model is significant at $p < .05$;

** model is significant at Holm corrected level (.00625 < p < .05 for cue phase models; .0083 < p < .05 for feedback phase models).

Table 5

Results of Linear Regression Analysis with ALC as Outcome Variable and curvature_{fMRI} and slope_{fMRI} as fMRI predictors, and Sensation Seeking (SS) as the personality predictor

Region	Model F(3, 51)	p	R ²	Predictor	b	p
<i>Regions from Cue Phase</i>						
L caudate	2.25	.095	.12	none		
L accumbens	1.46	.236	.08	none		
L putamen	2.46	.074	.13	none		
L thalamus	4.04	.012*	.20	slope _{fMRI}	-.37	.007
R caudate	2.64	.060	.14	slope _{fMRI}	-.27	.050
				SS	.27	.049
R accumbens	1.61	.198	.09	none		
R putamen	2.67	.058	.14	slope _{fMRI}	-.28	.047
R thalamus	4.24	.010*	.21	slope _{fMRI}	-.38	.005
<i>Region from Feedback Phase</i>						
L caudate	2.03	.123	.11	none		
L putamen	2.31	.088	.13	none		
L thalamus	2.98	.041*	.16	curvature _{fMRI}	.29	.046
R caudate	1.99	.128	.11	none		
R putamen	2.13	.109	.12	none		
R thalamus	2.50	.071	.14	none		

Note: Slope_{fMRI} refers to the coefficient for the linear fit of the fMRI incentive function. SS, UPPS Sensation Seeking. b, standardized parameter estimate.

* model is significant at p < .05;

** model is significant at Holm corrected level (.00625 < p < .05 for cue phase models; .0083 < p < .05 for feedback phase models).

Table 6

Results of Linear Regression Analysis with ALC as Outcome Variable and high-loss_{fMRI} and high-reward_{fMRI} as fMRI predictors, and Sensation Seeking (SS) as the personality predictor

Region	Model F(3, 81)	p	R ²	Predictor	b	p
<i>Regions from Cue Phase</i>						
L caudate	2.16	.105	.12	none		
L accumbens	1.44	.243	.08	none		
L putamen	2.48	.073	.13	none		
L thalamus	4.07	.012*	.20	high-loss _{fMRI}	.39	.008
R caudate	2.60	.063	.14	none		
R accumbens	1.49	.229	.09	none		
R putamen	2.71	.055	.15	high-loss _{fMRI}	.33	.042
R thalamus	4.04	.012*	.20	high-loss _{fMRI}	.38	.010
<i>Region from Feedback Phase</i>						
L caudate	1.88	.146	.11	none		
L putamen	1.90	.142	.11	none		
L thalamus	1.55	.214	.09	none		
R caudate	1.63	.194	.09	none		
R putamen	1.62	.196	.09	none		
R thalamus	1.39	.256	.08	none		

Note: High-loss_{fMRI} and high-reward_{fMRI} refer to the fMRI signal in the high-loss and high-reward conditions. b, standardized parameter estimate.

* model is significant at p < .05;

** model is significant at Holm corrected level (.00625 < p < .05 for cue phase models; .0083 < p < .05 for feedback phase models).