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Research paper

Motivational differences in unipolar and bipolar depression, manic bipolar, acute and stable phase schizophrenia

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ABSTRACT

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Keywords:

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Background: : Motivational anhedonia has been observed in patients with a wide range of mental disorders. However, the similarity and uniqueness of this deficit across diagnostic groups has not been thoroughly investigated.

Method: : The study compared motivational deficits in 37 patients with major depressive disorder (MDD), 32 with bipolar depression, 33 with manic bipolar disorder (BD), 30 with acute phase and 33 with stable phase schizophrenia, as well as 47 healthy controls. Participants were administered the Effort-Expenditure for Reward Task which measures allocation of effort between a high-effort and a low-effort task for monetary rewards at varying magnitudes and probabilities.

Results: Compared with healthy controls, BD manic, acute and stable phase schizophrenia patients were significantly less likely to choose the high-effort task in the high reward magnitude condition. BD manic and acute phase schizophrenia patients were significantly less likely to choose the high-effort task in the high probability condition. Acute and stable phase schizophrenia patients made less effort in the high estimated value condition. Bipolar manic patients made excessive effort in low estimated value but less effort in high estimated value. Contrary to expectations, both the unipolar and bipolar depression patients did not differ significantly from healthy controls in reward magnitude, probability, and estimated value conditions. Anhedonia and negative symptoms were associated with fewer high-effort task choices in schizophrenia patients.

Conclusion: : Motivation anhedonia showed distinct patterns across psychiatric patients: acute phase schizophrenia was the most severely affected, bipolar mania was similar to schizophrenia, but bipolar depression was similar to unipolar depression.

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1. Introduction

Motivational anhedonia manifests as reduced motivation to initiate goal-directed behaviors that could yield pleasurable outcomes (Treadway and Zald, 2011). In reward processing, motivational anhedonia is regarded as a lack of reward "wanting" rather than reward "liking"(-Berridge et al., 2009). One promising translational measure of motivation anhedonia is the Effortful Expenditure for Rewards Task (EEfRT) (Treadway et al., 2012). Reward wanting in healthy people is an ability to balance costs and benefits when selecting from multiple options (Treadway et al., 2009). However, it has been reported that patients with major depressive disorder (MDD), bipolar disorder (BD) and schizophrenia display reduced effort to gain reward and fail to respond optimally to uncertain rewards(Barch et al., 2014; Treadway et al., 2012; Wang et al., 2015; Yang et al., 2014; Zou et al., 2020).

In mood disorders, MDD patients showed less willingness to expend effort for rewards and also were less able to effectively use information about magnitude and probability of rewards to guide their choice behaviour (Treadway et al., 2012; Treadway et al., 2009). Such motivation deficits have also been displayed in individuals with subsyndromal depression, with the effect amplified in MDD patients, but dissipated in stable-phase MDD patients(Yang et al., 2014). Unlike individuals with MDD, BD manic patients displayed an excessive increase in approach-related motivation(Alloy et al., 2016; Nusslock and Alloy, 2017). They were less able to delay responding to rewards(Swann et al., 2009), demonstrated a preference for high-risk, high-reward choices (Burdick et al., 2014), and higher odds of choosing the "high effort" option on the EEfRT task when reward probability was low(Nusslock and Alloy, 2017). This increased reward motivation would appear to uniquely relate to manic symptoms. With respect to bipolar depression, few studies have examined motivational anhedonia. Using the progressive ratio task, which manipulates the reward value but not the probability, Hershenberg et al. (2016) found that motivational anhedonia was present across unipolar and bipolar depressed patients, with both exhibiting significantly less effort to gain reward (Hershenberg et al., 2016; Zou et al., 2020). Thus, additional research is needed to determine whether bipolar depression is similar to unipolar depression in terms of being characterized by reduced motivation, or whether, like bipolar mania, it involves increased motivation.

Unlike with mood disorders, there is a growing consensus that schizophrenia does not reflect a primary motivation deficit, but rather a difficulty in representing the value of rewarding experiences in cognition and working memory(Gold et al., 2008; Strauss et al., 2014). For example, individuals with schizophrenia do not exhibit an overall reduction in effort expenditure for reward (as demonstrated in individuals with MDD), but instead fail to select high effort options at times when it is most advantageous to do so(Barch et al., 2014; Chang et al., 2019; Cooper et al., 2019; McCarthy et al., 2016; Treadway et al., 2015). Negative symptoms were inversely related to decreased willingness to expend effort for reward(Barch et al., 2014; Fervaha et al., 2013; Strauss et al., 2016). Although mood disorders and schizophrenia display similar behavioural deficits on effort-cost tasks, these may result from very different mechanisms. The model of reward sensitivity proposes that risk for MDD and BD are characterized by extreme and opposite profiles of reward sensitivity, with blunted reward sensitivity serving as a risk factor for major depression(Pizzagalli, 2014; Treadway and Zald, 2013; Whitton et al., 2015), whereas abnormally elevated reward sensitivity is a risk factor for BD(Alloy et al., 2015; Johnson et al., 2012b). In patients with schizophrenia, the Aberrant Salience or Dopamine Hypothesis argues that negative and positive symptoms result from inappropriate (as opposed to chronically reduced or enhanced) dopamine release that fails to appropriately respond to meaningful reward cues(Nusslock and Alloy, 2017). Culbreth et al. (2018) proposed that reduced reward responsiveness in mood disorders may stem from blunted activation of the ventral striatum. For example, individuals do not select high-effort options because they do not find the incentive

offered sufficiently rewarding. In contrast, motivational anhedonia in schizophrenia may be due to dysfunction within the dorsolateral prefrontal cortex andthe anterior cingulate cortex, leading to inability to represent the value of potential rewards and using reward information to guide decision-making (Culbreth et al., 2018).

Relatively few transdiagnostic studies have compared distinct patient groups with motivation deficits(Hershenberg et al., 2016; Wang et al., 2020; Zou et al., 2020). Hershenberg et al. (2016) demonstrated that diminished effort was present across depressed patients who experienced either unipolar or bipolar depression. Zou et al. (2020) found that MDD, BD, and schizophrenia patients made fewer high-effort choices in an EEfRT task than healthy controls. Wang et al. (2020) reported that all patients with SCZ, MDD, and BD exhibited emotion-behavior decoupling compared with HC: an intact ability to enjoy positively valenced stimuli ("liking") but lacked the motivation to pursue positive outcomes ("wanting"). SCZ patients showed the poorest decoupling between emotion and behavior in both representational and evoked responding, whereas BD and MDD patients showed impaired motivational behaviour only in evoked responding. However, in these studies, participants in the various diagnostic groups were not further separated into subtypes.

Thus, the main aim of the current study was to compare effort-based decision-making in patients with MDD, BD mania and depression, acute and stable phase schizophrenia, as well as healthy controls, to identify shared and unique mechanisms of motivational anhedonia. Based on existing evidence for the reward deficits, it was hypothesized that all clinical groups would exhibit common motivation deficits with reduced effort toward rewards compared with healthy controls. Furthermore, patients with schizophrenia were hypothesised to make the fewest higheffort task choices among the five diagnostic groups, especially those with acute-phase schizophrenia according to the findings of Wang et al. (2020). Individuals with MDD and bipolar depression had both been found to show less willingness and less effort to gain reward (Hershenberg et al., 2016). However, individuals with bipolar mania had difficulty in evaluating the costs and benefits of a given set of reward information due to their dysfunctional beliefs and emotions (Johnson et al., 2012a; Johnson et al., 2012b). Based on these findings, it was hypothesized that bipolar depression would be similar to unipolar depression but not bipolar mania in effort-based decision-making behavior. It was further hypothesized that those with self-reported anhedonia and negative symptoms would be particularly prone to make fewer high-effort task choices in reward-based decision-making according to previous studies on each group (Treadway et al., 2012, 2015; Yang et al., 2014).

2. Materials and method

2.1. Participants

Thirty-seven unipolar patients with MDD, 33 currently depressed and 32 manic patients with BD, 33 acute-phase and 30 stable-phase patients with schizophrenia were recruited from the inpatient and outpatient units at the Hunan Brain Hospital. All patients met the diagnostic criteria for MDD, BD, and schizophrenia respectively according to the DSM-IV using the Structured Clinical Interview for DSMIV-Research Version(First, Michael B. et al., 2001). Inclusion criteria were 1) being aged between 18 and 50 years-old; 2) \geq nine years of education; 3) having MDD, BD, or schizophrenia as the main psychiatric condition; 4) no central nervous system disorders; 5) no drug abuse or brain injury history. 6) acute-phase schizophrenia patients defined as any new-onset or recurrent psychotic symptoms which required either initiation of antipsychotic treatment, change in existing treatment, or hospitalization. All acute-phase patients were recruited from the outpatient unit. Stable-phase schizophrenia patients were required to meet the following criteria based on the Positive and Negative Syndrome Scale (Andreasen et al., 2005): 1) scores of 3 or less

for: delusions, conceptual disorganization, hallucinatory behaviour, blunted affect, social withdrawal, lack of spontaneity, mannerisms and posturing, and unusual thought content. 2) All stable-episode patients had experienced at least 6 months of hospitalization. Within the bipolar sample, all manic patients had Bipolar Disorder-I. Ten BD manic patients and 2 BD depressed patients had psychotic symptoms. In the MDD sample, 3 patients had psychotic symptoms. Thirteen patients with MDD were first-episode and twenty-four were recurrent MDD.

For comparison, 43 healthy controls (HC) were recruited from the community. Volunteers were assessed with the SCID to exclude any psychiatric disorders. The Ethics Committee of the Hunan Brain Hospital approved the study protocol. All participants provided written informed consent.

2.2. Clinical Assessments

The Chinese version of the 24-item Hamilton Rating Scale for Depression (HRSD-24) was used to assess severity of depressive symptoms (Zhao, 1992, Zheng 1988). The Hamilton Rating Scale for Anxiety (HAMA) was used to assess severity of anxiety symptoms(Wang XD, 1999b). The Young Manic Rating Scale Questionnaire (YMRS) was used to assess severity of manic symptoms(Young et al., 1978). The HRSD, HAMA and YMRS were only administered to BD depression and mania, and MDD participants. The Positive and Negative Syndrome Scale (PANSS) was used to assess severity of schizophrenia symptoms(Wang XD, 1999a). The PANSS was only administered to schizophrenia acute-phase and stable-phase participants. Healthy controls were not assessed with these clinical scales.

2.3. Assessment of pleasure experience

The Chinese version of the Snaith–Hamilton Pleasure Scale (SHAPS) was used to assess anhedonic state over the last few days (Liu et al., 2012). The SHAPS has been validated with good internal consistency (Cronbach' s $\alpha = 0.93$) and test–retest reliability (r= 0.85). It consists of 14 items each answered on a 4-point Likert scale (totally false for me) to (totally true for me), with a higher total score indicating higher levels of anhedonia.

The Chinese version of the Temporal Experience of Pleasure Scale (TEPS) was used to evaluate trait anticipatory and consummatory anhedonia (Chan et al., 2010). Four factors (abstract anticipatory, concrete anticipatory, abstract consummatory pleasure, and concrete consummatory) have been validated with good internal consistency (Cronbach' s α = 0.83) and test–retest reliability (*r*= 0.79). The present study combined the abstract and contextual anticipatory factors to create an anticipatory anhedonia subscale (TEPS-ANT), and abstract and contextual consummatory factors to create a consummatory anhedonia subscale (TEPS-CON). The inventory consists of 20 items each answered on a 6-point Likert scale (1 (totally false for me) to 6 (totally true for me)), with lower TEPS scores indicating higher levels of anhedonia.

2.4. Effort-Expenditure for Rewards Task (EEfRT)

The task used in the present study was a modified version of the Effort Expenditure for Rewards Task (Yang et al., 2014). First, the participants had to choose between the high and low effort tasks. The high-effort task was 20 button-presses with the non-dominant pinky finger within 4s while the low-effort task was 10 button presses with the dominant index finger within 4s. For the low-effort task, participants were eligible to win ¥0.5 for each successfully completed trial. For the high-effort task, participants were eligible to win two higher monetary rewards (reward magnitude: ¥0.8 and ¥5). In each trial, reward probability was manipulated into three levels (low: 20%, medium:50%, high: 80%), which meant that it was not guaranteed to obtain a monetary reward even if the physical effort was successfully exerted. After choosing a task, participants had to exert the effort and a reward would be presented. The EEfRT task was a 2 (reward magnitude) \times 3 (reward probability) design. Each cell condition was repeated 6 times, yielding 36 trials in total. The task lasted for 10 minutes. Fig. 1 illustrates the trial procedure. All trials began with a 1-second fixation cross, following a 4-second choice period in which participants were presented with information regarding the probability of receiving a reward and the reward magnitude of the high-effort task. Participants were told that if they did not make a choice within 4 seconds, they would be randomly assigned to either the easy or the high-effort task for that trial. After making a choice, they were shown a 1-second "Ready" screen and then completed the task. Following task completion, participants were shown a 2-second feedback screen informing them that the task was successfully or unsuccessfully completed. After participants completed the entire study, they were debriefed and were given their reward of approximately 50~80 RMB according to their performance on the task.

2.5. Procedures

All data was collected between March 2016 and September 2018. The clinical study population consisted of individuals with a psychiatric diagnosis whose symptoms were severe enough to require hospitalization. Patients and their doctors were informed about the study's aims and methods. Interviews and measurements of psychiatric symptoms and the EEfRT task were conducted in a private meeting room on the ward. Acute schizophrenia patient assessments were conducted at the outpatient clinics before hospitalization. All psychometric tests were conducted in a single day for each participant.

2.6. Medication use

Medication reports closest to the date of testing were searched for mention of antidepressant, antipsychotic, or mood stabilizer use. This information was used to create binary variables to examine potential effects of psychiatric medication use on EEfRT performance.

2.7. Data Analysis

Data was analysed using Generalized Estimating Equation (GEE) models in line with previous studies (Wang et al., 2015; Yang et al., 2014). GEE models allow for trial-by-trial modelling of both time-varying parameters (e.g., changes in reward magnitude and probability of the hard task for each trial) as well as allowing for the exclusion of the influence of fatigue when number of trials was included as an additional covariate. The working correlation matrix was an independent model in the present study. The binary distributions to model were constructed to examine the main effect of probability, reward magnitude, estimated value (EV: probability \times reward magnitude) of high-effort task choices and group, the interaction between group and probability, reward magnitude and EV. Trial number, age, gender, education, medication use and current nicotine use were included as covariates. Post-hoc tests with bonferroni correction were conducted when significant main effects and interactions were detected. Pearson correlations were calculated to determine the association between clinical symptoms and high-effort task choices in the patient groups. Following the method employed by previous studies (Barch et al., 2014), four EEfRT performance indices were chosen: (1) percentage of choices in 80% probability condition; (2) percentage of choices at high reward condition; (3) difference in choices between 20% and 80% probability conditions; and (4) difference in choices between low and high reward conditions.

3. Results

3.1. Demographic and clinical characteristics

Sample characteristics are shown in Table 1. There was no significant



Fig .1. Modified version Effort Expenditure for Rewards Task (EEfRT) trial.

Table 1

Demographic and clinical characteristics of participants.

	MDD (n=37)	BD Depression (n=32)	Mania (n=33)	Schizophrenia Acute (n=30)	Stable (n=33)	HC (n=43)	$F/t/\chi 2$	р
Gender	18/19	25/7	22/11	12/18	8/25	17/26	25.59	<.001
Education	$13.43{\pm}2.80$	$13.94{\pm}2.50$	$13.45 {\pm} 2.36$	$13.63 {\pm} 2.72$	$12.76{\pm}2.20$	$13.40{\pm}2.00$	0.83	0.53
Age	$26.16 {\pm} 7.56$	$27.28{\pm}7.87$	$26.94{\pm}6.31$	$24.8 {\pm} 4.50$	$34.85{\pm}8.66$	$27.02{\pm}5.83$	8.64	<.001
Age of onset	$21.81{\pm}7.11$	$21{\pm}6.16$	$18.79 {\pm} 2.90$	$21.07 {\pm} 4.44$	$21.58{\pm}5.22$	-	1.65	0.16
Duration of illness(years)	$4.32{\pm}5.38$	$6.28 {\pm} 4.89$	$8.15{\pm}6.39$	$3.93{\pm}3.91$	$13.37{\pm}8.56$	-	13.19	<.001
Duration of treatment(day)	$10.65{\pm}22.52$	$168.09{\pm}533.02$	$356.12{\pm}602.60$	$15.83{\pm}11.38$	$789.09{\pm}362.92$	-	22.53	<.001
Current smoker (no/yes)	29/8	29/3	28/5	18/12	24/9	42/1	20.79	<.002
Antidepressant(no/yes)	19/18	1/32	32/1	25/5	32/1	43/0	92.22	<.001
Mood stabilizer(no/yes)	35/2	10/22	0/33	33/0	29/1	43/0	122.30	<.001
Antipsychotics(no/yes)	29/8	16/16	10/23	8/22	0/33	43/0	50.16	<.001
TEPS_ANT	$27.84{\pm}7.25$	$32.97{\pm}6.27$	38.12 ± 7.33	$33.13{\pm}5.37$	32.52 ± 5.96	$34.30{\pm}6.00$	7.72	<.001
TEPS_CON	$32.68{\pm}5.87$	$37.84{\pm}8.14$	43.76±7.37	$38.13{\pm}6.33$	$37.76 {\pm} 7.42$	41.65±7.39	9.38	<.001
SHAPS	$33.19{\pm}6.12$	$26.41 {\pm} 6.58$	$22.18{\pm}5.21$	$27.43 {\pm} 6.77$	$25.85{\pm}5.02$	$27.51{\pm}12.00$	10.34	<.001
HRSD	24.11 ± 7.68	16.06 ± 8.39	$5.88{\pm}2.90$	-	-	-	15.00	<.001
HAMA	$10.27{\pm}6.49$	$6.88{\pm}6.61$	$2.85{\pm}3.07$	-	-	-	62.76	<.001
YMRS	$0.32{\pm}0.78$	$1.63{\pm}2.32$	$13.55 {\pm} 5.35$	-	-	-	160.40	<.001
PANSS_P	-	-	-	$22.07 {\pm} 4.84$	$8.67 {\pm} 3.92$	-	146.96	<.001
PANSS_N	-	-	-	$10.10{\pm}2.72$	$18.09{\pm}3.89$	-	87.51	<.001
PANSS_G	-	-	-	$29.47{\pm}5.14$	$32.21{\pm}8.11$	-	2.52	0.12

Note: PANSS=Positive and Negative Syndrome Scale, PANSS_P=the positive subscale, PANSS_N=the negative subscale, PANSS_G=The general psychopathology subscale, HRSD= the 24-item Hamilton Rating Scale for Depression, HAMA= Hamilton Anxiety Rating Scale, YMRS=The Young Manic Rating Scale. SHAPS=S-naith-Hamilton Pleasure Scale; TEPS_ANT=Anticipatory subscale in the Temporal Experience of Pleasure Scale, TEPS_CON=Consummatory subscale in the Temporal Experience of Pleasure Scale

difference in years of education between MDD, BD depression, BD mania, acute-phase and stable-phase schizophrenia, and healthy controls. However, there were more males, an older age and more smokers in the stable-phase schizophrenia group and more females in the BD mania group. Duration of illness was significantly different among patients($F_{(4,160)} = 13.19$, p < 0.001, $\eta^2 = 0.25$), with patients with stable-phase schizophrenia having a longer duration than patients. No significant difference was found for age of onset between the five clinical groups. The MDD group had a significantly higher HRSD than the bipolar depressed group. The stable-phase schizophrenia group had a significantly lower PANSS positive subscale score and higher negative subscale score than the acute-phase schizophrenia group.

TEPS-ANT($F_{(5,202)} = 9.38$, p < 0.001, $\eta^2 = 0.19$), TEPS-CON($F_{(5,202)} = 10.34$, p < 0.001, $\eta^2 = 0.20$) and SHAPS ($F_{(5,202)} = 7.72$, p < 0.001, $\eta^2 = 0.16$) were significantly different among the MDD, BD mania, BD depression, acute-phase and stable-phase schizophrenia and HC groups. Pairwise comparisons are presented in the Supplemental Table 1 The MDD group reported more severe scores on the three types of anhedonia compared with stable-phase and acute-phase schizophrenia, BD mania, BD depression, and HC (all p < 0.05). The BD mania group reported less anhedonia compared with the MDD, BD depression, stable-phase and acute-phase schizophrenia groups (all p < 0.05) but did not differ from HCs. Moreover, the BD depression, stable-phase and acute-phase schizophrenia groups did not differ from HC on the three types of anhedonia.

3.2. Generalized Estimation Equation (GEE)

All participants completed both the high-effort and low-effort tasks

throughout the experiment. There was no significant group difference in the completion rate (high-effort task: $F_{(5,202)} = 1.92$, p = 0.09, $\eta^2 = 0.05$), or in mean choice reaction time ($F_{(5,202)} = 2.01$, p = 0.79, $\eta^2 = 0.05$). Table 2 shows the results of the GEE model using an independent working correlation matrix. Adjusting for gender, age, trial number, medication use and current nicotine use, group showed no main effect on high-effort task choices. However, the main effects of reward, probability and EV were all significantly predictive of high-effort task choices with increasing probability and reward magnitude.

A significant group x reward magnitude interaction (b=-.027, p= 0.006) was found, suggesting that reward magnitude was a significant

Table 2					
Generalized	Estimation	Equation	result o	of decision	making

	1	0	
	b coefficient	SE	р
Age	.008	.004	.032
Gender	.037	.065	.566
Education	.021	.012	.072
Trail number	.002	.001	.191
Reward	.155	.029	<.001
Probability	1.046	.178	<.001
Expected value (EV)	091	.034	.008
Smoker	035	.092	.702
Antidepressant	.138	.065	.034
Mood stabilizer	.089	.071	.213
Antipsychotics	.030	.070	.665
Group	.052	.047	.267
Group \times reward	027	.010	.006
Group \times probability	124	.064	.052
Group \times EV	.026	.013	.042

predictor of high-effort task choices between the patient and the healthy control groups. Compared with the healthy controls group, BD mania (b =-0.22, p=.002), acute-phase schizophrenia (b =-.40, p<.001) and stable-phase groups (b = -0.37, p<.001) were significantly less likely to choose high-effort tasks for high-reward magnitude, see Fig. 2A.

The interaction between group and probability was marginally significant (*b*=-0.12, *p*=0.052). Further analysis showed that, compared with HCs, acute-phase schizophrenia patients (*b*=-0.31, *p*=0.001) made less high-effort task choices under 50% probability conditions. BD mania (*b*=-0.25, *p*=.003) and acute-phase schizophrenia patients (*b*=-0.35, *p*<.001) made fewer high-effort task choices under 80% probability conditions. There was no difference between the stable-phase schizophrenia, unipolar and bipolar depression groups, and HCs in the three probability conditions, see Fig. 2B.

The interactive effect between group and EV was significant (*b*=0.03, *p*=0.043). Further simple effects tests showed BD mania patients (*b*=0.42, *p*=.008) made more high-effort task choices than HCs under the lowest estimated value of 0.16. The stable-phase schizophrenia group (*b*=-0.40, *p*=.005) made fewer high-effort task choices at high reward and low probability (EV 1). The stable-phase (*b*=-0.42, *p*<.001) and acute-phase schizophrenia groups (*b*=-0.56, *p*<.001) made fewer high-effort task choices at high reward and medium probability (EV 2.5). At high reward and high probability (EV 5), BD mania and acute-phase schizophrenia groups (*b*=-0.38, *p*=.002) made fewer high-effort task choices, see Fig. 2C.

To further examine the differences across the five patient groups in the high-effort task choice, an alternative GEE model was conducted with clinical characteristics as covariates. Antidepressant use (b=0.16, p=.026) and education (b=0.03, p=.042) were significantly predictive of high-effort task choices. Age, gender, duration of illness, smoker status, group and three interactions (group and reward, group and probability group and EV) were not significant.

3.3. Correlation between high-effort task choices and self-reported anhedonia

No significant relationship in the unipolar and bipolar depression groups, as well as the BD mania group, was found. However, among those with stable-phase schizophrenia, SHAPS was negatively associated with high-effort task choices in high reward magnitude (r = -0.41, p =0.009). Among those with acute-phase schizophrenia, TEPS-ANT was positively associated with high-effort task choices in high probability (r =0.38, p = 0.02) and the increase in high-effort task choice from 20% to 80% probability (r = 0.45, p = 0.006). TEPS-CON was positively associated with high-effort task choices in high probability (r = 0.48, p =0.004) and high reward magnitude task choices (r = 0.39, p = 0.017). SHAPS was negatively associated with high-effort task choices in high probability (r = -0.51, p = 0.002) and high reward task choices (r = -0.43, p = 0.008). All but two of these significant correlations remained after a Bonferroni correction (p = 0.004). The results of the correlations are provided in the Supplementary Table 2.

3.4. Correlation between high-effort task choices and clinical symptoms

Age of onset was not significantly associated with high-effort task choices within diagnostic groups. However, among those with MDD, duration of illness was positively associated with high-effort task choices in high probability (r = -0.31, p = 0.03) and the increase in high-effort task choice from 20% to 80% probability (r = -0.45, p = 0.003). Among those with schizophrenia, negative symptoms were negatively associated with the increase in high-effort task choice from low to high magnitude in the stable-phase (r = -0.31, p = 0.04) and acute-phase schizophrenia group (r = -0.35, p = 0.03). For acute-phase schizophrenia patients, disorganization symptoms were negatively associated with the increase in high-effort task choice from 20% to 80% probability (r = -0.38, p = 0.02). Duration of treatment was negatively associated with high-effort task choices in high reward (r = -0.36, p = 0.024) and the increase in high-effort task choice from low to high magnitude (r =-.430; p = 0.009). However, no findings remained significant after a Bonferroni correction. No significant relationship was found for clinical symptoms between bipolar depression and bipolar mania.

4. Discussion

The present study investigated the similarities and uniqueness in motivation deficits across multiple psychiatric disorders using a physical effort allocation paradigm. Compared with healthy controls, BD manic, acute-phase and stable-phase schizophrenia patients were significantly less likely to choose a high-effort task with high reward magnitude. Furthermore, BD manic and acute-phase schizophrenia patients were significantly less likely to choose a high-effort task with high probability. Acute-phase and stable-phase schizophrenia patients were both less able to use information about reward magnitude and probability to guide their choice behavior. Bipolar manic patients displayed atypical effortful choice behaviour, with excessive effort in low estimated value conditions but less effort in high estimated value conditions. Contrary to expectations, both the unipolar and bipolar depression patients did not differ from healthy controls in reward magnitude, probability, and estimated value conditions. Anhedonia and negative symptoms were associated with fewer high-effort task choices in schizophrenia patients.

Across stable-phase and acute-phase schizophrenia groups, participants displayed low effortful behaviour compared to controls, with fewer high-effort task choices under maximizing reward/probability conditions after accounting for the confounding effects of antipsychotic medication and nicotine use. This is consistent with two recent transdiagnostic studies (Wang et al., 2020; Zou et al., 2020). Zou et al. (2020)



Fig.2. (A) Interaction of group and reward magnitude. (B) Interaction of group and reward probability. (C) Interaction of group and estimated value. Error bar represents standard error. *: p < 0.05; **: p < 0.01. MDD = major depressive disorder; BD = bipolar depression; BM= bipolar mania; aSCZ = acute-phase schizo-phrenia; sSCZ = stable-phase schizophrenia; HC = healthy control.

showed schizophrenia patients to exhibit both deficits in effort for rewards and in sensitivity to information about the reward magnitude and probability when compared with BD and MDD patients and HCs. Wang et al. (2020) reported that schizophrenia patients showed the most serious emotion-behaviour decoupling when compared with BD, MDD and HC groups. The poor performance in schizophrenia may be due to disorganization in reward processing and cognitive function, including inappropriate energy expenditure and focus on irrelevant cues (Lambert et al., 2018; Whitton et al., 2015). This further supports the notion that an excessive and dysregulated firing of dopamine neurons in striatal dopamine release may result in blunting of phasic dopamine responses for relevant rewarding-cues, in particular high-value/high-probability reward, and therefore resulting in an impaired ability to optimally allocate effort for reward maximization(Maia and Frank, 2017). Importantly, this inefficient cost/benefit decision-making policy was especially the case in patients with acute-phase schizophrenia who showed fewer high-effort task choices in both high reward and high probability conditions. According to the model of aberrant salience, positive symptoms may be driven by excessive striatal dopamine release and lead to inability to represent the value of outcomes and plans in the task because the allocation of attentional resources and cognition are impaired(Whitton et al., 2015). Moreover, stable-phase schizophrenia patients still exhibited reduced overall motivation although they had less psychiatric symptoms than acute-phase schizophrenia. Previous studies also reported similar findings that patients with first-episode, chronic and clinical-stability schizophrenia showed reduced willingness to expend effort for reward (Barch et al., 2014; Cooper et al., 2019; McCarthy et al., 2016; Treadway et al., 2015; Wang et al., 2015; Zou et al., 2020). Additionally, these effort-based decision-making impairments were most pronounced in individuals with negative symptoms. This could be due to the fact that some negative symptoms such as poverty of speech and anhedonia remained unchanged during the stable episode because these symptoms were not sensitive to standard treatment (Dollfus and Petit, 1995). In general, evidence suggests that patients with BD are willing to expend more effort toward rewarding stimuli and increase goal pursuit following an initial reward(Johnson et al., 2012b). In the present study, EV results showed patients with bipolar mania exhibited more choices towards high-effort tasks when both reward magnitude and probability were low. In contrast, they chose fewer high-effort tasks when both reward magnitude and probability were high. This atypical effortful choice behaviour in BD patients may reflect a disorganized incentive motivation, more ambitious goal-striving when the reward salience was low and losing motivation when reward salience was high. These individuals have difficulty in evaluating the costs and benefits of a given set of reward magnitude and probabilities due to their dysfunctional belief and emotion (Johnson et al., 2012a; Johnson et al., 2012b). Previous literature found that abnormal decision-making in manic BD patients may arise due to elevated reward sensitivity and increased approach motivation (Adida et al., 2008; Burdick et al., 2014), and these processing abnormalities have been associated with elevated activity within the dopamine-rich ventral striatum and ventrolateral prefrontal cortex during reward processing (Alloy et al., 2015; Alloy et al., 2016; Phillips and Swartz, 2014). Except for the atypical effortful choice behaviour, BD manic patients showed the same pattern as acute schizophrenia patients who made fewer high-effort task choices in high reward and probability conditions. However, no similarity was found between BD mania and unipolar/bipolar depression. These findings suggest that BD mania may be similar to schizophrenia in its effort-based decision-making presentation. This finding also supports a parallel to the equifinality perspective (Whitton et al., 2015), the theory that a common motivational deficit observed across different disorders may be driven by distinct pathophysiological mechanisms (reward hypersensitivity model of bipolar, aberrant salience model of schizophrenia) across these two disorders.

It is unexpected that both unipolar and bipolar depression

participants exhibited similar patterns of effortful making decision to healthy controls. However, in most previous studies, patients with unipolar depression were found to have reduced reward motivation and were characterized by reward hyposensitivity (Pizzagalli, 2014; Treadway and Zald, 2013; Whitton et al., 2015). In the present study, compared with healthy controls, participants with unipolar and bipolar depression did not differ in probability and reward magnitude, nor estimated value. That said, depressed patients showed the same capacity in pursuit of rewards as healthy controls. Our unipolar (BDI, 26.95 ± 12.03) and bipolar depressed (BDI, 18.47 ± 11.08) participants had significantly fewer depression symptoms than first-episode drug-naïve MDD participants (BDI, 32.50±7.67) in our previous study (Yang et al., 2014), which may explain the intact motivational behaviour observed in the present study. Prior studies found depression severity to be related to impaired decision-making although this difficulty was not present in stable-phase MDD patients (Yang et al., 2014). Recently, decreased activity in the posterior ACC related to the EEfRT task in first-episode drug-naïve MDD participants was found to dissipate after one year follow-up when depressive symptoms stabilised (Yang et al., 2020). Importantly, BD depressed patients displayed similar motivational behaviour to MDD but not BD mania. This finding provided evidence that the mechanisms underlying reward motivation may be different in the subsets of manic and depressed BD patients: reward hypersensitivity is related to bipolar mania, but reward hyposensitivity is related to bipolar depression. Replication studies will be required to further clarify this relationship.

We also found significant differences in anhedonia in the five clinical groups: consistent with previous studies(Wang et al., 2020; Yang et al., 2014), MDD patients showed the most severe anhedonia whereas BD mania showed the least anhedonia and even more state pleasure experience than HCs. This indicates that reward hyposensitivity of unipolar depression and hypersensitivity of BD mania reflect self-reported anhedonia(Whitton et al., 2015). Similar to our results in schizophrenia participants, Schlosser et al. (2014) also found no significant impairment in anticipatory and consummatory anhedonia in individuals with early course or late-course schizophrenia (Schlosser et al., 2014). However, contrary to MDD patients, BD depression showed the same pleasure capability as HCs, suggesting bipolar depression showed similar depressive symptoms but having different hedonic capability impairments. Our EEfRT results supported that both disorders show depression-related motivation performance, but their anhedonia symptoms were distinctive and opposite features. This encourages further efforts to understand shared mechanisms of reward and motivation dysfunction across psychiatric disorders(Nusslock and Alloy, 2017). Within the clinical groups, several associations between the EEfRT performance and clinical variables were observed. First, duration of illness predicted fewer high-effort task choices in MDD group. This is consistent with previous MDD studies reporting motivational deficits to be associated with a poorer illness course(Treadway et al., 2012; Yang et al., 2014). Among both stable-phase and acute-phase schizophrenia patients, the relationship between negative symptoms, anhedonia and aberrant effortful performance was replicated, supporting the idea that greater deficits in effort allocation were associated with worse negative symptoms and severe anhedonia. Although none survived Bonferroni correction, these results are thus partially in keeping with some prior studies reporting that more severe negative symptoms are related to fewer high-effort task choices in the effort-based decision-making.

This study has several limitations. Firstly, the relatively small sample size may have limited the possibility to discover statistically significant differences and the six comparison groups were not matched in gender proportion and age. Secondly, not all clinical groups were assessed with all clinical rating measures, such as the PANSS, the YMRS, and the HAMD. Thirdly, medication usage and illness duration differed across groups, which may accentuate anhedonia or amotivation. Most patients were taking more than one psychotropic medication, making stratification for concomitant medication status unfeasible. In this study, we attempted to minimize this confounding factor by controlling for medication treatment in the analysis. Finally, cognitive function tests, IQ, and psychomotor activity were not assessed, which may have affected our results.

In summary, the present study has provided empirical evidence of impaired reward motivation in a transdiagnostic psychiatric sample by demonstrating similar and unique patterns of effort expenditure decision-making among patients. This work may ultimately provide insight into the neural mechanisms that underlie affective and psychotic disorders.

Author contribution

Authors Xinhua Yang designed the study, analyzed the data and wrote the first draft. Jia Huang help to analyse the data. Guangya Liu interviewed all patients using the DSM–IV. Kai Tian and Dongfang Wang participated in the data collection. Phillippa Harrision and Matthew E. Roser gave their critical revision of the manuscript. All authors contributed to and have approved the final manuscript.

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Supplementary materials

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X. Yang et al.

Journal of Affective Disorders 283 (2021) 254-261

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