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Atypical contributions of reward decisions to momentary mood in individuals with methamphetamine use disorder

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Abstract

Background Individuals with Methamphetamine use disorder (MUD) are often accompanied by severe mood dysregulation, leading to more frequent irrational decisions such as drug-seeking behavior. Existing research indicates that the impairment of the reward system is central to the development of addiction. However, it remains unclear how the abnormal reward processing affects the mood regulation abilities of individuals with MUD. In this study, we explored the cognitive and computational mechanisms through which the subjective mood of individuals with MUD is influenced by reward information during decision-making.

Methods We recruited 76 male participants (27 with MUD, 49 healthy controls, HC) who completed a risk gambling task. In this task, participants were asked to choose between two options with certain or uncertain rewards. After every 2–3 gambling trials, participants also rated their momentary subjective happiness. We constructed multiple computational models to predict how various reward information (such as reward prediction error) influenced the short-term fluctuations in participants' subjective mood during risk decisions.

Results Individuals with MUD exhibited significantly more irrational decisions compared to the HC group. Computational modeling revealed that, compared to healthy controls, individuals with MUD showed a significantly weaker influence of various reward information (e.g., expected value, EV; reward prediction error, RPE) on their subjective mood. Importantly, the EV- and RPE-mood associations predict the degree of substance abuse.

Conclusions Our findings provide computational evidence that individuals with MUD lack effective regulation of mood by the reward system. This process leads to more substance abuse. These results shed new light on the mood issues in individuals with MUD from the perspective of reward processing, thereby helping to reduce drug use.

Clinical trial Not applicable.

Keywords Methamphetamine use disorder, Mood regulation, Decision-making, Reward processing

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Introduction

Substance use disorder is characterized by persistent consumption of specific substances, despite that individuals are fully aware of the harmful consequences, namely an inability to control drug-seeking desires and behaviors [1]. Among various substances, drug use significantly impairs both physical and mental health, and drives individuals toward irrational decision-making that jeopardizes social stability and public safety [2, 3]. Recent epidemiological studies have highlighted a global increase in the use of amphetamine-type stimulants such as methamphetamine and methcathinone [4–6], which have surpassed cannabis as the most commonly abused stimulant due to their potency and accessibility [7, 8]. Even more concerning, compared to other commonly abused stimulants, methamphetamine use disorder (MUD) is often associated with more severe cognitive decline and mood dysregulation [9], further exacerbating societal issues such as family disruption and a rising rate of deaths [10, 11].

Individuals with MUD are often associated with profound mood dysregulation. A substantial body of research has documented anxiety, depression, anhedonia, and emotional instability in individuals with MUD [12–15]. Over 50% of individuals with MUD have self-reported depressive symptoms [16, 17]. Functional neuroimaging studies reveal abnormal connectivity between the prefrontal cortex and the limbic system during emotional processing, supporting the presence of the impaired mood regulation in individuals with MUD [18]. Such mood dysregulation not only amplifies psychological distress but may also contribute to drug relapse [19]. According to the "negative reinforcement" model [20], the escape and avoidance of negative affect is the prepotent reason for addictive drug use. Drug taking exacerbates negative affect during the process of seeking temporary relief by compulsive drug taking, thereby creating the addiction cycle and hedonic comorbidities that are associated with addiction [21]. Therefore, identifying and addressing the underlying mood dysregulation in individuals with MUD is pivotal for improving clinical rehabilitation and mitigating relapse risk.

A bulk of human and animal studies have suggested abnormal reward processing as an important underlying mechanism of mood dysregulation in individuals with substance use disorders [22–25]. The aberrant reward processing may contribute to mood dysregulation in MUD via two distinct neurobiological mechanisms. First, methamphetamine exposure has been shown to induce diminished sensitivity to non-drug natural rewards (e.g., monetary gain and palatable food), leading to reduced pleasure and persistent anhedonia [26–28]. This reward hyposensitivity is thought to be associated with decreased dopaminergic transmission and reduced neural activation within the striatum and other reward-related regions [29, 30]. Second, the heightened sensitivity to drug-related cues results in overwhelming craving, which causes severe psychological distress and impairs mood regulation, particularly during withdrawal. Methamphetamine consumption directly alters neural circuits involving the striatum, limbic, and paralimbic regions, generating exaggerated motivational salience that contributes to anxiety and depressive symptoms during withdrawal and abstinence [31–33]. These results demonstrate a clear disruption in the integration of reward processing and affective states in individuals with MUD.

Despite substantial evidence for abnormal reward processing as a potential mechanism of mood dysregulation in MUD, several issues remain unclear. First, although past research has highlighted the long-term consequences of drug-taking on mood dysregulation, little is known about the short-term momentary mood fluctuations that occur during trial-and-error in sequential decision-making. Understanding these dynamics is crucial, as maladaptive decisions in MUD often prioritize immediate gratification over long-term controllable benefits. Second, how different types of reward information (e.g., reward prediction error, RPE) modulate real-time mood in MUD is not well understood. Addressing these gaps will enhance our knowledge of the interaction between compromised reward circuits, mood dysregulation, and maladaptive decision-making in MUD, guiding more precise interventions targeting mood regulation.

This study systematically examined computational mechanisms of atypical mood regulation during risky decision-making in males with MUD and matched controls. Participants performed a risky gambling task while reporting real-time subjective happiness as a measure of mood state. Combining behavioral experiments and computational modeling, our approach yields two key advancements: disentangling the effects of reward information (e.g., RPE) on mood fluctuations and showing how these reward-mood associations predict substance use severity. Our findings provide direct evidence that impaired reward processing underlies mood dysregulation in MUD and highlight its clinical relevance in maladaptive decisions and substance-seeking behaviors.

Methods and materials

Participants

We recruited 50 individuals with MUD from the First Drug Rehabilitation Center of Yunnan Province between July and August 2023. Fifty-seven healthy control participants were also recruited in Shanghai between February and July 2024. All participants were male because the First Drug Rehabilitation Center of Yunnan Province only received male patients. All participants had normal intelligence and were capable of understanding the

experimental procedures. Methamphetamine dependence was diagnosed according to the "Measures for the Identification of Drug Addiction" revised by the Ministry of Public Security of China in 2017 [34]. Participants were classified as methamphetamine-dependent if they met the following criteria: (i) positive drug tests from blood, urine, or saliva samples indicating the presence of drugs; (ii) evidence of drug use behavior; (iii) presence of withdrawal symptoms or historical evidence of drug use, including being apprehended by the police, undergoing voluntary detoxification, or testing positive for drugs in hair samples. Eleven patients were excluded during the screening process for using only heroin and not methamphetamine. We also applied the following exclusion criteria to all participants:

- Serious or unstable organic diseases (e.g., cancer, cardiovascular diseases, or head injuries);
- Other psychiatric disorders;
- Treatment for psychological or physical illnesses prior to recruitment.

These participants were also required to complete several questionnaires for further analysis. These questionnaires included basic demographic information, the Wechsler Adult Intelligence Scale (WAIS) -matrix reasoning for nonverbal IQ, the Self-Rating Depression Scale (SDS), the Self-Rating Anxiety Scale (SAS), the Barratt Impulsiveness Scale (BIS), the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) report [35–38], and questions about drug use and comorbidity history.

Four participants in the MUD group withdrew from the study for personal reasons. An additional 27 participants in both groups were excluded due to failure to follow the task instructions (e.g., constant mood ratings or decision-making patterns throughout the experiment). Some questionnaires were not completed due to participants' dropouts or unidentified contact information. Ultimately, data from 27 individuals with MUD (aged 16–50) and 49 healthy controls (aged 17–52) were included in the analysis.

The detailed demographic data are presented in Table 1.

Risky gambling tasks

The risky gambling task is illustrated in Fig. 1. Our risky gambling task followed the structure of previous studies [39]. At the beginning of the task, each participant was provided with a base virtual capital of 500 RMB. Their objective was to maximize their earnings throughout the task. In each trial, participants made a binary choice between an uncertain option (including two potential payoffs) and a certain option (offering a fixed payoff) within a 3-second time window. If no decision was made within this time window, the participant received the lowest reward among the three possible payoffs. The payoff of the certain option was constrained to fall between the two potential payoffs of the uncertain option. After a choice was made, the chosen option (either certain or uncertain) remained on the screen for 2 s, while the unchosen option disappeared. If the certain option was selected, the participant immediately received the corresponding payoff at the end of the 3-second display. If the uncertain option was selected, the uncertain option remained on the screen for 3 s, followed by 1-second outcome feedback. A fixation cross, randomly presented for 2–5 s (mean = 3 s), appeared before the next trial. The uncertain option offered two potential payoffs with equal probability, while the participant directly obtained its payoff once choosing the certain option.

After every two or three decision trials, participants completed a mood rating trial: "How happy are you at this moment?". Participants were asked to report their mood on a 100-point scale, ranging from "very unhappy" to "very happy", without time limits.

The entire experiment consisted of 60 decision trials and 22 mood-rating trials, and the whole risky gambling task lasted approximately 14 min. Prior to the main experiment, participants completed the practice session. The setup of the practice session was identical to that of the main experiment, except that the practice session only contained 6 decision trials and 2 mood rating trials. All experimental stimuli were programmed using jsPsych7 (Josh de Leeuw, Corp.) [40], and presented via a web browser.

Computational modelling construction

We constructed a computational model to account for moment-to-moment subjective mood [39]. The model has two key assumptions. First, mood ratings exhibit a linear dependence on temporally accumulated reward components from all preceding trials, specifically incorporating three parameters: chosen certain rewards (CRs), expected values (EVs), and reward prediction errors (RPEs). Second, the cumulative influence of preceding trials on current mood decays exponentially.

$$\begin{aligned} Happiness\,(t) = w_0 + w_1 \sum\nolimits_{j=1}^{t} \gamma^{\,t-j} CR_j \\ + w_2 \sum\nolimits_{j=1}^{t} \gamma^{\,t-j} EV_j + w_3 \sum\nolimits_{j=1}^{t} \gamma^{\,t-j} RPE_j \end{aligned} \quad (1)$$

Where $0 \le \gamma \le 1$ is the decay factor that simulates the forgetting of past events. t and j are trial numbers. Weights (w_1, w_2, w_3) of each component indicate the contribution of this component to mood ratings. w_0 is the baseline mood. The RPE and EV for the certain option and the CR for the uncertain option were set to zero. In addition to this model, we also constructed several other computational models that have different reward components.

Table 1 Demographic and clinical data and (standard deviations) by group

	MUD	HC	Stats. value	*p* value
Age (M ± SD, *n* = 27/49)	30.296 ± 8.691	35.163 ± 9.310	*t* = -2.232	0.029
Sex (male/female, *n* = 27/49)	27/0	49/0		
Drug intake (M ± SD, g/day, *n* = 25)	3.432 ± 4.780			
Withdrawal (M ± SD, month, *n* = 25)	10.680 ± 6.663			
Comorbidity history (yes/no, *n* = 25)	2/23			
SDS (M ± SD, ≤ 1 week, *n* = 25/40)	44.280 ± 7.760	37.650 ± 5.531	*t* = 4.019	< 0.001
SAS (M ± SD, ≤ 1 week, *n* = 25/40)	41.400 ± 10.516	32.050 ± 5.607	*t* = 4.673	< 0.001
BIS (M ± SD, *n* = 25/40)				
Motor	25.480 ± 11.136	22.725 ± 6.555	*t* = 1.258	0.213
Cognition	30.360 ± 10.230	23.425 ± 5.134	*t* = 3.629	< 0.001
No plan	30.120 ± 11.028	22.900 ± 6.983	*t* = 3.238	0.002
Drug type (*n* = 25)				
Crystal meth	*n* = 7			
Yaba	*n* = 14			
Crystal meth + Yaba	*n* = 4			
Drug addiction (M ± SD, now, *n* = 25)				
Drug desire	14.200 ± 7.331			
Drug negative reinforcement	8.400 ± 5.058			
Drug control	4.360 ± 2.885			
DSM-5 self-report (M ± SD, ≤ 2 week, *n* = 25/40)				
Depression	1.840 ± 1.818	2.300 ± 1.381	*t* = -1.155	0.252
Anger	1.120 ± 1.269	0.775 ± 0.733	*t* = 1.391	0.169
Manic	1.760 ± 1.589	2.300 ± 1.381	*t* = -1.447	0.153
Anxiety	2.040 ± 2.051	2.450 ± 1.934	*t* = -0.812	0.420
Somatization	2.320 ± 2.193	1.275 ± 1.601	*t* = 2.217	0.030
Suicide	0.600 ± 0.957	0.275 ± 0.599	*t* = 1.687	0.097
Psychiatric symptom	0.880 ± 1.333	0.650 ± 1.075	*t* = 0.764	0.447
Sleep	1.120 ± 1.166	1.050 ± 1.131	*t* = 0.240	0.811
Memory	0.760 ± 0.970	0.550 ± 0.714	*t* = 1.003	0.320
Repeat thoughts/action	1.920 ± 2.197	1.575 ± 1.679	*t* = 0.818	0.416
Dissociation	0.800 ± 1.000	0.550 ± 0.904	*t* = 1.041	0.302
Personality	1.840 ± 2.230	1.575 ± 1.866	*t* = 0.517	0.607
Substance use	2.200 ± 2.041	1.075 ± 1.509	*t* = 2.549	0.013

All details of computational models are documented in Supplementary Note 1.

We estimated model parameters for each individual using nonlinear least-squares regression implemented in MATLAB R2024b (The MathWorks, Inc.) [41], with the lsqnonlin function from the Optimization Toolbox. The objective function minimized the sum of squared errors between predicted and observed mood ratings. To ensure robust convergence and to avoid local minima, the fitting procedure was repeated 80 times with randomly initialized starting values. The parameter set yielding the lowest residual sum of squares was retained as the best fit for each participant. Parameter recovery analysis demonstrated excellent agreement between true and estimated parameters (see Supplementary Figure S2). Codes are publicly available via https://github.com/GITSyfX/CCNN-Decisionhappy.

Statistical analysis

To evaluate the behavioral signature of risky decision, we calculated the best choice rate and the uncertain choice rate of each participant. The best choice rate is the proportion of trials where a participant chose the option yielding a higher mean payoff. The best choice rate indicates the optimality of decision-making. The uncertain choice rate is the proportion of trials where a participant chose the uncertain option. The uncertain choice rate indicates the extent of risk-seeking propensity.

To assess the severity of substance use among participants, we computed the total score of the substance use subscale from the DSM-5 report. This subscale comprises three items evaluating the frequency and impact of substance use over the past two weeks (e.g., "Using any of the following medicines on your own, that is, without a doctor's prescription, in greater amounts or longer than

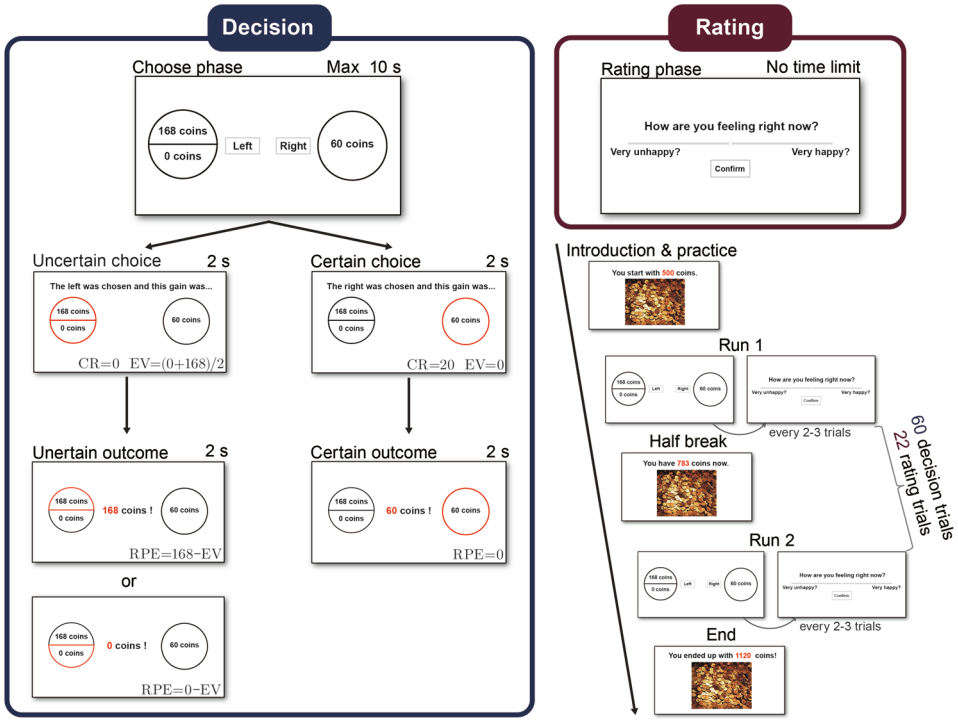

Fig. 1 Task design. Shown in the blue boxed line is the flow of a decision trial subset, participants made a choice between a certain option and an uncertain option. If participants made a certain choice, the outcome (i.e., 60 coins) would be presented immediately. If participants made an uncertain choice, they first saw two possible outcomes (i.e., 0 vs. 168 coins) and then saw the outcome (i.e., 0 or 168 coins). We show here the computation of CR, EV, and RPE in one trial and label the process where the computation takes place. Subjects will need to perform the calculations themselves during the actual task and will not see this content. Shown in the red boxed line is detail of a rating task. participants were instructed to indicate "How are you feeling right now?" by moving the squares to the appropriate position with the mouse. The lower right part of the figure shows the complete flow of the experiment. In the actual experiment, all text has been converted to Chinese

prescribed?"). Each item was rated on a 5-point Likert scale ranging from 0 ("none") to 4 ("severe"). The total score was obtained by summing the item responses, with higher scores reflecting greater severity of substance-use problems. Given the high comorbidity of anxiety and depression in the MUD group, we additionally assessed anxiety and depressive symptoms using the SAS and SDS, both consisting of 20 items rated on a 4-point Likert scale, with higher scores indicating greater symptom severity.

For all behavioral, model parameter, and symptom analyses, linear mixed model and Spearman correlation analysis were performed in JASP 0.19.3 (https://jasp-stats.org/) [42]. Marginal means adjusted for the effects were estimated using the Holm adjustment in JASP to specify contrasts (*t-tests*) between the MUD and HC groups. Our sample size was comparable to several previous studies employing similar experimental designs and computational modeling approaches [39, 43, 44].

Results

Atypical decision patterns of MUD in value-based decision-making

We first examined the behavioral performance of individuals with MUD in the risky gambling task. A series of linear mixed-effects models was constructed in JASP. In each model, *group* (MUD vs. HC) was included as a fixed effect, and *SAS* and *SDS scores* were entered as covariates to account for the high comorbidity of anxiety and depressive symptoms typically observed in individuals with MUD [45–47]. The dependent variables included log-transformed *reaction time* (with outliers beyond ±2 SDs from the mean excluded, *mood ratings*, *total earnings*, and *choice rate* (see Methods for details). In models for dependent variables assessed at the trial level (i.e., *reaction time*, *mood ratings*, and *choice rate*), *participant identity* was included as a random effect to account for inter-individual variability.

There was no evidence for a group effect in reaction time ($t_{(60.99)}$ = -0.305, p = 0.762, *Estimate* = -0.020, *SE* = 0.067, 95% *CI* = [-0.155, 0.114]). The mood ratings of individuals with MUD were slightly higher (though non-significantly so) than those of HCs ($t_{(61.00)}$ = 1.905, p = 0.062, *Estimate* = 7.097, *SE* = 3.726, 95%*CI* = [-0.354,

14.550]). The total earnings of individuals with MUD were significantly lower than those of HCs ($t_{(61.00)}$ = -2.185, p = 0.033, *Estimate* = -409.943, *SE* = 187.58, 95%*CI* = [-785.03, -34.85]; Fig. 2A).

Importantly, using the same model, we found that the individuals with MUD exhibited a significantly lower best choice rate than those of HCs ($t_{(61.00)}$ = -2.564, p = 0.013, *Estimate* = -0.095, *SE* = 0.037, 95%*CI* = [-0.169, -0.021]; Fig. 2B), indicating that the MUD group made less optimal decisions. There was no significant group difference in the uncertain choice rate ($t_{(61.00)}$ = -1.835, p = 0.071, *Estimate* = -0.092, *SE* = 0.050, 95%*CI* = [-0.193, 0.008]).

The subjective mood of individuals with MUD was less sensitive to reward information

In order to better understand the computational mechanisms of reward-based mood regulation in the two groups, we constructed 10 computational models that assume various reward components in previous trials impact mood ratings. These reward components include: (i) certain reward (CR), which indicates the amount of reward for the certain option in a trial; (ii) expected value (EV), which indicates the averaged reward for the uncertain option in a trial; (iii) reward prediction error (RPE), which indicates the difference between the outcome of the uncertain option and EV in a trial. We detail these components of an example trial in the caption of Fig. 1. Notably, the influence of reward components in previous trials on mood ratings in the current trial follows an exponential decay. We also considered other forms of reward components, such as uncertain reward (UR), which indicates the actual reward for the uncertain option in a trial. All 10 computational models incorporated different combinations of these reward components (see more details in Supplementary Note 1 and Supplementary Figure S1).

We quantitatively compared these models on all participants. The results showed that the model, including CR, EV, and RPE, and assuming the cumulative influence of all preceding trials on current mood decays exponentially, was the best-fitting model (Model 1, Eq. 1; Fig. 3A). The best-fitting model outperformed other models according to the Bayesian Information Criteria (BIC). The model was also the best-fitting model in the MUD and HC subgroups. We also calculated the posterior exceedance probability (PXP) and observed similar findings across the overall sample (Supplementary Figure S3). This model captured the trial-by-trial fluctuation of subjective mood ($r^2 = 0.529 \pm 0.218$, $t_{(75)} = 21.169$, $p < 0.001$; Fig. 3B).

This model allows us to quantify the extent to which different reward components contribute to momentary mood fluctuations by the weighting coefficients including the baseline mood w_0, CR coefficient w_1, EV coefficient w_2, and RPE coefficient w_3. Therefore, we defined these coefficients as reward-mood associations. The model also includes a decay factor γ.

Group comparisons revealed that individuals with MUD exhibited a significantly higher baseline mood w_0 compared with HCs (w_0: $t_{(74.00)} = 2.916$, $p = 0.005$,

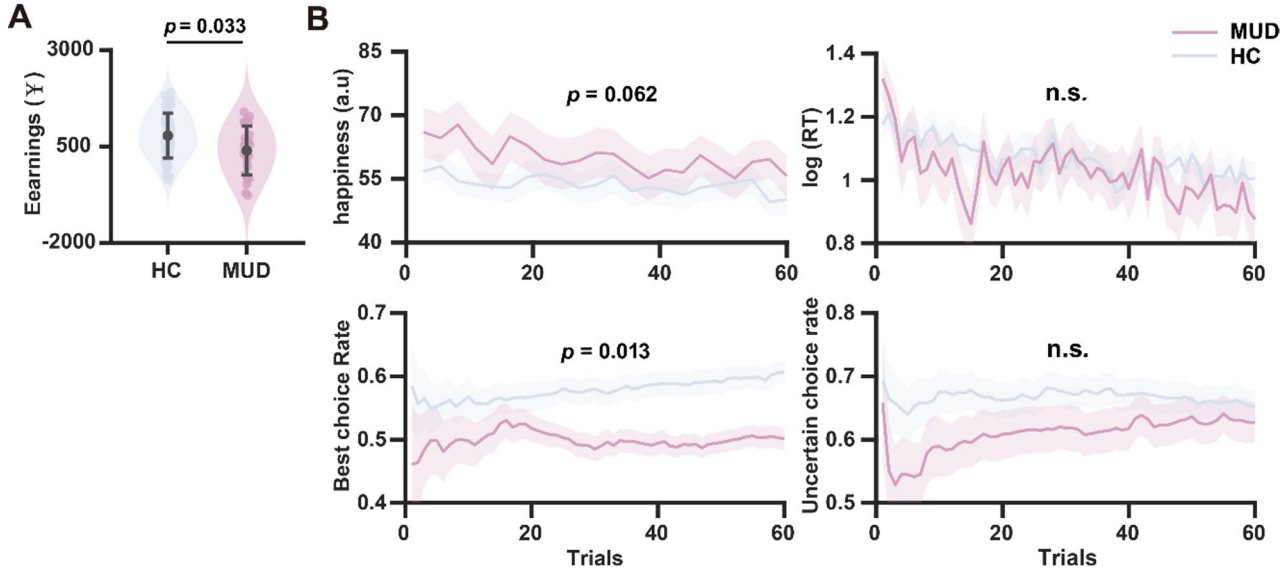

Fig. 2 Comparison of behavioral signatures in the risky decision-making task. (**A**) Total earnings. Total earnings (y-axis) are displayed for the MUD and HC groups (x-axis). The black dot and bar indicate the mean and standard deviation, respectively. Individual participant data are shown as scatter points, with shaded areas representing the data distribution. (**B**) Trial-level behavioral difference. The y-axis represents trial-by-trial behavioral indices, with reaction time (RT) log-transformed. The x-axis represents trial number. The lines indicate the mean trajectories for the MUD (purple) and HC (blue) groups, with shaded areas representing the standard error. Significance symbol convention is n.s.: non-significant

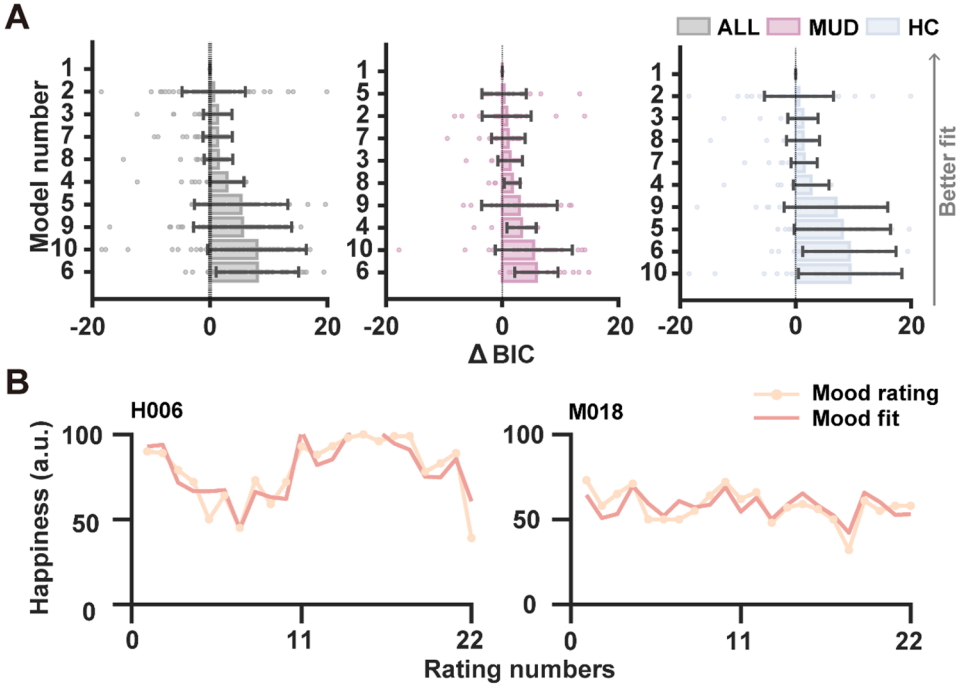

Fig. 3 Model fit results **A**. Model comparison. Discrepancies in BIC between each model and the best-fitting model (Model 1, Eq. 1) are shown as Δ values. The y-axis denotes the model number, with models arranged in order of fit quality, and the best-fitting model positioned at the top. Δ values are averaged across all subjects, with smaller Δ values indicating better model fit. **B**. Model fit in example participants. Mood ratings (y-axis) of two example participants are shown across all 22 trials (x-axis). The orange line with dots represents the observed mood ratings, and the red line indicates the fitted mood ratings

Estimate = 13.290, *SE* = 4.557, 95%*CI* = [4.210, 22.370]). In contrast, individuals with MUD exhibited significantly lower CR coefficient w_1 and EV coefficients w_2 (w_1: $t_{(74.00)}$ = -2.824, p = 0.006, *Estimate* = -0.158, *SE* = 0.056, 95%*CI* = [-0.270, – 0.047]; w_2: $t_{(74.00)}$ = -2.758, p = 0.007, *Estimate* = -0.073, *SE* = 0.026, 95%*CI* = [-0.125, -0.020]), as well as a marginally lower RPE coefficient w_3 (w_3: $t_{(74.00)}$ = – 1.935, p = 0.057, *Estimate* = -0.062, *SE* = 0.032, 95%*CI* = [-0.126, 0.002]). These results indicate attenuated reward-mood associations in individuals with MUD. No significant group difference was observed in decay factor γ (γ: $t_{(74.00)}$ = 1.348, p = 0.182, *Estimate* = 0.088, *SE* = 0.066, 95%*CI* = [-0.042, 0.219]).

To account for the potential confounding effects of anxiety and depressive symptoms, *SDS* and *SAS scores* were additionally included as covariates. After controlling for these factors, individuals with MUD continued to show a significantly higher baseline mood w_0 relative to HCs (w_0: $t_{(61.00)}$ = 2.228, p = 0.030, *Estimate* = 11.955, *SE* = 5.365, 95%*CI* = [1.226, 22.684]). Moreover, individuals with MUD exhibited marginally lower CR coefficient w_1 and significantly lower EV coefficient w_2 (w_1: $t_{(61.00)}$ = -1.995, p = 0.050, *Estimate* = -0.148, *SE* = 0.074, 95%*CI* = [-0.296, 0.000]; w_2: $t_{(61.00)}$ = -2.269, p = 0.027, *Estimate* = -0.077, *SE* = 0.034, 95%*CI* = [-0.154, -0.009]; Fig. 4). No significant group difference was observed in the RPE coefficient w_3 and decay factor γ after controlling for SDS and SAS scores (w_3: $t_{(61.00)}$ = – 1.696, p = 0.095, *Estimate* = -0.070, *SE* = 0.041, 95%*CI* = [-0.152, 0.012]; γ: $t_{(61.00)}$ = 0.363, p = 0.718, *Estimate* = 0.028, *SE* = 0.078, 95%*CI* = [-0.127, 0.184]).

Model parameters predict the severity of substance use

The above parameter analyses revealed group differences in multiple reward-related coefficients. We further examined how these reward-mood associations were associated with clinical symptom severity. Based on participants' self-reported assessments, we specifically assessed the severity of substance use, depressive, and anxiety symptoms (see Methods).

Except for CR coefficient w_1, both the EV coefficient w_2 and RPE coefficient w_3 were negatively correlated with substance use severity in the overall sample (w_1 ρ = -0.228, p = 0.068, 95%*CI* = [-0.456, 0.020]; w_2 ρ = -0.389, p = 0.001, 95%*CI* = [-0.583, -0.153]; w_3 ρ = -0.257, p = 0.039, 95%*CI* = [-0.477, -0.007]; Fig. 5). Similar negative correlations were observed in the HC group (w_1 ρ = -0.325, p = 0.041, 95%*CI* = [-0.562, -0.039]; w_2 ρ = -0.383, p = 0.015, 95%*CI* = [-0.616, -0.105]; w_3 ρ = -0.447, p = 0.004, 95%*CI* = [-0.681, -0.150]; see Supplementary Figure S4). No significant correlations were found in the MUD group (w_1 ρ = 0.102, p = 0.628, 95%*CI* = [-0.349, 0.513]; w_2 ρ = -0.158, p = 0.451, 95%*CI* = [-0.558, 0.306]; $w_3\rho$ = 0.193, p = 0.356, 95%*CI* = [-0.226, 0.548]).

Given the high comorbidity of depression and anxiety among individuals with MUD, we further examined

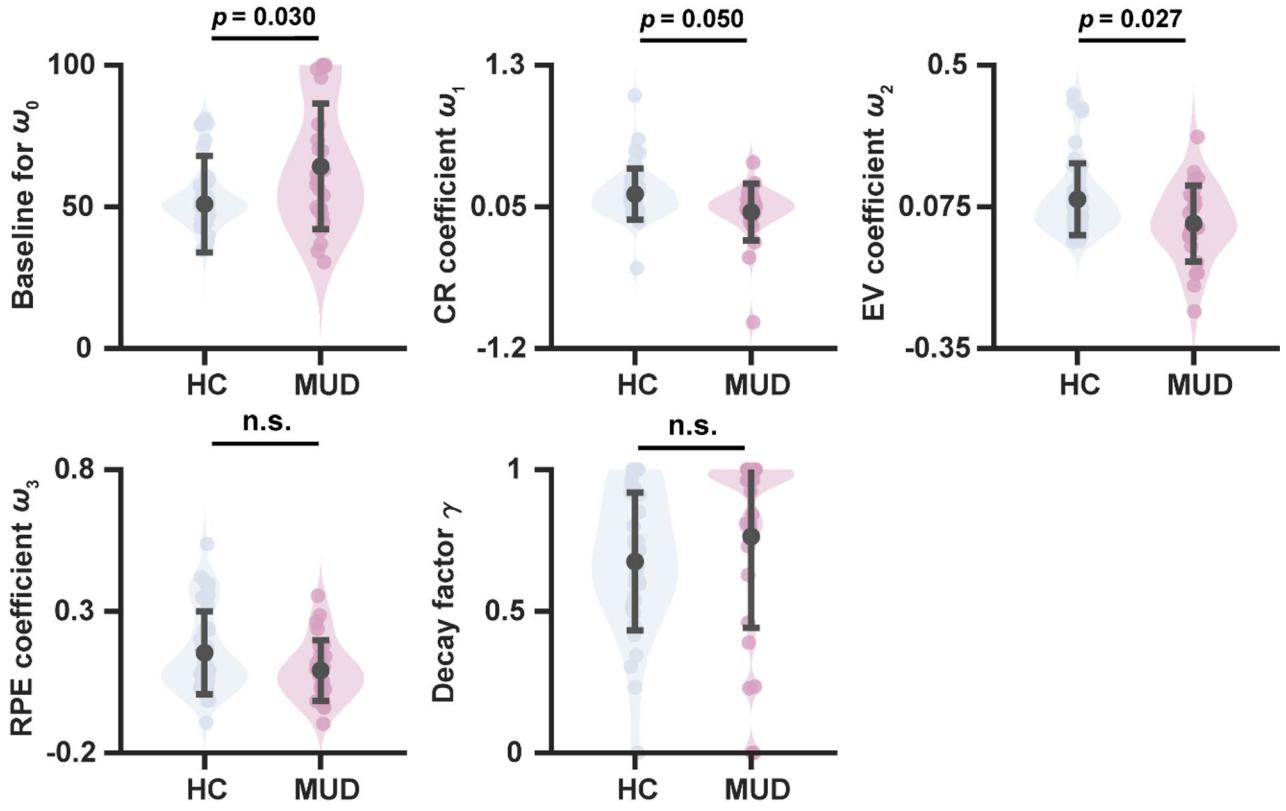

Fig. 4 Comparison of model parameters. Model parameters (y-axis) are shown for the MUD and HC groups (x-axis). The black dot and bar indicate the mean and standard deviation, respectively. Individual participant data are shown as scatter points, with shaded areas representing the data distribution. Significance symbol convention is n.s.: non-significant

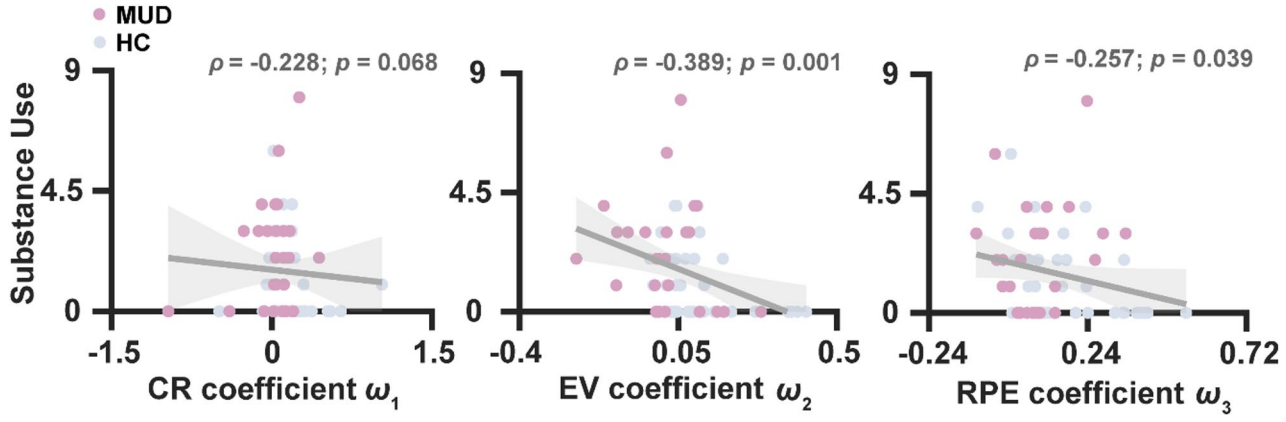

Fig. 5 Correlation between reward-related coefficients and substance use severity. The y-axis represents the substance use severity, and the x-axis represents the coefficient values. Scatters for the MUD (purple) group and the HC (blue) group are plotted alongside fitted lines (light gray) for overall sample. Shaded areas indicate the 95% confidence intervals of the fitted lines

whether the reward-mood associations were related to depressive or anxiety symptom severity. No significant correlations were found between any of the reward-related coefficients (CR, EV, or RPE) and depressive or anxiety symptom severity in any group (see Supplementary Figure S5 for details).

Discussion

This study systematically examined how reward processing influences the momentary mood in individuals with MUD during risk gambling tasks. We found that individuals with MUD made significantly less optimal decisions and showed attenuated reward-mood associations compared to HCs. Additionally, reduced EV/RPE-mood associations predicted more severe substance abuse

symptoms. These findings provide computational evidence for the aberrant reward processing as a key mechanism underlying impaired mood regulation in MUD.

The finding of lower decision-making optimality in individuals with MUD suggests that they struggle to select the most rewarding options through effective value comparison. This behavioral pattern aligns with computational theories proposing that addiction involves an imbalance between two reinforcement learning systems: a goal-directed system (model-based, MB) that supports flexible, outcome-sensitive decision-making, and a habitual system (model-free, MF) that governs rigid, stimulus-response behaviors [48, 49]. In healthy individuals, goal-directed control allows actions to be guided by anticipated outcomes, whereas habitual control dominates when behavior becomes automatic through repetition [50]. Extensive evidence indicates that chronic substance use gradually shifts behavior from goal-directed to habitual control [51–53]. For example, one study employing the two-stage task combined with reinforcement-learning modeling has demonstrated that individuals with MUD exhibit lower weights on the model-based component, indicating a stronger tendency toward habitual learning and reduced reliance on goal-directed control [54]. Such an imbalance may impair the ability of outcome representations to effectively control responding [1]. In line with this framework, our findings show that individuals with MUD tend to overlook high-value goals or outcomes, resulting in reduced total reward acquisition (Fig. 2A). This behavioral inefficiency reflects a compromised goal-directed system and supports the notion that impaired value-based decision-making is a core feature of substance-use disorders. Considering the elevated rates of criminal behavior and relapse among individuals with MUD in real life [55–57], these findings highlight the importance of incorporating decision-making intervention and cognitive remediation strategies into treatment programs for MUD.

The finding of attenuated reward-mood associations highlights an impaired reward system in individuals with MUD. This diminished coupling between reward and mood may reflect a reduced sensitivity to natural rewards such as monetary gain or food, which has been widely documented in addiction research [58, 59]. Neurobiological evidence supports this interpretation: methamphetamine exposure leads to decreased dopamine D2 receptor availability and disrupted cortical-striatal system, both of which are critical for encoding the motivational value of rewards [60–62]. Such dysfunction is thought to blunt the neural response to non-drug rewards, manifesting as reward hyposensitivity [63–65], and leading to attenuated emotional and behavioral reactivity to everyday rewarding experiences. Consistent with this view, neuroimaging studies have reported hypoactivation of the reward system (e.g., striatum and medial prefrontal cortex) in response to natural rewards among individuals with substance use disorders [66–68]. Clinically, this blunted reward sensitivity results in reduced motivation and diminished hedonic responses to non-drug rewards, contributing to mood dysregulation, anhedonia, and related symptoms in substance users, including those with MUD [69, 70]. From a computational perspective, our study extends this literature and provides quantitative evidence linking reward processing deficits to mood dysregulation in individuals with MUD.

More importantly, we found that EV/RPE-mood association predicted the substance use severity in the control group, but not in the MUD group. Although this finding provides preliminary computational evidence for a close link between reward processing abnormalities, mood dysregulation, and substance use in healthy individuals, the clinical implications remain unclear, given that the relationship between symptoms and model parameters was observed only in the control group. One possible explanation is that greater clinical heterogeneity among the participants with MUD, including differences in comorbidities, withdrawal phase and treatment status, may have introduced additional noise that obscured parameter-symptom relationships. Previous studies have shown the translation of reward information into effective cues for mood can guide individuals toward better decision-making [71]; however, aberrant reward processing combined with pronounced mood dysregulation may impair one's ability to make adaptive choices and increase the tendency to seek drugs [70, 72]. Our approach was intend to characterize this process through computational modeling. Future studies using longitudinal designs and rigorous characterization of substance use trajectories will be necessary to explore the potential of this novel computational metric for assessing the latent risk of developing substance use disorders in healthy individuals, and to determine whether these computational associations can reliably predict clinical outcomes across different stages of dependence and recovery.

Our study has some limitations. First, our sample comprised only male individuals with MUD. While the literature remains inconclusive, accumulating evidence suggests that females may exhibit greater susceptibility to developing substance addiction than males [73]. Future studies should therefore include female participants and extend the investigation to other forms of addiction (e.g., opioid, cocaine) to examine the generalizability of aberrant reward-mood associations across sex and addiction subtypes. Second, we used money as a reward cue, but drug users may show different computational and behavioral patterns for rewards related to drug cues [69]. Future studies may employ task paradigms including drug cues. Lastly, although the behavioral and computational

signatures of mood dysregulation are evident in our study, it remains unclear what the neural underpinnings of such aberrant reward-mood association are. Future studies that combine multimodal imaging and computational modeling are imperative to further reveal the specific role of the striatum-frontal-limbic network in individuals with MUD.

Abbreviations

MUD	Methamphetamine use disorder
HC	Healthy controls
EV	Expected value
RPE	Reward prediction error
CR	Certain reward
UR	Uncertain reward
WAIS	Wechsler Adult Intelligence Scale
SDS	Self-Rating Depression Scale
SAS	Self-Rating Anxiety Scale
BIS	Barratt Impulsiveness Scale
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
BIC	Bayesian Information Criteria
PXP	Posterior exceedance probability

Supplementary Information

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Supplementary Material 1

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Author contributions
R-Y.Z. conceived and designed the study. Y-F.X. prepared the computer program for the behavioral task. Z.F. checked and verified the task. Y-F.X., Y-Y.G., Z-J.C., and W.L. collected the data. Y-F.X. organized and analyzed the data. Y-F.X. wrote the first draft of the manuscript. T.K., L.G., and H.J. supervised the study. All authors revised the manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of Science and Technology Research Involving Humans at Shanghai Jiao Tong University (Approval No: H20240606C) and the Biomedical Ethics Committee of Nankai University (Approval No: NKUIRB2023090). All experimental procedures were conducted in accordance with the principles outlined in the Declaration of Helsinki. All participants voluntarily participated in the study and provided informed consent.

Consent for publication
All authors gave their consent for the publication of this manuscript.

Competing interests
The authors declare no competing interests.

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