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Research Article

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Neurocomputational mechanisms of reward-based online mood regulation in adolescents with bipolar disorder and major depressive disorder

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Abstract

Background **The overlapping symptoms between bipolar disorder (BD) and major depressive disorder (MDD) pose a challenge in diagnosis and treatment. A prevailing hypothesis suggests that mood dysregulation may be linked to impairments in the reward system, but the neurocomputational differences between BD and MDD remain elusive. This study investigates whether atypical reward processing affects subjective mood in adolescents with BD and MDD. Our research aims to elucidate the behavioral and neural differences between the two groups, facilitating more accurate and timely diagnosis and intervention.**

Methods **Forty-five adolescents (aged $\leq$ 19 years) diagnosed with BD-II in depressed mood states ($N = 25$) or MDD ($N = 20$) completed a risky gambling task while their brain responses were recorded using functional magnetic resonance imaging (fMRI). Several computational models were constructed to uncover the associations between various reward components (e.g. reward prediction errors, RPE) and trial-wise fluctuations in subjective mood during the task.**

Results **Adolescents with BD exhibited a lower best choice rate and a higher uncertain choice rate compared to those with MDD. Computational modeling and mediation analysis suggested a tripartite mediating relationship between RPE-mood association, decision rationality, and symptom severity. Using fMRI, we observed significant RPE-related activation in the ventral striatum, which showed a slight positive correlation with the RPE-mood association. We also noted subtle differences in several brain regions (i.e. medial orbitofrontal cortex) between the BD and MDD groups. These differences were further associated with manic symptoms.**

Conclusion **Decision rationality mediated the association between RPE-mood association and symptom severity. Relative to adolescents with MDD, those with BD showed decreased decision rationality, along with modest but distinct reward-related neural patterns on fMRI. These findings highlight the crucial role of reward processing in mood regulation and provide preliminary neurocomputational evidence that may inform future diagnostic biomarker development.**

Keywords bipolar disorder, major depressive disorder, decision-making, functional magnetic resonance imaging, reward prediction error

Introduction

Bipolar disorder (BD) and major depressive disorder (MDD) are two of the most common mood disorders (Zhang and Rong, 2019; Yang *et al.*, 2023). MDD is characterized by depressed mood, diminished interests, impaired cognitive function, and vegetative symptoms (Otte *et al.*, 2016). BD is usually characterized by recurring depressive and manic or hypomanic episodes (Carvalho *et al.*, 2020). Both are typical in adolescents. Approximately 60% of individuals with BD experience their first onset before reaching adulthood (Perlis *et al.*, 2004). The first episode of MDD occurs slightly later. More than 40% of individuals with MDD are less than 21 years old at onset (Klein *et al.*, 1999), and the peak age is 19.5 years (Solmi *et al.*, 2022). Relevant research on adolescent populations is par-

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ticularly valuable for the timely diagnosis and intervention of the two most common mood disorders.

The high risk of misdiagnosis for BD and MDD when they first come to the clinic is the central clinical challenge. About 50–75% of individuals with BD were initially misdiagnosed as MDD (Hirschfeld *et al.*, 2003; Tondo *et al.*, 2014), and 40–50% of those diagnosed with MDD may have BD (Benazzi, 1997; Angst *et al.*, 2011). The misdiagnoses result in high monetary losses and considerable delays in treatment (Menzin *et al.*, 2009), and inappropriate use of antidepressant medication even worsens symptoms of BD (Tohen *et al.*, 2018). Therefore, it is a central question in clinical practice to identify behavioral biomarkers to distinguish BD from MDD and predict the progression of BD, especially in adolescents.

Mood dysregulation has been documented as one of the most common symptoms of BD and MDD. A number of studies have attempted to distinguish the differences in mood dysregulation between the two disorders, but the conclusions are controversial. In clinical practice, it is well established that individuals with BD often present with depressive episodes during their initial onset (Young and MacPherson, 2018; Whitton and Pizzagalli, 2022), which is also the core symptom of MDD. Existing studies also suggest that, compared with MDD, individuals with BD can better adjust to immediate happiness and sadness (Rive *et al.*, 2015) but exhibit severe anhedonia (Fang *et al.*, 2021). However, some evidence has suggested no significant differences in anhedonia between MDD and BD, especially when individuals with BD are experiencing depressive episodes (Perlis *et al.*, 2006; Mula *et al.*, 2010). These findings highlight the difficulty of distinguishing the two disorders purely based on their explicit behavioral symptoms and self-reports (Smith and Craddock, 2018).

What are the mechanisms underlying mood dysregulation? One prevailing assumption is that mood dysregulation may stem from inaccurate estimates of potential costs and benefits from the environment when individuals make decisions, or from heightened or diminished sensitivity to reward information (Russo and Nestler, 2013; Berridge and Kringelbach, 2015; Alloy *et al.*, 2016; Nusslock *et al.*, 2025). For individuals, subjective mood states elicited by rewards can be tracked and used to guide future behavior, such that individuals preferentially select actions that restore or maintain these rewarding affective states (Dayan and Daw, 2008). When reward processing is impaired, however, individuals may fail to experience appropriate affective responses and thus cannot effectively update reward contingencies in the environment, leading to maladaptive behaviors. Based on this perspective, it has been increasingly recognized that mood dysregulation in MDD and BD may primarily reflect reward motivational rather than hedonic deficits (Nusslock *et al.*, 2025). Supporting this theoretical account, a growing body of evidence indicates that dysfunction of cortico-striatal circuitry represents a key neural mechanism linking such atypical reward processing to mood dysregulation. Convergent evidence from functional magnetic resonance imaging (fMRI) studies indicates that atypical activation or altered functional connectivity of the striatum, orbitofrontal cortex (OFC), and cingulate cortex during reward processing is associated with immediate affective responses and increased risk for mood disorder onset (Deveney *et al.*, 2013; Satterthwaite *et al.*, 2015; Anderson *et al.*, 2023). Notably, reward system deficits contributing to mood dysregulation are especially pronounced during adolescence (Forbes and Dahl, 2011; Zubovics *et al.*, 2021) and have further been linked to the emergence of BD and MDD in this developmental stage (Davey *et al.*, 2008; Urošević *et al.*, 2018).

A growing literature has compared atypical reward processing between MDD and BD, but has not drawn conclusions (Chase *et al.*, 2013; Redlich *et al.*, 2015; Weinstock *et al.*, 2018). Some findings indicate that MDD is often associated with reduced reward sensitivity (Alloy *et al.*, 2016; Takamura *et al.*, 2017; Kumar *et al.*, 2018), whereas BD, particularly in manic states, involves heightened sensitivity to reward (Mason *et al.*, 2012; Caseras *et al.*, 2013; Damme *et al.*, 2017; Alloy and Nusslock, 2019). However, studies of individuals with BD in syndromic remission or euthymic phases have reported reduced reward sensitivity, similar to that observed in MDD (Schreiter *et al.*, 2016; Pouchon *et al.*, 2023). Given the unstable state of BD at diagnosis, the differences in reward functioning between BD and MDD remain inconclusive.

Although a bulk of existing studies have examined differences in mood regulation and reward processing between MDD and BD, several critical issues remain elusive. First, most studies have examined BD and MDD separately, with few systematically comparing the two disorders within the same context of experimental conditions and tasks. Second, prior research has largely focused either on reward processing or on mood regulation, without addressing the intrinsic link between them. Third, existing experimental paradigms have primarily focused on basic decision behaviors or directly measured mood states. Only a few quantitative models have been constructed to capture how reward processing impacts mood regulation. Modeling momentary subjective feelings can improve our understanding of affective processes by quantifying the simultaneous influence of multiple factors on affective dynamics (Kao *et al.*, 2023). In other words, modeling has the potential to disentangle the stable and dynamic components of affective processes, thereby helping us distinguish the different mechanisms that may underlie similar mood dysregulation in BD and MDD. Moreover, a large body of studies has used latent variables derived from computational models to perform neuroimaging analyses (Gläscher *et al.*, 2010; Rutledge *et al.*, 2014; Kumar *et al.*, 2018). This approach provides a powerful framework for linking algorithmic-level cognitive processes with their neural implementations. Lastly, no studies have yet examined the effects of reward processing on mood regulation, particularly in the adolescent population, who represent a critical group in developmental psychopathology.

This study aimed to investigate the neurocomputational mechanisms linking reward processing and mood regulation in adolescents with BD and MDD. Our primary focus was on direct comparisons between BD and MDD, and therefore, we did not include a healthy control group. While including such a group could provide additional context, our rationale was that the clinical challenge lies primarily in distinguishing BD from MDD, particularly in adolescents. In contrast, differentiating either disorder from healthy populations has been extensively addressed in previous studies (Rutledge *et al.*, 2017; Johnson *et al.*, 2019). Accordingly, our emphasis was on identifying BD-MDD differences, which remain highly clinically relevant.

Adolescents diagnosed with BD and MDD completed a risky gambling task (Rutledge *et al.*, 2014), during which momentary variations in subjective mood were intermittently measured. The combined measurement of reward-based decision behavior and momentary mood provides a unique opportunity to examine their relationship within the same experimental context. Notably, we

developed a computational model to quantify how different reward components [i.e. expected value (EV) and reward prediction error (RPE)] contribute to fluctuations in momentary mood. This model not only offers a direct, quantitative link between decision behavior and mood regulation but also enables further exploration of their neural substrates. Our findings revealed a tripartite relationship between decision behaviors, model parameters, and clinical symptoms. Furthermore, given that our study focused on the cortico-striatal circuitry, including deep subcortical nuclei, fMRI provides one of the best available non-invasive approaches to obtain imaging data from these regions. Moreover, our study design builds on prior work, where fMRI has been widely employed to examine the neural mechanisms of reward and mood processing (Jiang *et al.*, 2024; Zhuang *et al.*, 2025), particularly during risky gambling tasks (Rutledge *et al.*, 2014, 2017). Consistent with this literature, we recorded whole-brain activity using fMRI to test whether abnormalities within this circuitry differentiate adolescents with BD from those with MDD. As a result, we observed robust RPE-related activation in the ventral striatum across all participants, as well as subtle group differences in regions such as the right frontal pole during the task.

Materials and methods

Ethics and participants

All experimental protocols were approved by the institutional review board of Shanghai Mental Health Center. All research was conducted in accordance with relevant guidelines and regulations. Written informed consent was obtained from all participants and their parents or legal guardians.

We recruited 62 adolescents (age $\leq$ 19 years old) with the first episode of MDD and bipolar disorder type II (BD- II) between January and August 2021 from the Shanghai Mental Health Center. The diagnosis of MDD and BD-II was conducted by licensed psychiatrists using the Structured Clinical Interview for DSM-V-Clinician version (SCID-5-CV) (First *et al.*, 2016). Adolescents with BD-II had moderate or severe depressive symptoms at the time of enrollment. Specialist clinicians then assessed these participants' symptoms using the Hamilton Depression Scale (HAMD) and the Hypomania Symptom Checklist-32 (HCL-32) (Hamilton, 1960; Angst *et al.*, 2005). Five participants were excluded because either their HAMD score (for MDD and BD-II) or HCL score (only for BD-II) was below 14 (i.e. a conventional definition of moderate severity). The remaining exclusion criteria included

- serious or unstable organic diseases (i.e. malignant cancer, cardiovascular disease, head injuries, or alcohol/nicotine abuse);
- comorbidity with any other psychiatric disorder;
- receipt of medication or physical therapy for the current episode immediately before enrollment;
- contraindications for MRI scanning, including the presence of metal implants, dental braces, or a fear of claustrophobia.

Seven participants dropped out during the experiment, and five participants were excluded from data analysis because they did not follow the task instructions (i.e. mood or decision responses remained constant throughout the experiment). Data from 46 participants (12–19 years, 10 males) were included for further statistical analysis. Both groups were matched for age and sex (see Table 1).

Risky gambling task

The order of stimulus presentation in the scanning task with the general flow is shown below (Fig. 1C). Our risky gambling task was consistent with previous studies (Rutledge *et al.*, 2014, 2017). At the beginning of the task, each participant was given 500 RMB as their base virtual capital. Their task was to earn as much money as they could in this task (Fig. 1A). On each trial, participants made a binary choice between an uncertain option (including two uncertain rewards, URs) and a certain option (including one certain reward, CR) within a 3-s time window; otherwise, they received the least reward among the three possible outcomes. The uncertain option contained two potential rewards with equal probability. In contrast, participants chose a certain option to gain its reward directly. The reward value of the certain option was constrained to fall between the two potential outcomes of the uncertain option, thereby establishing these uncertain outcomes as the designated gain and loss conditions.

After a choice was made, the chosen option (no matter certain or uncertain) lasted 3 s on the screen, and the other unchosen option disappeared. If participants chose a certain option, they received a CR immediately after the 3 s. If participants chose an uncertain option, after a 3-s presentation of the chosen uncertain option, the outcome feedback lasted 1 s. A fixation (random from 2 to 5 s, with a mean of 3 s) was presented before the next trial. After every two or three decision trials, participants were presented with a mood rating trial—"How happy are you at this moment?" (Fig. 1B). Participants had 3 s to report their mood along the 7-point scale labeled from "very unhappy" to "very happy".

The whole experiment included a total of 60 decision trials and 22 mood-rating trials. All 82 trials were divided into two consecutive fMRI scanning runs. The entire risky gambling task lasted approximately 14 min in the scanner.

Prior to the scan, participants completed the practice session containing 30 decision trials and 12 mood rating trials in the waiting room. The setup of the exercise session was identical to the main experiment, except that participants could see their cumulative earnings in each trial. In the main experiment, the cumulated earnings were presented at the end of the experiment. All experimental stimuli were presented in MATLAB R2013a (MathWorks, Inc.).

Computational modeling of mood regulation

We constructed several computational models to account for momentary variations in subjective mood (Rutledge *et al.*, 2014, 2017). The best-fitting model has two basic assumptions. First, the mood ratings are influenced by the reward components from all previous trials. These reward components include (i) CR, which indicates the amount of reward for the certain option in a trial; (ii) EV, which indicates the averaged reward for the uncertain option in a trial; and (iii) RPE, which indicates the difference between the outcome of the uncertain option and EV in a trial. Here, we assumed a linear relationship between the three reward components and

Table 1 Demographic and clinical characteristics by group.

	MDD ($N = 20$)	BD ($N = 25$)	Statistic test	*P*-value
Female, no. (%)	15(75%)	20(80%)	$\chi 2 = 0.161$	0.689
Age, M ± SD	14.500 ± 1.732	15.360 ± 1.800	$t = 1.619$	0.113
HAMD, M ± SD	20.050 ± 3.502	19.560 ± 3.267	$t = -0.484$	0.631
HCL, M ± SD	3.950 ± 4.466	20.440 ± 3.852	$t = 13.294$	<0.001***
Illness duration (years)	2.313 ± 3.092	2.180 ± 1.759	$t = -0.181$	0.857
Self-mutilation, no. (%)	10(50%)	15(60%)	$\chi^2 = 0.450$	0.502
Suicide attempt, no. (%)	2(10%)	3(12%)	$\chi^2 = 0.045$	0.832
Hospitalization, no. (%)	0(0%)	5(20%)	$\chi^2 = 4.500$	0.034*
Typical antipsychotic, no. (%)	1(5%)	0(0%)	$\chi^2 = 1.278$	0.258
Atypical antipsychotic, no. (%)	13(65%)	21(84%)	$\chi^2 = 2.172$	0.141
Any antidepressant, no. (%)	12(60%)	15(60%)	$\chi^2 = 0.000$	1.000
Lithium, no. (%)	7(35%)	11(44%)	$\chi^2 = 0.375$	0.540
Any anticonvulsant, no. (%)	9(45%)	19(76%)	$\chi^2 = 4.543$	0.033*
Any psychotherapy, no. (%)	1(5%)	0(0%)	$\chi^2 = 1.278$	0.258

HAMD, Hamilton scale for depression; HCL, hypomania checklist.
Significance symbol conventions are $^{*}P < 0.05$, $^{***}P < 0.001$.

mood ratings. Second, the influence of reward components in previous trials on the mood rating in the current trial decays exponentially.

$$\text{Mood}_{(t)} = w_0 + w_1 \sum_{j=1}^{t} \gamma^{t-j} \text{CR}_j + w_2 \sum_{j=1}^{t} \gamma^{t-j} \text{EV}_j + w_3 \sum_{j=1}^{t} \gamma^{t-j} \text{RPE}_j, \quad (1)$$

where $0 \leq \gamma \leq 1$ is the decay factor. 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.

We also fitted nine alternative models and a baseline model (see Supplementary Note 1). To quantitatively compare these models, we calculated the Akaike information criterion and Bayesian information criterion (BIC) for each participant, and protected exceedance probability for each group. All models were fitted using nonlinear least squares in the optimization toolbox in MATLAB R2023a (MathWorks, Inc.). Code is publicly available via https://github.com/GITSyfX/CCNN-23BPhappy.

fMRI data acquisition and preprocessing

All MRI data were acquired on a 3T Siemens scanner with a 32-channel head coil. The scanner was located at the Shanghai Mental Health Center. All participants' heads were positioned with foam position pillows. A T1-weighted anatomical scan was performed with a 3D MPRAGE sequence [1 mm^3 voxel size, 256 mm^2 field of view, TR/TE/TI = 2530/3.65/1100 ms, 7° flip angle, 180 HZ/Pixel bandwidth, 8.5 ms echo spacing, in-plane acceleration (GRAPPA) factor of 2, A→P phase encoding, 1 mm slice thickness] for each participant. T2*-weighted functional images were collected with a one-shot echo-planar imaging pulse sequence [3 mm^3 voxel size, 220 mm^2 field of view, TR/TE = 2000/30 ms, 50 slices, 1 mm slice thickness, 77° flip angle, multi-band accelerated factor of 2, 2330 Hz/Pixel bandwidth, 0.51 ms echo spacing, P→A phase encoding, 208 TRs]. To correct the image distortion along the phase encoding direction, we also collected functional images with the identical protocol except that it set the reversed phase encoding direction (A→P phase encoding) and a much shorter duration (20 TRs).

Preprocessing was performed using customized scripts based on AFNI 24.1.11 (Cox, 1996). At the initial step of fMRI data preprocessing, the DICOM series was converted to NIfTI (`dcm2niix_afni`). The preprocessing of data started with the removal of the spike from the blood-oxygen-level-dependent (BOLD) time series (`3dDespike`). All slices were then time-corrected for each EPI brain volume to the same temporal origin at the first TR of the first scanning run (`3dTshift`). Then, functional data were reverse-polarity phase-encoding corrected (`3dNwarpApply`) and motion-corrected based on the volume with the smallest outlier by using a six-parameter affine transform (`3dvolreg`). Before aligning datasets to standardized anatomy, all functional data were aligned to the corresponding anatomical image (`align_epi_anat.py`). We manually checked the effect of the alignment in each participant based on whether the image edges and the shapes of major structures (e.g. the corpus callosum) were aligned. After that, the preprocessed data were nonlinearly transformed to the Montreal Neurological Institute (MNI) standard space (`3dNwarpApply`). Next, functional images were smoothed with a 4 mm FWHM Gaussian kernel (`3dmerge`). Ultimately, the response amplitude for each vertex on the cortical surface was transformed into percentage units of BOLD signal change.

fMRI general linear modeling

We fitted three general linear models (GLMs) to voxel-wise parametric statistical maps using the AFNI `3dDeconvolve` function. In GLM1, the model includes the choice onset and the feedback onset as separate regressors. Here, the choice onset indicates the moment when a participant pressed the choice button. The feedback onset indicates the moment when a participant receives the outcome feedback from either a certain or uncertain option. In

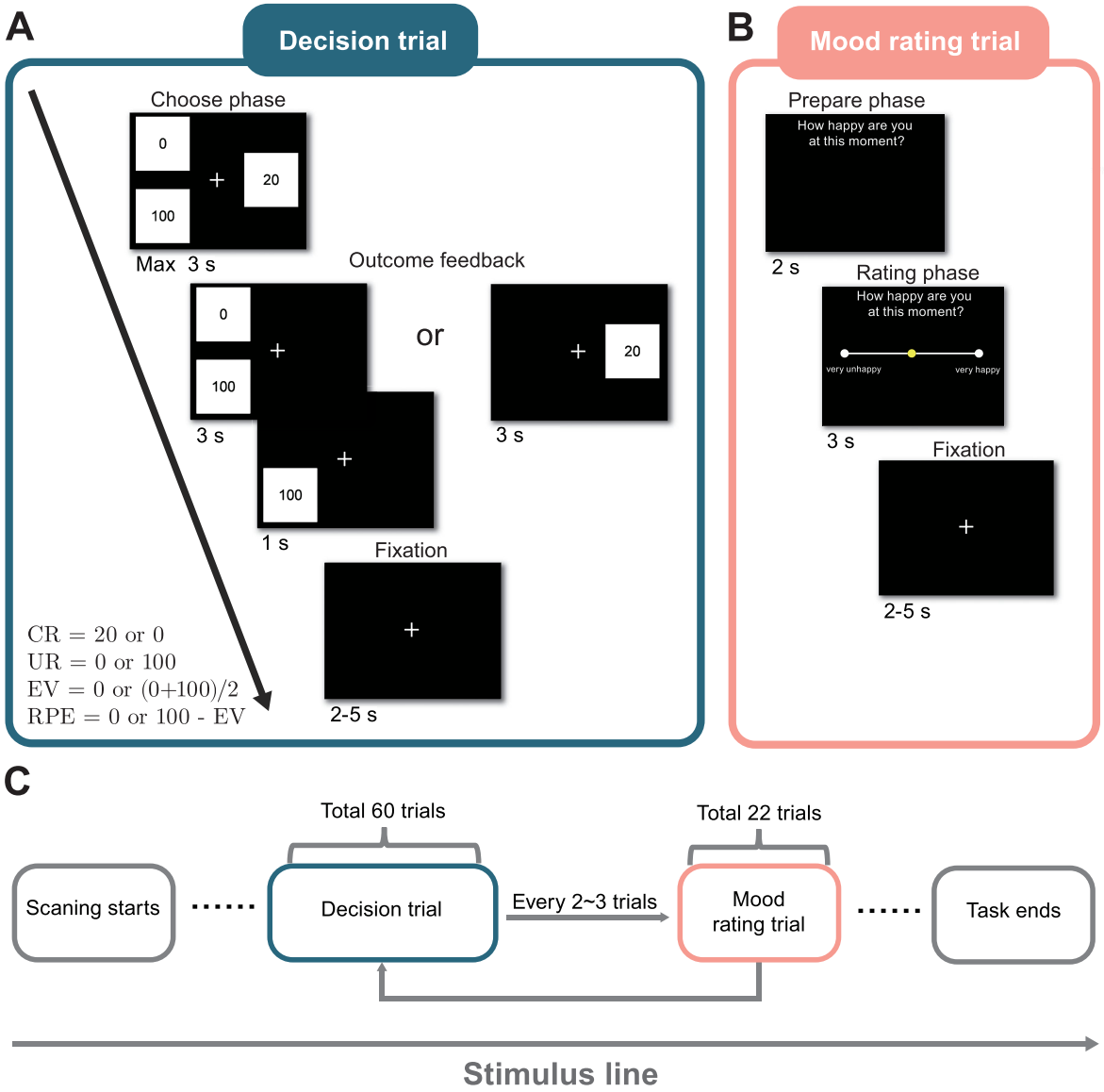

Figure 1 Risky gambling task. (A) Task design. Participants chose between a certain option and an uncertain option. If a certain option was chosen, the outcome (i.e. 20 yuan) was presented immediately. If an uncertain option was selected, participants first saw two possible outcomes (i.e. 0 vs. 100 yuan) and then saw the final reward (i.e. 100 yuan). In this example, the certain reward is 20 or 0 yuan; the expected value is 0 or $(0 + 100)/2 = 50$ yuan; the reward prediction error is 0 or $100–50 = 50$ yuan. And the uncertain reward is 0 or 100 yuan. (B) Rating task. Participants were instructed to indicate "How happy are you at this moment?" by using a customized keyboard in fMRI to move a yellow circle button. In the actual experiment, all text was converted to Chinese. (C) Stimulus line. Participants completed a mood rating trial every 2–3 decision trials. Following this cycle, participants completed the decision task in a total of 60 trials with 22 mood ratings.

GLM2, the regressor of choice onset is parametrically modulated by CR and EV. The regressor of feedback onset was parametrically modulated by RPE. In GLM3, the regressor of choice onset is the same as GLM2, and the regressor of feedback onset is parametrically modulated by UR (see calculation in Supplementary Fig. S1) and EV.

The GLMs also include demeaned head-motion parameters and constant, linear, and quadratic polynomial terms as nuisance predictors. We concatenated the time series of all the runs during each scanning session. All the analyses of the main experiment data were performed based on the GLM results (i.e. beta weights) on the voxel level. A standard second-level contrast analysis was implemented. Specifically, we ran a two-sample *t-test* for each regressor of interest. Statistical significance was determined using a two-stage thresholding approach: (1) initial voxel-wise thresholding at $P < 0.001$ (uncorrected) and (2) subsequent cluster-level family-wise error (FWE) correction at $P < 0.05$. All second-level results for the combined group were reported using cluster-level thresholds ($P < 0.05$, FWE-corrected). No suprathreshold clusters surviving the FWE correction in second-level between-group contrasts, as such, we present findings using a voxel-wise threshold ($P < 0.001$, uncorrected).

We extracted parameter estimates from clusters where all voxels were significant at uncorrected $P < 0.001$ in the group-level analyses. We then extracted the mean beta weights for each cluster, and performed Pearson correlation analyses between

these mean values, computational model parameters, and clinical symptom scores.

Statistical analysis

Data on behaviors, model parameters, and clinical symptoms were analyzed using one-way analysis of covariance (ANCOVA) and Pearson correlation tests in JASP 0.19.3 (Love *et al.*, 2019). Group comparisons of 3D imaging data were performed with two-sample *t*-tests using the `3dtest++` function in AFNI, employing the `-covariates` option. Mediation analyses were conducted with the PROCESS version 4.2 (Andrew F. Hayes, Corp.) plug-in for SPSS.A simple mediation model (Model 4) was specified, with 5000 bootstrap samples and 95% confidence intervals to estimate the indirect effect. In all group-level comparisons, *group* (BD vs. MDD) was included as a fixed effect, and *hospitalization* and *any anti-convulsant use* were included as covariates to control for variables showing significant group differences.

Our sample size was consistent with several previous studies using a similar experimental design and computational models (Rutledge *et al.*, 2014, 2017). Post hoc power analysis for sample size was conducted using G*power 3.1 software (Faul *et al.*, 2009). Parameters included a significance level of $\alpha = 0.05$ and a total sample size of 45 participants (BD group: 25; MDD group: 20). For the ANCOVA, the maximum observed effect size (partial $\eta^2 = 0.118$) yielded a power of 0.667. For Pearson correlation tests, the maximum observed effect size ($\rho = 0.413$) yielded a power of 0.821.

Results

Adolescents with BD exhibit more risk-seeking decision behaviors

We first examined the behavioral performance of the two groups in the risky gambling task. We found no significant group difference in the total earnings ($F_{(1,41)} = 0.843$, $P = 0.364$, partial $\eta^2 = 0.020$), reaction time ($F_{(1,41)} = 0.619$, $P = 0.436$, partial $\eta^2 = 0.015$), and their averaged mood ratings across trials ($F_{(1,41)} = 0.952$, $P = 0.335$, partial $\eta^2 = 0.023$; Fig. 2A and Table 2).

We further compared the decision patterns between the two groups. We calculated the best choice rate—the proportion at which participants chose the option with the larger EV. The higher best choice rate indicates a more optimal decision. We also calculated the uncertain choice rate—the proportion at which participants chose the uncertain option. The higher uncertain choice rate indicates a more risk-seeking decision. Adolescents with BD showed a significantly lower best choice rate ($F_{(1,41)} = 5.467$, $P = 0.024$, partial $\eta^2 = 0.118$; Fig. 2B) compared to those with MDD. They also exhibited a significantly higher uncertain choice rate ($F_{(1,41)} = 4.311$, $P = 0.044$, partial $\eta^2 = 0.095$), implying that adolescents with BD may make more irrational decisions.

Computational modeling of subjective mood in BD and MDD

In order to better understand the computational mechanisms of reward-based mood regulation in the two groups, we constructed ten computational models along with a baseline model. Each computational model assumes that various reward components from previous trials influence mood ratings. These reward components include CR, EV, and RPE. We detail these components of an example trial in the caption of Fig. 1. Notably, the influence of previous reward components on mood ratings follows an exponential decay. We also considered other forms of reward components, such as 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).

Consistent with previous results (Rutledge *et al.*, 2014; Vanhasbroeck *et al.*, 2021), we conducted quantitative model comparisons on all participants, and the results showed that the model, including CR, EV, and RPE, was the best-fitting model for mood rating. The best-fitting model (Model 1, Equation (1)) outperformed other alternatives according to BIC (Fig. 3B). This model was also the best-fitting model after splitting participants into MDD and BD subgroups. The result indicated that CR, EV, and RPE played important roles in mood rating. Also, this best-fitting model could successfully predict momentary mood ratings in both groups ($r^2 = 0.507 \pm 0.176$, $t_{(44)} = 19.343$, $P < 0.001$; see example in Fig. 3A).

After identifying the best-fitting model, we further examined the parameter differences between groups in this model. We compared the weighting coefficients—CR coefficient w_1, EV coefficient w_2, and RPE coefficient w_3 (Equation (1))—between the two groups. We found that none were statistically significant (CR $F_{(1,41)} = 0.128$, $P = 0.723$, partial $\eta^2 = 0.003$; EV $F_{(1,41)} = 0.255$, $P = 0.616$, partial $\eta^2 = 0.006$; RPE $F_{(1,41)} = 0.035$, $P = 0.852$, partial $\eta^2 = 0.001$). No significant between-group differences were found for baseline mood w_0 ($F_{(1,41)} = 1.961$, $P = 0.169$, partial $\eta^2 = 0.046$) or the decay factor γ ($F_{(1,41)} = 0.216$, $P = 0.645$, partial $\eta^2 = 0.005$) either.

RPE-mood exacerbating symptoms through irrational decision behavior

We further analyzed the relationships between the contribution of reward components to mood, decision behaviors, and symptom severity. In this section, we were particularly interested in RPE coefficient w_3 because a bulk of previous literature has reported the critical role of RPE in mood regulation (Mula *et al.*, 2010; Chase *et al.*, 2013; Eldar *et al.*, 2018; Kumar *et al.*, 2018; Macoveanu *et al.*, 2020; Liu *et al.*, 2021). Henceforth, we termed the RPE coefficient w_3 as RPE-mood association because it indicated the influence of RPE on mood ratings. Relevant results about the CR coefficient w_1 and the EV coefficient w_2 are reported in Supplementary Fig. S2.

First, we explored the relationship between RPE-mood association and decision behaviors. Indeed, we found a negative correlation between the RPE-mood association and the best choice rate ($r = -0.346$, $P = 0.020$; Fig. 4A) across all participants, indicating that the stronger the RPE-mood association, the more irrational decision being made. Second, we explored the relationship between decision behaviors and symptom severity. The negative correlation was found between participants' best choice rate and symptom severity (HAMD $r = -0.361$, $P = 0.015$; HCL $r = -0.354$, $P = 0.017$), indicating that participants tended to make more irrational decisions as their symptoms became more severe.

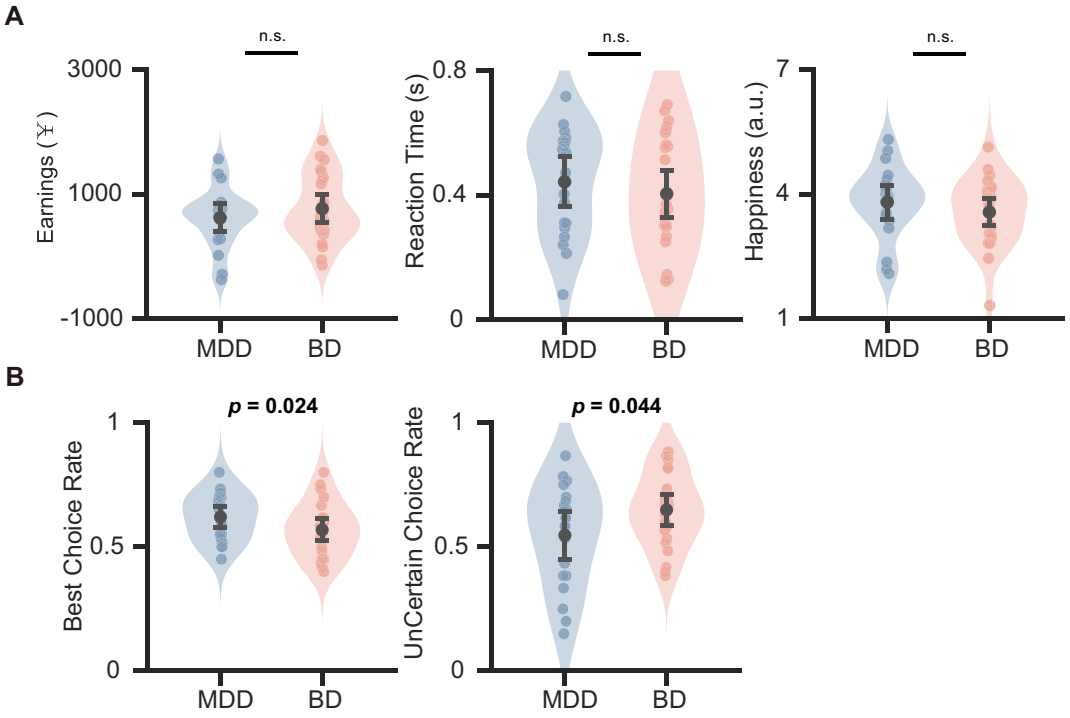

Figure 2 Decision behavior comparison. (A) Decision performance. Decision performance (*y*-axis) of MDD and BD groups (*x*-axis), including earnings (left), reaction time (middle), and mood ratings (right). The black bar and dot represent the standard error and mean, respectively. The scatter indicates the data for each participant, and the shaded area shows the distribution of the data. (B) Decision patterns. Decision patterns are denoted by the best choice rate (left) and uncertain choice rate (right). Significance symbol convention is n.s.: non-significant.

Table 2 Behavioral performance, decision patterns, and weighting coefficients by group.

	MDD ($N = 20$)	BD ($N = 25$)	Statistic test	*P*-value
Behavioral performance, M ± SD				
Earnings	620.880 ± 108.653	768.400 ± 106.864	$F = 0.843$	0.364
Reaction time	1.579 ± 0.058	1.523 ± 0.056	$F = 0.619$	0.436
Happiness	3.807 ± 0.195	3.567 ± 0.161	$F = 0.952$	0.335
Decision patterns, M ± SD				
Best choice rate	0.620 ± 0.021	0.568 ± 0.022	$F = 5.467$	0.024
Uncertain choice rate	0.547 ± 0.046	0.649 ± 0.030	$F = 4.311$	0.044
Weighting coefficients, M ± SD				
Baseline mood w_0	3.969 ± 0.225	3.501 ± 0.212	$F = 1.961$	0.169
CR coefficient w_1	0.005 ± 0.002	0.004 ± 0.003	$F = 0.128$	0.723
EV coefficient w_2	0.004 ± 0.001	0.004 ± 0.001	$F = 0.255$	0.616
RPE coefficient w_3	0.009 ± 0.002	0.008 ± 0.001	$F = 0.035$	0.852
Decay factor γ	0.744 ± 0.054	0.682 ± 0.061	$F = 0.216$	0.645

Finally, we considered all three behavioral measurements together by constructing a mediation model from the RPE-mood association to symptoms through decision behaviors. Interestingly, the mediation analysis showed that the total effects of RPE-mood association on symptom severity were not significant (HAMD $c = 1.242$, $P = 0.394$, 95% CI = [−1.666, 4.150]; HCL $c = 0.210$, $P = 0.959$, 95% CI = [−7.897, 8.316]). With the influences of decision behaviors being controlled, the direct effects of RPE-mood association on symptom severity were also not significant (HAMD $c' = 0.056$, $P = 0.970$, 95% CI = [−2.896, 3.008]; HCL $c' = -3.427$, $P = 0.399$, 95% CI = [−11.542, 4.688]). However, RPE-mood association had a negative effect on best choice rate ($a = -0.103$, $P = 0.020$, 95% CI = [−0.188, −0.017]; Fig. 4B), and the best choice rate had a negative effect on symptoms (HAMD $b = -11.552$, $P = 0.024$, 95% CI = [−21.507, −1.597]; HCL $b = -35.429$, $P = 0.012$, 95% CI = [−62.795, −8.063]). Most importantly, the decision behavior (i.e. best choice rate) acted as a significant mediator within the prediction from RPE-mood association to symptoms (HAMD $ab = 1.186$, $P < 0.001$, 95% CI = [0.143, 2.651]; HCL $ab = 3.637$, $P < 0.001$, 95% CI = [0.202, 8.373]).

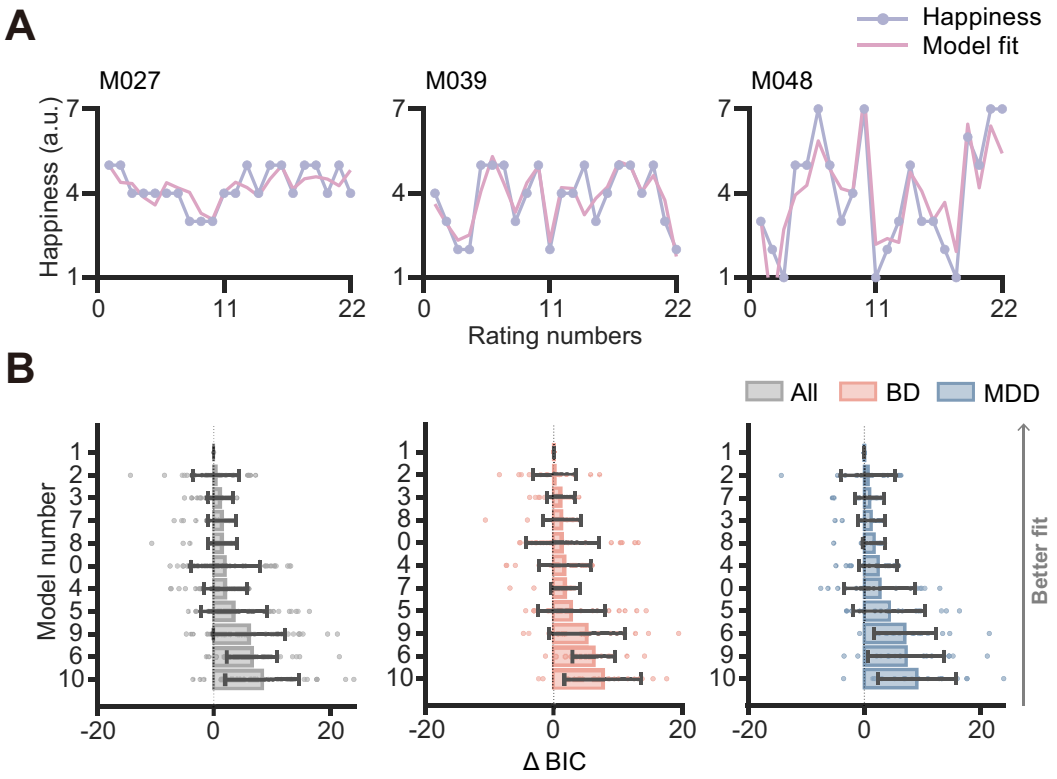

Figure 3 Model fit. (A) Model fit in example participants. Mood ratings (*y*-axis) of the three example participants across all 22 trials (*x*-axis). The purple line with dots is the actual mood ratings, and the pink line is the fitted mood ratings. (B) Model comparison. ΔBIC values were calculated as the difference in BIC between each model and the main model (Model 1, Equation (1)). Models are displayed on the *y*-axis in descending order of fit quality, with the best-fitting model positioned at the top. ΔBIC is averaged across all participants. A smaller ΔBIC signifies a more favorable model fit.

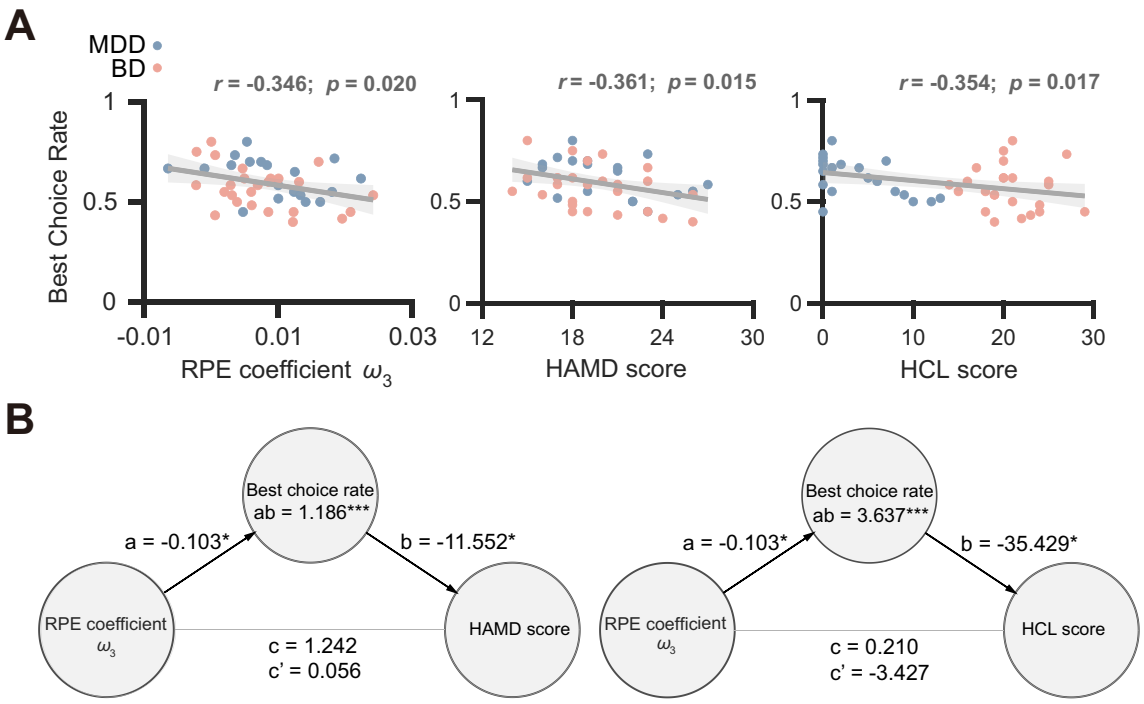

Figure 4 Correlation and mediation tests. (A) Correlation between the best choice rate and RPE coefficient w_3 as well as symptom scores. The *y*-axis illustrates the best choice rate. The *x*-axis illustrates RPE coefficient w_3 (left), HAMD score (middle), and HCL score (right). Scatters for MDD (blue) and BD (red), and fitted lines (light gray) for all participants are shown simultaneously. Shaded areas are 95% confidence intervals for the fitted lines. (B) Simple mediation models. The path reflects the association between RPE coefficient w_3 and symptoms mediated by the best choice rate. Numbers on the paths and circles represent the effect sizes. Significance symbol conventions are *: $P < 0.05$; ***: $P < 0.001$.

Table 3 Brain regions in BD and MDD associated with decision-making tasks.

Brain regions	MNI coordinates, mm	Cluster size	*z* peak values
Overall GLM2, feedback onset × RPE			
Right ventral striatum	16, 16, −10	161	4.734
Left ventral striatum	−13, 8, −12	137	5.262
Left posterior cingulate cortex	−6, −40, 36	43	4.058
BD minus MDD GLM2, feedback onset × RPE			
Left ventral striatum	−8, 4, −7	21	−4.176
GLM1, choice onset			
Left medial orbitofrontal cortex	−1, 49, −10	189	5.061
Left parahippocampal gyrus	−20, −47, −14	62	4.546
Right parahippocampal gyrus	30, −44, −12	74	4.475
Left anterior cingulate cortex	−1, 13, −10	42	4.417
Left posterior cingulate cortex	−13, −52, 38	42	4.356

Neural representation of RPE in adolescents with BD and MDD

We further investigated the neural mechanisms of reward processing in the gambling task. We were also particularly interested in the neural representations of RPE and its relationship to decision behaviors and symptoms. We set the trial-by-trial RPE as a parametric modulator and examined its influences on neural activity. Consistent with previous studies (Rutledge *et al.*, 2014, 2017; Parker *et al.*, 2016; Kumar *et al.*, 2018), significant RPE-related neural activity was found in the bilateral ventral striatum (left $z_{(44)} = 5.262$, $P < 0.01$ FWE-corrected; right $z_{(44)} = 4.734$, $P < 0.01$ FWE-corrected; Fig. 5A) across all participants. In addition, we also found significant RPE signals in the left posterior cingulate cortex ($z_{(44)} = 4.058$, $P < 0.05$ FWE-corrected). See Table 3 for more details on the relevant brain regions.

We then explored the relationships between RPE-related responses, model parameters, and decision behavior. We found that there was a trend of positive correlation between RPE signals in the bilateral ventral striatum and RPE-mood association ($r = 0.287$, $P = 0.056$; Fig. 5B) across all participants. This result suggested that the stronger RPE signals the more RPE one may use to regulate mood. We further found that the RPE signals in the bilateral ventral striatum were negatively correlated with the uncertain choice rate ($r = -0.413$, $P = 0.005$), and the RPE signals in the left posterior cingulate cortex were positively correlated with the best choice rate ($r = 0.333$, $P = 0.026$).

Differential neural responses in BD and MDD during the risky gambling task

The central aim of our study was to identify the different neural underpinnings of BD and MDD in adolescents. We examined group differences in neural responses during the risky gambling task, focusing on participants' activity at choice onset (when they pressed the choice button) and feedback onset (when they received the outcome).

Results showed that, in response to RPE, adolescents with BD exhibited modestly weaker neural activity in the left ventral striatum compared to those with MDD ($z_{(43)} = -4.176$, $P < 0.001$ uncorrected; Fig. 6A). They also showed stronger activation in the left medial orbitofrontal cortex (mOFC $z_{(43)} = 5.061$, $P < 0.01$ FWE-corrected) and the bilateral parahippocampal gyrus (left $z_{(43)} = 4.546$, $P < 0.05$ FWE-corrected; right $z_{(43)} = 4.475$, $P < 0.05$ FWE-corrected; see Table 3) when making a choice. Additionally, adolescents with BD exhibited modestly stronger activation in the left anterior cingulate cortex ($z_{(43)} = 4.417$, $P < 0.001$ uncorrected) and left posterior cingulate cortex ($z_{(43)} = 4.356$, $P < 0.001$ uncorrected) when making a choice. More importantly, activity in the left ventral striatum ($r = -0.297$, $P = 0.048$; Fig. 6B) and the left mOFC ($r = 0.373$, $P = 0.012$) significantly predicted HCL scores across all participants.

Discussion

In this study, we systematically compared the behavioral performance and neural mechanisms of mood regulation in adolescents with BD-II in depressed mood states and MDD during a risk gambling task. Compared to adolescents with MDD, those with BD exhibited lower decision rationality, reflected by a reduced best choice rate and increased risk preference. Individual variations in decision rationality were found to mediate the relationship between RPE-mood association and symptom severity. Leveraging fMRI, we further identified distinct neural response patterns across several brain regions during task performance in adolescents with BD-II. Taken together, these findings provide insight into the neurocomputational mechanisms underlying reward-based mood regulation in BD and MDD, and highlight potential pathological distinctions between the two disorders.

The observed lower best choice rate and higher uncertain choice rate in adolescents with BD indicate a marked decrease in decision rationality, reflecting both suboptimal choice behavior and heightened risk preference. This pattern is consistent with previous findings suggesting that individuals with BD show a propensity for making less advantageous or more uncertain decisions (Adida *et al.*, 2011; Ramírez-Martín *et al.*, 2020; He *et al.*, 2025). Given that choices in our task consistently required participants to weigh the possibility of obtaining larger rewards against the risk of greater losses, this bias may stem from heightened sensitivity to reward-related information (van Enkhuizen *et al.*, 2014; Alloy *et al.*, 2016). Compared to healthy controls, individuals with BD exhibit an excessive focus on reward cues, resulting in heightened responses even to small rewards (Ramírez-Martín *et al.*, 2020). Such hypersensitivity may contribute to both increased risk-taking and decreased decision rationality in pursuit of uncertain outcomes. However, our study also observed reduced striatal activation in BD during outcome feedback, suggesting a more nuanced and complex pattern of reward sensitivity. Indeed, whether BD is characterized by reward hypersensitivity or hyposensitivity remains a subject of ongoing debate. One possible explanation is that findings of reward hypersensitivity primarily pertain to the anticipatory phase of reward processing, whereas reward hyposensitivity is more commonly observed during the

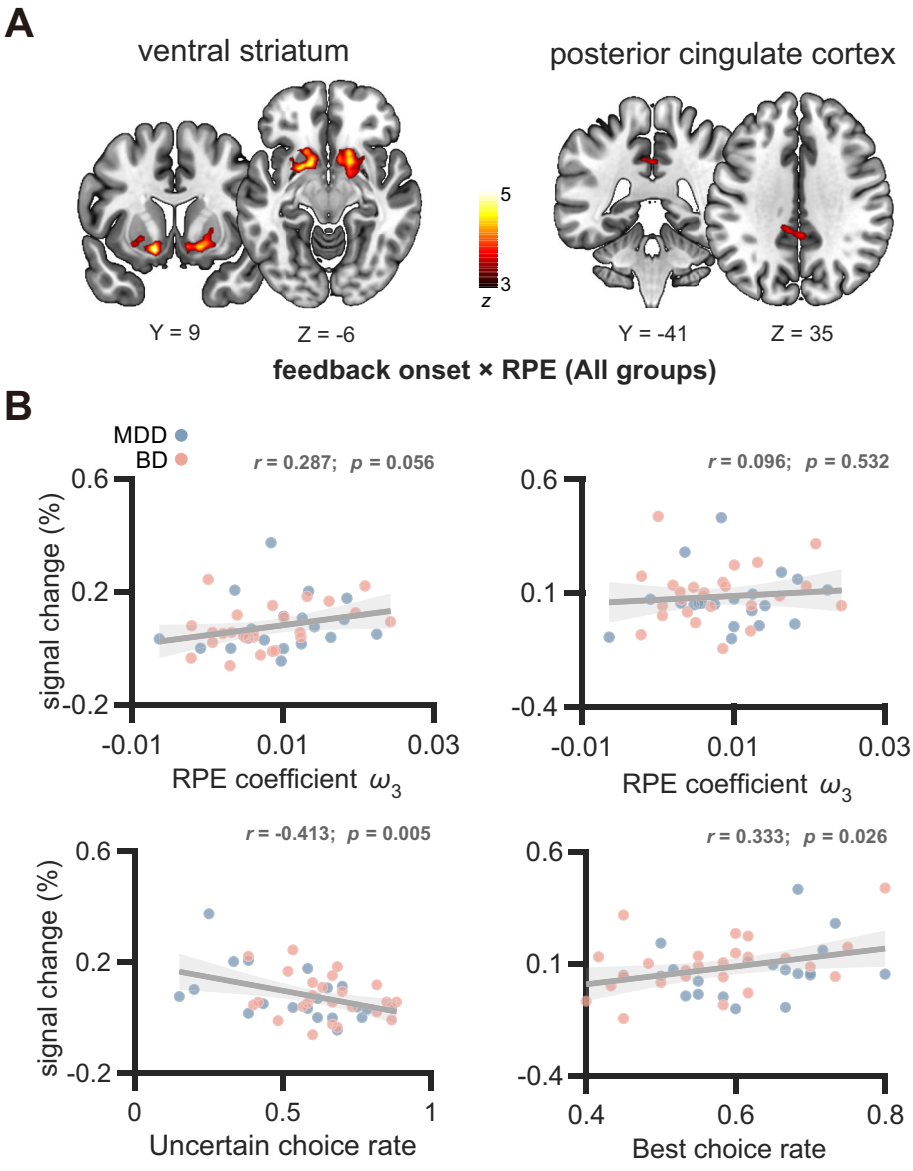

Figure 5 Neural activation correlates with RPE. (A) RPE-related signals in the ventral striatum and the left posterior cingulate cortex. Orange shaded regions indicate clusters in the bilateral ventral striatum and the left posterior cingulate cortex where activity was significantly modulated by RPE at feedback onset. Voxels with $|z| > 5$ are shown in saturated color. (B) Correlation between brain activation and parameters/behaviors. Signal change (y-axis) in the ventral striatum (left) and the left posterior cingulate cortex (right) at feedback onset modulated by RPE correlated with varying degrees of w_3 (top) and behavioral indicators (bottom). Scatters for MDD (blue) and BD (red), and fitted lines (light gray) for all participants are shown simultaneously. Shaded areas are 95% confidence intervals for the fitted lines.

outcome or learning phase (Redlich *et al.*, 2015; Mason *et al.*, 2017; Johnson *et al.*, 2019; Long *et al.*, 2022; Pouchon *et al.*, 2023; Nusslock *et al.*, 2025). These interpretations, however, warrant further investigation given the limited number of studies directly addressing reward processing abnormalities in BD during depressed mood states. Importantly, suboptimal decision-making and risk preference in BD have been linked to longer and more severe manic episodes (Swann *et al.*, 2007; Meade *et al.*, 2010), higher likelihood of suicide in high-risk populations (Zakowicz *et al.*, 2021), and associations with impulsive personality characteristics, genetic traits, and emotional fluctuations (Di Nicola *et al.*, 2010; Muhtadie *et al.*, 2013; Hindley *et al.*, 2021). Taken together, such maladaptive decision behavior may contribute to the greater life impairment experienced by adolescents with BD as compared to those with MDD.

More importantly, our study revealed modest but noteworthy neural activation differences between BD and MDD in the context of risky decision-making. Prior research has shown that differences in reward processing between BD and MDD are associated with distinct patterns of activation across multiple reward-related brain regions (Chase *et al.*, 2013; Whitton *et al.*, 2015; Wang *et al.*, 2022). For instance, individuals with BD exhibit reduced response to reward feedback in the nucleus accumbens, caudate nucleus, thalamus, insula, and prefrontal cortex (Redlich *et al.*, 2015). In the present study, we identified the mOFC as a potential region that may differentiate reward- and mood-related pro-

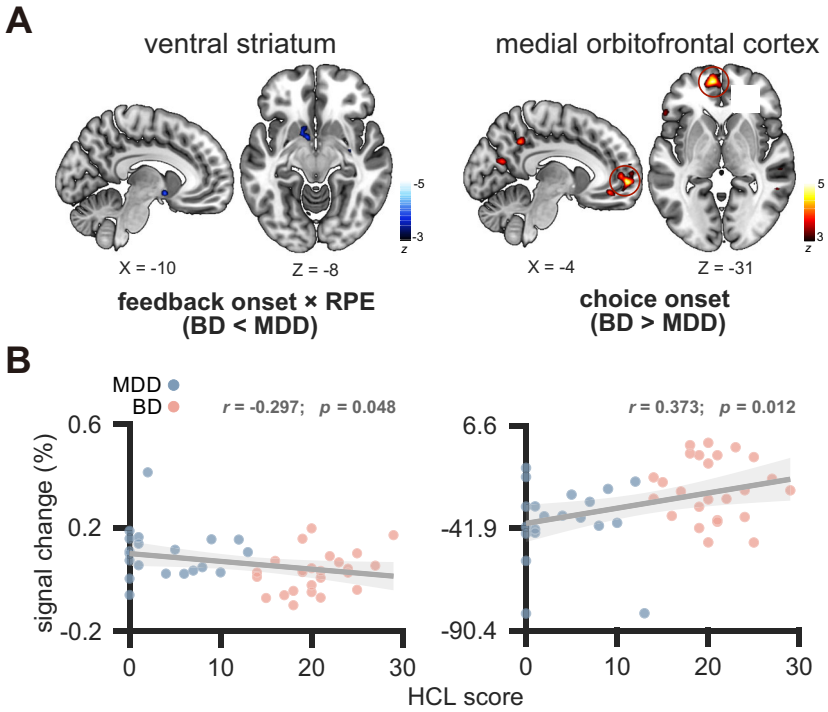

Figure 6 Differences in neural activation between BD and MDD. (A) Differences in brain activation. Blue shaded regions (left) indicate clusters in the left ventral striatum. Orange shaded regions (right) with red circle indicate clusters in the left mOFC. Voxels with $|z| > 5$ are shown in saturated color. (B) Correlation between brain activation and symptoms. Signal change (*y*-axis) in the left ventral striatum (left) at feedback onset modulated by RPE and the left mOFC (right) at choice onset is correlated with HCL score. Scatters for MDD (blue) and BD (red), and fitted lines (light gray) for all participants are shown simultaneously. Shaded areas are 95% confidence intervals for the fitted lines.

cessing between BD and MDD. Numerous studies have also indicated that the OFC is the key brain area in emotion, and in the representation of reward value and non-reward, i.e. not obtaining an expected reward, with close associations to depressive symptoms (Rolls *et al.*, 2020). While some regions identified in the current study (i.e. parahippocampal gyrus) are not traditionally considered core regions of mood regulation, their involvement may reflect broader disruptions in cognitive control and reward-based decision-making. Notably, we found that individual differences in activation within the ventral striatum and mOFC were associated with manic symptoms. This pattern provides preliminary support for the idea that alterations in reward sensitivity may contribute to differences in manic symptoms between BD and MDD. Our findings may serve as an initial step toward identifying candidate neural markers that warrant replication and further investigation in larger samples.

Another key question in our study is how reward processing contributes to subjective mood and whether this contribution is associated with clinical symptoms. In our model, the contribution of RPE to subjective mood is quantified by the RPE-mood association (i.e. RPE coefficient w_3). We found decision rationality as a mediator within the prediction from RPE-mood association to symptoms. A substantial body of research has demonstrated the links between subjective mood, decision behavior, and clinical symptoms. For example, reward-induced subjective mood impairs rational decision-making (Phelps *et al.*, 2014). Maladaptive decision-making behaviors also negatively impact symptoms in patients with mood disorders (Alexander *et al.*, 2017). Importantly, our study takes a further step in unifying the triple relationship between reward-based subjective mood, decision behavior, and symptom severity. Our findings provide a complete conceptual framework that bridges cognitive computation, behavior, and the progression of psychopathology in both MDD and BD patients.

Our study did not find significant differences between adolescents with BD and MDD in their neural representation of RPE, nor did we observe group differences in the influence of reward information on subjective mood. This finding may be consistent with a spectrum concept of mood disorders (Cassano *et al.*, 2004; Angst and Cassano, 2005), which posits that manic and depressive symptoms exist along a continuum rather than reflecting a strict unipolar–bipolar dichotomy. Increasing evidence suggests that BD and MDD may not be separated by discrete boundaries, but instead represent different positions along a dimensional trajectory of mood dysregulation (Moreno *et al.*, 2012; Wallace *et al.*, 2016; Angst *et al.*, 2018). In line with this perspective, prior work has also suggested that reward processing in non-manic BD patients may resemble that of healthy controls or MDD (Chase *et al.*, 2013; Edge *et al.*, 2013; Johnson *et al.*, 2019), whereas much of the evidence regarding atypical reward processing in BD comes from studies of manic episodes (Mason *et al.*, 2012; Caseras *et al.*, 2013; Damme *et al.*, 2017). These findings highlight the importance of considering mood symptoms within a dimensional framework. At the same time, we observed significant behavioral differences and functional activation differences in multiple brain regions during decision-making between BD and MDD adolescents. As noted in

our previous discussion, these positive findings can be viewed as markers that may aid traditional categorical diagnosis. However, from a spectrum perspective, these findings may also reflect differences along specific symptom dimensions that cut across diagnostic categories, such as variation in manic symptom severity across individuals. Overall, while our results do not fully support a strict categorical distinction between MDD and BD as traditionally defined, they imply that classifying patients according to manic-depressive symptom dimensions, or into finer-grained subgroups along this continuum, may become a better approach to capture the heterogeneity of mood disorders than rigid diagnostic boundaries.

Our study also has several limitations. First, the sample included a relatively small number of adolescents with BD and MDD, which may have limited the statistical power of some analyses. Accordingly, the results should be interpreted as relative differences between BD and MDD, rather than as deviations from normative functioning. To draw stronger conclusions regarding disorder-specific mechanisms and exaggerated variants of normative processes, future studies should incorporate larger samples, including healthy participants, for direct comparisons of multiple groups or integrate findings with other studies that include such groups.

Second, our model relied on relatively simple, linear decision values, whereas psychiatric disorders such as BD may involve more complex maladaptation, including impaired learning under environmental volatility. Reinforcement learning models that track behavioral updating under changing contexts may provide more sensitive markers of disorder-specific features. More broadly, while computational models can decompose cognitive processes beyond traditional approaches, the complexity of psychiatric disorders constrains what a single model can capture. For example, some mood dimensions may be more strongly influenced by threat than by reward. Integrating multiple computational models into a broader "computational fingerprint" may therefore offer a more comprehensive characterization of psychiatric conditions.

Finally, our study was limited to cross-sectional comparisons of behavioral and neural measures, and some effects in comparisons between the BD and MDD groups reached only trending significance. These findings, therefore, require further validation and replication. Future research should consider conducting joint analyses on more demographic and biological information, such as somatic symptoms, familial susceptibility, personality traits, and brain networks (Perlis *et al.*, 2006; Araujo *et al.*, 2016; Chen *et al.*, 2022; Nimarko *et al.*, 2022; Qin *et al.*, 2022), and incorporate longitudinal designs to track developmental trajectories of adolescents with BD and MDD. Such integrative approaches may help reduce the risk of misdiagnosis and facilitate the development of more precise, personalized interventions.

Conclusion

In conclusion, our findings underscore the critical role of reward processing in mood regulation. Adolescents with BD exhibited reduced decision rationality. Individual differences in decision rationality appeared to mediate the relationship between RPE-mood association and clinical symptoms. RPE-related activation was observed in the ventral striatum and showed a slight positive correlation with the RPE-mood association across all participants. Subtle differences were observed in several brain regions between BD and MDD. Activation in these regions was further associated with manic symptoms. These patterns may point to candidate neural markers, such as the mOFC, that may differentiate the two groups. Future research should utilize more sophisticated reinforcement learning models and integrate multi-modal data to comprehensively identify MDD and BD and help reduce misdiagnosis.

Supplementary data

Supplementary data are available at *Psychoradiology Journal* online.

Author contributions

Yu-Feng Xia (Data curation, Formal Analysis, Writing – original draft, Writing – review & editing), Yingyan Zhong (Data curation, Validation, Writing – review & editing), Zi-Jian Cheng (Data curation, Validation, Writing – review & editing), Enzhao Cong (Funding acquisition, Supervision, Writing – review & editing), Yifeng Xu (Supervision, Writing – review & editing), Ru-Yuan Zhang (Conceptualization, Funding acquisition, Supervision, Writing – original draft, Writing – review & editing)

Conflicts of interest

The authors declare no competing financial interests.

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