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The effects of reward and frustration in patients with bipolar disorder: Evidence from a computerized task with non-contingent feedback

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ABSTRACT

Background: Bipolar disorder (BD) is characterized by mood changes that implies alterations in reward sensitivity and frustration tolerance. This study examined the effects of monetary reward and frustration on attentional performance and on affective experience across mood states in BD. Methods: An Affective Posner Task in which the nature of contingencies are divided in the three successive blocks (baseline condition, monetary reward and non-contingent feedback) was applied to BD individuals in their different episodes: mania ($n = 30$), depression ($n = 30$), and euthymia ($n = 30$) as well as to a group of healthy controls ($n = 30$). Results: Monetary reward improved performance (in terms of faster response times) in the euthymic group and the control group, whereas it impaired performance in the manic group and has not significant effect in the depressed group. In addition, an increased interference of frustration on response accuracy was exhibited in the three groups of BD patients (including euthymia) compared with healthy controls. Limitations: Participants' affective experience was self-informed by a Likert scale, so the reliability of this measure can be undermined in symptomatic patients in terms of stability and objectivity. Although it was statistically controlled, at the time of testing, all BD patients were medicated. Conclusions: A dissociated effect of reward and frustration was found between symptomatic and euthymic states in BD: whereas the benefit from monetary reward is affected only during symptomatic episodes (i.e., a state), the notably increased interference of frustration is exhibited also during euthymia (i.e., a trait).

Introduction

Bipolar disorder (BD) is a chronic and severe psychiatric disorder characterized by mood changes that implies alterations in goal-directed activity, reward sensitivity, and frustration tolerance (Johnson et. al., 2012). To understand the interaction between mood regulation and goal-directed behavior management in BD, it is fundamental to examine how individuals with BD in their different episodes (mania, depression, euthymia) emotionally react to the reward and frustration elicited by environmental contingencies (Rich et al., 2005). In the present experiment we do so by means of a computerized attentional task (the Affective Posner Task; henceforth, APT) as it can be used to analyze the effect of monetary reward and frustration by means of non-contingent feedback (see Rich et al. 2005, 2007, 2010).

Two theoretical models contribute to the comprehension of goal-directed behavior in BD. Firstly, the Behavioral Approach System (BAS) model (Gray, 1987, 1990) posits that the affective symptoms in BD are related to the dysregulation of two neurobiological systems that underlay goal-directed behavior (Harmon-Jones et al., 2008): the BAS manages the approach behavior to attain rewards, whereas the Behavioral Inhibition System (BIS) inhibits ongoing behavior in response to frustration. Indeed, mania has been related to the hyperactivity of the BAS and the hypoactivity of the BIS, so manic patients would focus on achieving rewards and would continue striving goals despite frustrating conditions (Alloy et al., 2006; Harmon-Jones et al., 2002;). In contrast, depression has been associated to the hypoactivity of the BAS and the hyperactivity of the BIS (Alloy et al., 2008; Meyer et al., 2001), so depressed patients would react with lower sensitivity to reward and would focus on avoiding frustration. Interestingly, the BIS/BAS model has identified some alterations in goal-directed behavior also during

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euthymia, where there is a tendency to invest in difficult-to-attain goals and to over-react to cues of goal progress versus thwarting (Johnson et. al., 2012). Thus, if goal-directed behavior is altered in patients with BD by the changes in the processing of potential reward and frustration, individuals in the different affective episodes in BD (mania, depression, and euthymia) would react differently to reward and frustration in a well-control experimental scenario (i.e., the APT). Secondly, according to the Affective Events Model (Weiss and Cropanzano, 1996), corrective feedback may act as an emotional event that induce emotional reactions. These emotional reactions, in turn, impact both the task performance (via reaction times and error rates) and the self-reported affective experience after finishing the task. In this sense, reward elicits positive emotional reactions that benefit task performance (via shorter reaction times without accuracy cost; see Rich et al. (2005), with the APT; and García-Blanco et al. (2016), with the Emotional Dot Probe Task), and it produces pleasant mood after the task (Mouratidis et al., 2008). In contrast, frustration elicits negative emotional reactions that impair task performance (via lower accuracy despite shorter reaction times; see Rich et al. (2005), and Tseng et al. (2017), with the APT) and it results in unpleasant mood (García-Blanco et al., 2016; Ball et al., 2010). Therefore, if altered reactivity to reward and frustration are exhibited in BD (Gruber et al., 2011; Mason et al., 2012), it would provide valuable information the examination of how affective symptoms differently modulate the emotional reactions to reward and frustration across the different episodes of BD (see Fig. 1).

At an empirical level, this issue has been investigated by the introduction of rewarding and frustrating feedback in computerized tasks. In the first case, studies focusing on reward system abnormalities in BD have predominantly utilized monetary reward paradigms. Ernst et al. (2004) applied a two-choice decision-making task in which pediatric patients with BD (not differed by clinical episode) were asked to select one of two options based on the likelihood of a gain/loss and the magnitude of that gain/loss (e.g., 30% chance of winning/loosing $2 and 70% chance of winning/loosing nothing). They found that higher rates of missed selections were associated to manic symptoms when patients were exposed to a potential loss, whereas they were associated to depressive symptoms when they were exposed to a potential winning. Moreover, self-affective experience was assessed after each trial and patients with BD reported being happier after winning and sadder after losing. In addition, Pizzagalli et al. (2008) administered a signal-detection task in which euthymic patients with BD had to classify a short or long mouth presented into a face. Importantly, for each participant one of the stimuli (short mouth trials or long mouth trials) was rewarded more frequently ("rich stimulus"). They found that, for rich stimuli, euthymic patients with BD showed lower response bias (i.e., lower preferred selection) and higher rates of missed selections compared with controls. Moreover, patients showed increased miss rates in trials where a "rich stimulus" had been immediately preceded of a rewarded "lean stimulus" or preceded of a non-rewarded "rich stimulus", suggesting higher interference of non-congruent feedback conditions. In their study, Hayden et al. (2008) applied a card-sorting task in which euthymic and symptomatic (including mania, depression, hypomania, and mixed episodes) patients with BD could win money by sorting as many cards as possible. Results found that euthymic patients with BD sorted more cards than symptomatic patients with BD and controls, whereas greater manic and depressive symptoms were associated to decreasing card sorting. Furthermore, Mueller et al. (2010) applied a pro-antisaccade task with monetary reward in which adolescent patients with BD (not differed by clinical episode) had to attend (prosaccade trial) or not to attend (antisaccade trial) a neutral visual target, and they were previously informed about if they were going to win (incentive trial) or not win (no incentive trial) money. Results showed that, for antisaccade trials, healthy controls improved their task performance (lower error rates) during incentive trials, but patients with BD did not. In sum, the above-discussed studies pointed to an altered monetary reward processing in BD, which would be exhibited by the lack of benefit with the inclusion of contingent monetary-reward (Hayden et al., 2008; Mueller et al., 2010) and by the task disengagement when the likelihood of winning or losing is at stake (Ernst et al., 2004; Pizzagalli et al., 2008).

Regarding to frustration, studies have used non-contingent feedback (i.e., feedback was manipulated and administered independently from participants' performance). Minassian et al. (2004) applied a two-choice prediction task in which manic patients with BD and healthy controls were required to guess the potential location (right or left) of a visual stimulus. Non-contingent negative feedback was applied to all subjects in three levels: 50% error rate for the first block, 80% for the second one, and 20% for the third one. Results found that manic patients were more likely to change their choices at the high error rate block, thus suggesting heightened responsiveness under frustrating conditions. In addition, Ruggero and Johnson (2006) applied a concept-formation task to euthymic patients with BD and controls who were instructed on trying to determine which value the experimenter had selected by listening to the feedback (social reward) given after each decision. Critically, non-contingent feedback had been randomly assigned in three different levels: (i) no failure feedback on all four blocks, (ii) failure feedback on one of the four blocks, and (iii) failure feedback on all four blocks. Immediately after, the participants' performance in a cognitive task and their self-reported emotional reactions were registered. Interestingly, in the total failure feedback condition, patients with BD showed slower

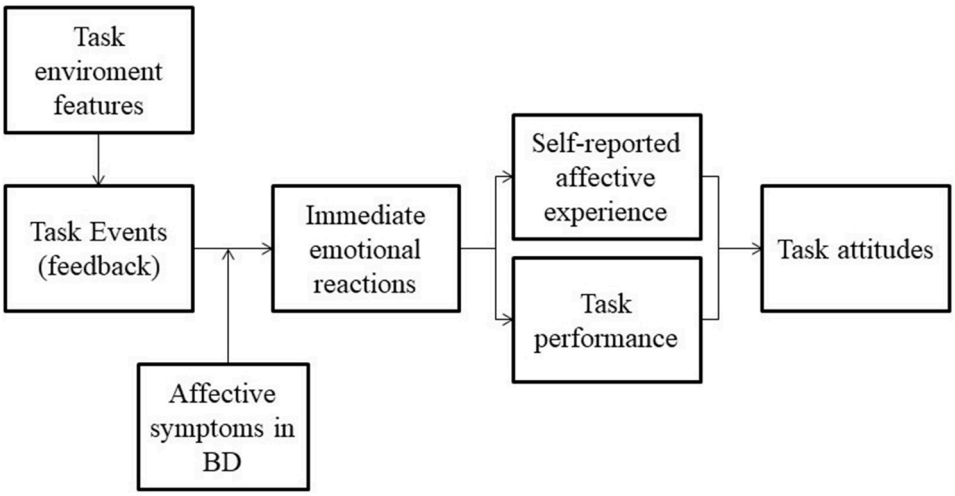

Fig 1. Schematic depiction of the affective events model (adapted from Weiss & Cropanzano, 1996).

latencies to solve the anagram compared to healthy controls, suggesting that emotional reactions to frustration would interfere with cognitive performance also in a euthymic state. However, no significant differences were found in self-reported emotional reactions between groups. In addition, Edge et al. (2015) assessed emotional reactivity to frustration in euthymic patients with BD, applying a video game in which participants navigated a vehicle and avoided obstacles. During two periods of 30 seconds the game was programmed to respond only intermittently to participants' key presses, so they were unable to avoid obstacles and, thus, lost money. The experimenters registered the performance in the task (via key presses, collisions with obstacles, and collection of power-ups), as well as affect ratings, heart rates and facial behavior. Results showed that, although both groups increased task engagement (i.e., they pressed the keys more frequently) and displayed angrier expressions during the frustrating condition, the euthymic patients with BD did not display greater reactivity than did the control group. Thus, the hypotheses about increased reactivity to frustration posited in the BAS model have not been strictly supported by empirical data -particularly during euthymia-, so the interest in a better characterization of the processing of frustration in BD is highlighted.

Although prior research is informative and suggests the existence of altered task performance and self-affective experience outcomes with rewarding and frustrating feedback in BD, some limitations must be considered. Firstly, the effect of reward has been mainly examined manipulating the magnitude (e.g., Ernst et al., 2004; Hayden et al., 2008) or the frequency (e.g., Pizzagalli et al., 2008) of reward. Interestingly, the inclusion of a prior baseline condition (i.e., a block without monetary contingencies) would allow to examine -in itself- the effect of monetary incentives, improving the characterization of the processing of reward in BD. Secondly, the jointly analysis of the effect of reward and frustration cannot be thoroughly inferred since these studies did not include contingent and non-contingent feedback in a single design. In our experiment, we aim to overcome these limitations by means of the APT paradigm (see Perez-Edgar and Fox, 2005; see also Rich et al. (2005, 2007, 2010) in patients with BD), which combines a baseline condition, the addition of monetary reward, and the inclusion of non-contingent feedback in a single design. Thus, the APT quantifies in the same task the effect of reward and frustration on performance (reaction times and accuracy) and on self-reported affective experience (see Tseng et al. (2017), for an examination of APT reliability and validity). In this paradigm, the nature of the contingencies is divided in three successive blocks that allow to measure the effect of reward (by the comparison between performance in Block 1 [baseline condition] and Block 2 [monetary reward]) and the effect of frustration (by the comparison between performance in Block 2 [contingent feedback] and Block 3 [non-contingent feedback]).

To the best of our knowledge, four prior studies have applied APT in pediatric patients with BD (Rich et al., 2005, 2007; Rich et al. 2010; Ross et al., 2020). For the three studies conducted by Rich (Rich et al., 2005, 2007; Rich et al. 2010), the effect of reward and frustration in BD group and healthy controls was conducted by the analysis of the comparisons within group (i.e., 20 euthymic pediatric patients with BD vs. 20 healthy controls) and across blocks (i.e., baseline condition vs. monetary reward; contingent-feedback vs. non-contingent feedback) for trials after negative and after positive feedback. In relation to the effect of reward, results revealed that, in trials after negative feedback, healthy controls improved their task performance (i.e., shorter reaction times) in the Block 2, whereas no significant effect was found in patients with BD. In addition, for the effect of frustration in trials after negative feedback, both healthy controls and patients with BD showed shorter reaction times in Block 3 than Block 2, although patients with BD were significantly slower than controls. In the case of trails after positive feedback, no significant effects were found. In relation to self-report emotional ratings, patients with BD reported being significantly unhappier and more aroused after the task. More recently, Ross et al. (2020) applied a fMRI paradigm using APT in a sample of 20 young patients with BD (not differentiated by clinical episode) and 20 healthy controls. In contrast, they did not find any significant effect of frustration in the task performance or in the self-affective responses of the patients with BD compared to healthy controls. However, the fMRI imaging data revealed that patients with BD showed greater activation in the limbic system, which is involved in threat processing, arousal, and reactive aggression.

With this in mind, it should be considered that the above-discussed studies were focused on pediatric patients, and they did not examine the effect of affective symptoms in itself (note that Rich et al. (2005, 2007), and Rich et al. (2010) applied APT in euthymic patients, whereas Ross et al. (2020) did not differentiate by clinical episodes). Therefore, these findings may not be strictly generalizable to symptomatic adult patients with BD since these two factors must be considered. Firstly, the clinical features of pediatric BD are substantially different from the adult disorder. For instance, children with BD usually present more rapid cycling and mixed symptoms, mood instability in pediatric BD is more defined by irritability rather than by depressive or manic symptoms, psychotic features during acute states are not as frequent as in adults, among others (see Youngstrom and Algorta 2014). Secondly, regarding the clinical episode, affective symptoms may critically impact on the emotional reactions to feedback, as suggested by the Affective Events Model (Weiss and Cropanzano, 1996). This effect should be studied thoroughly by the inclusion of one group per each episode in BD for comparison (mania, euthymia, and depression).

In the present experiment, we focused on examining how monetary reward and frustration impact on attentional task performance and self-affective experience in BD, placing the affective episode as a relevant element. From this assumption, two main questions would arise: (i) whether the effect of monetary reward (via additional monetary incentives to a baseline condition) and the effect of frustration (via non-contingent feedback) would be differentially modulated by the affective episode in patients with BD, and (ii) whether these effects are a state (i.e., patients with BD in depressive and manic episodes should exhibit an altered feedback effect of monetary reward or frustration on reaction times or accuracy rates, while no differences should be found between euthymic patients with BD and healthy controls), or a trait (i.e., patients with BD, regardless of their episode, should show an altered feedback effect of monetary reward or frustration relative to healthy controls).

The predictions are as follow. First, if reward-attaining behavior in BD is altered by the increase of BAS sensitivity during mania and its decrease during depression (Johnson et. al., 2012), one would expect an altered effect of monetary reward for symptomatic patients with BD, but not for euthymic individuals. That is, monetary reward -in contrast to the baseline condition- would benefit task performance (e.g., faster reaction times and/or higher accuracy) in euthymic individuals and healthy controls but not in manic and depressed BD individuals (i.e., the effect of monetary reward would be a state in BD). More specifically, in line with the decreased sensitivity to reward during depression (Meyer et al., 2001), we expected a lack effect of monetary reward in the depressed patients' task performance (see Ernst et al. (2004), and Hayden et al. (2008), for similar findings with computerized tasks in a monetary reward paradigm). Regarding to mania, we hypothesized an impaired task performance (slower reaction times and/or lower accuracy) with the introduction of monetary reward—the underlying idea is that manic patients would consider the monetary incentives as repetitive and uninspiring (see Hayden et al. (2008), for similar findings using a card-sorting task). This would be in line with prior research that reported that manic patients are more focused on the attainment of grandiose goals (Johnson, 2005; Johnson and Carver, 2006) and tend to get dysregulated with delayed monetary incentives (Mason et al., 2012). Second, given that goal-pursuit behavior in BD is altered by the over-reactivity to cues of goal progress versus thwarting and the increased engagement to difficult goals even during euthymia (Harmon-Jones et al., 2008; Wright et al., 2008), one would expect an increased negative impact of frustration (slower reaction times and/or increased error rates) in both symptomatic and non-symptomatic

patients with BD. Thus, when frustration is at stake, all patients with BD (and not only those symptomatic) would stay overly emotionally dysregulated as they become more frustrated, so their performance would be hindered to a greater extent than healthy controls (i.e., the effect of frustration would be a trait in BD). In particular, both euthymic and manic individuals may initially value the possibility of overcoming the obstacle and they would keep engaged to the task despite frustration, so they would become increasingly upset and would impair performance (Minassian et al., 2004). In contrast, depressed individuals may value the obstacle as too large to overcome, responding with inhibition to frustration and disengaging of the task effort (Winer and Salem, 2016). Finally, for self-reported affective experience, we hypothesized an increase in upsetting reactions (unhappier and/or more aroused reactions) after the task in BD symptomatic patients, in line with evidence of altered emotional reactions to feedback contingencies in BD (Ernst et al., 2004; Farmer et al., 2006; Rich et al., 2005; Rich et al., 2010; Roiser et al., 2009).

Method

Participants

The participants were 90 patients with BD from the Psychiatry Department (49 from in-patient wards and 41 from the outpatient Bipolar Disorder Unit) at the University and Polytechnic Hospital La Fe (Valencia, Spain) and 30 healthy individuals. Patients fulfilled the DSM-5 criteria (American Psychiatric Association, 2013) for BD type 1 as the primary diagnosis, and they were included in the manic ($n = 30$), depressed ($n = 30$), or euthymic ($n = 30$) group at the time of assessment. The control group ($n = 30$) was recruited by advertisement in the community. All participants were Caucasian.

No participant reported neurological history or major medical disorders likely to affect cognition. Additional exclusionary criteria were the use of non-psychotropic medication that could affect cognition (e.g., treatment with corticosteroids), and having undergone electroconvulsive therapy in the previous three months. No healthy control showed any type of psychiatric history. A total of five participants were excluded from the original sample (four patients and one healthy controls) based on these criteria. The Clinical Research Ethic Committee of the Health Research Institute La Fe approved the study protocol (Ref: 2011/0502). Written informed consent was obtained from all subjects before enrolment.

Selection criteria

Patients with BD were invited by their attending clinicians to participate in the study. The treating psychiatrist corroborated the diagnosis based on a case note review and an in-depth intake interview at the clinic. The assessment included all pertinent items from the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I; (First and Gibbon, 2004). The Beck Depression Inventory-II (BDI-II; Beck et al., 1996) and Young Mania Rating Scale (YMRS; Young et al., 1978) were used to exclude mixed states as well as the absence of affective symptoms in euthymic patients and healthy participants (BDI-II scores < 9, except in depressed group > 18; YMRS scores < 6, except in the manic group > 20). Additionally, every participant filled out the Beck Anxiety Inventory (BAI; Beck et al., 1988) to measure anxiety –scores were classified as minimal anxiety (0 to 7), mild anxiety (8 to 15), moderate anxiety (16 to 25), and severe anxiety (30 to 63)–, and the Social Adaptation Self-Evaluation Scale (SASS; Bosc et al. 1997) to measure social functioning – the total score ranged from 0 to 60 (the higher score denoted better functioning, and social maladjustment was defined as a score of less than 25). See Table 1 for sociodemographic and clinical data for the final sample.

Table 1
Demographic and clinical data from control group, depressed, euthymic and manic patients. Data shown are averages and standard deviations.

	Control ($n = 30$)	Euthymic ($n = 30$)	Depressed ($n = 30$)	Manic ($n = 30$)	*p*
Female [*n* (%)]	12 (40%)	13 (43.3%)	19 (63.3%)	9 (30%)	0.068
Age	42.6 (12.5)	44.3 (11.0)	49.2 (8.9)	44.5 (14.7)	0.185
Primary Studies [n (%)]	18 (60%)	3 (10%)	13 (43.3%)	11 (36.7%)	
SASS[1]	45.5 (3.4)	30.2 (8.5)	30.8 (7.3)	32.4 (11.7)	0.000
BAI[2]	0.5 (1.1)	15.2 (9.3)	17.4 (9.6)	7.8 (5.3)	0.000
BDI[3]	0.2 (0.6)	9.2 (10.0)	27.5 (11.6)	3.9 (5.5)	0.000
YMRS[4]	0.0 (0.0)	0.5 (1.4)	0.2 (0.9)	25.5 (7.2)	0.000
Medication (% of patients)					
Lithium (%)	-	73.1	50.0	45.0	.00
Antipsychotic (%)	-	50.0	59.1	95.0	.11
Antidepressive (%)	-	23.1	68.2	00.0	.00
Antiepileptic (%)	-	53.9	31.9	20.0	.05
Anxiolytic (%)	-	50.0	86.4	95.0	.00

[1] SASS: Social Adaptation Self-evaluation Scale
[2] BAI: Beck Anxiety Inventory
[3] BDI: Beck Depression Inventory
[4] YMRS: Young Manic Rating Scale.
Note. The p values correspond to Chi-squared test for gender and studies, and to ANOVA for the rest of the variables.

Materials

The experimental computer-based task was an adapted version of the Posner Paradigm (Perez-Edgar and Fox, 2005; Posner (2016); see also Rich et al. (2005, 2007, 2010) for variations of the task applied to patients with BD. The task consisted of presenting a fixation cross in the center of the screen for 750 ms, replaced by two boxes of equal distance from the fixation point on each side of the screen (right and left) for 300 ms. Immediately after, a cue (i.e., a blue square) appeared inside one of the squares for 300 ms (50% at right and 50% at left). This cue was substituted by the target (i.e., a black square). The target appears in the same square as the cue in 50% of the trials (valid trials), but in the other 50% of trials the target appears in the opposite square (invalid trials). Participants were instructed to press as fast as possible the "Z" key when the target appeared on the left side of the screen, and to press the "M" key when the target appeared on the right side. After the response, feedback was shown during 100 msec if subjects responded, or 500 msec if they failed to respond (in this case, longer feedback display was designed in order to garner the person`s attention). After this feedback, a next trial was initiated.

The paradigm was divided into three conditions (Block 1, Block 2, and Block 3) depending on the emotional feedback. Block 1 (baseline condition; 48 trials): feedback without contingencies was provided according to the participant' response accuracy (i.e. "Good" for correct responses or "Bad" for incorrect responses); Block 2 (monetary reward; 48 trials): participants won or lost ten cents on each trial, based on performance (i.e. "Good, you earned 10 cents", for correct responses, "Bad, you lost 10 cents", for incorrect responses); and, Block 3 (non-contingent reward; 96 trials): the feedback was similar to the second condition, but in 56% of the trials it was randomly manipulated regardless of the participants' response (i.e. in 56% of this condition a negative feedback [i.e. "Too slow, you lost 10 cents"] appeared even if the response was correct; see Fig. 2). Note that as in previous experiments with this procedure (see Deveney, 2019; Rich et al., 2005; Tseng et al., 2017), the final block induced frustration and was not counterbalanced. This was done to prevent performance in the following blocks from being affected by residual emotions (Pérez-Edgar and Fox, 2005).

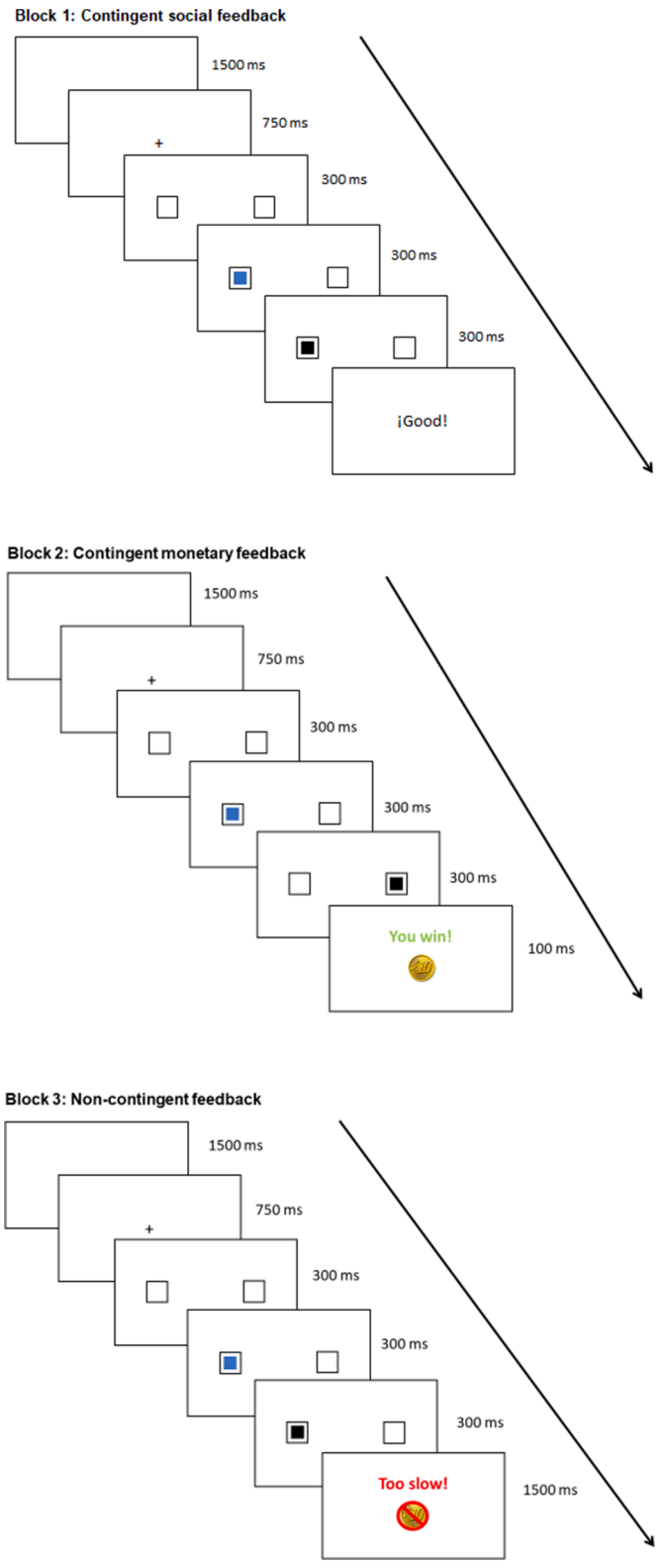

Fig 2. Affective posner task. sequence of trials in each block. Block 1 and 3 are examples of valid trials, and Block 2 is an example of invalid trial.

At the end of the experiment, each participant received the total amount of money that he had won depending on his accuracy rate. The maximum winning amount was 14.40€ (17.05$), but due to the manipulation of non-contingent feedback in Block 3, participants only could gain up to a maximum of 3.60€ (4.26$).

Prior studies that applied affective versions of the Posner task also assessed the affective experience of participants (Deveney, 2019; Lugo-Candelas et al., 2017; Rich et al., 2005, 2010). For this reason, prior to the beginning of the experiment (pre-test), and at the end of it (post-test), participants had to fill out or respond to a self-reported mood two-item scale. The first item measured the degree of arousal on a 5-point Likert scale ("How nervous do you feel?" on a scale of 1= "None" to 5= "Too nervous"). The second item measured the degree of valence on a 5-point Likert scale ("How are you feeling?" on a scale of 1= "very bad" to 5= "very good").

Procedure

Participants were tested individually in a quiet room. After signing an informed consent form, all participants responded to a demographic interview and the SASS, BAI and BDI-II rating scales. Additionally, patients completed a clinical interview and the YMRS. Afterwards, the APT was administered. Before starting the task, the experimenter explained the instructions to each participant, and he ensured that the task procedure had been correctly understood when the participant read the instructions in the computer screen before starting each block. Presentation of stimuli and recording of responses were controlled by DMDX software (Forster and Forster, 2003). Participants were seated approximately 60 cm in front of the monitor in a height-adjustable chair. The experimenter was in the room and monitored the stimulus presentation in each trial. The whole session lasted approximately 35-40 min.

Data analyze

The socio-demographic and clinical data for each group were analyses with *t*-tests for quantitative variables and with the Chi-square test for categorical variables. The dependent variables were: Reaction time (RT; i.e., time of response after a target presentation), Error rate (i.e., the percentage of responses that did not correspond to the target location per condition), and Self-reported arousal and valence scales. To guarantee that the responses were based on actual responses to the target location (see Rich et al., 2010; Whelan, 2008), very brief RTs (less than 200 ms) and those RTs beyond 2.5 standard deviations above each participant's mean were excluded from the analyses (less than 2% of all responses). We also excluded the incorrect RTs from the latency analyses.

Firstly, to examine the effect of reward, an omnibus analysis of variance (ANOVA) was conducted with Group (control, euthymic, depressed, manic) as between-subjects factor, and Block (1 [baseline condition] and 2 [monetary reward]) and Validity (valid and invalid trials) as within-subject factors.

Secondly, to the effect of frustration, an omnibus ANOVA was carried out with Group (control, euthymic, depressed, manic) as between-subjects factor, and Block (2 [contingent feedback] and 3 [non-contingent feedback]) and Validity (valid and invalid trials) as within-subject factors.

Finally, to test self–reported affective experience (i.e., valence and arousal) before and after the task application, omnibus ANOVAs were conducted with Group (control, euthymic, depressed, manic) as the between-subjects factor and Time (pre-test and post-test) as the within-subject factor.

In addition, we applied the Bonferroni correction for multiple tests with $\alpha_{familywise} = 0.05$ for cross-group comparisons (see García-Blanco et al. (2016), for a similar procedure). All the analyze were conducted using IBM SPSS v26.0.

Results

The descriptive data of RT and error rates for each block are displayed in Table 2.

Table 3 displays the omnibus ANOVA tables for the effects of reward

Table 2
Descriptive data of reaction times and percentage of errors for each experimental block, and self-reported arousal and valence for each group (control group, depressed, euthymic and manic patients).

			Control (n = 30)		Euthymic (n = 30)		Depressed (n = 30)		Manic (n = 30)	
Variables			Mean	SD	Mean	SD	Mean	SD	Mean	SD
	Block 1	Valid	444	125	512	132	669	208	560	225
Reaction Times		Invalid	466	122	594	144	716	214	597	196
	Block 2	Valid	420	112	494	140	688	258	602	230
		Invalid	429	105	545	153	733	250	636	211
	Block 3	Valid	331	38	373	72	555	237	510	256
		Invalid	346	33	425	91	604	221	562	231
	Block 1	Valid	2.92	4.26	1.95	3.91	12.10	17.38	15.43	19.40
Percentage of Errors		Invalid	3.33	6.53	2.65	4.58	12.06	17.75	17.06	21.38
	Block 2	Valid	2.13	4.21	0.42	1.29	10.56	20.08	11.10	17.23
		Invalid	0.46	1.41	0.85	2.34	10.71	20.35	14.90	17.92
	Block 3	Valid	3.35	3.84	6.42	7.72	15.82	16.01	20.02	17.87
		Invalid	2.78	3.18	11.23	12.38	19.16	18.35	27.48	19.12
Arousal		Pre-test	4.83	2.71	6.42	1.89	4.85	1.87	5.25	2.70
		Post-test	5.07	2.91	6.47	1.87	5.03	1.83	5.47	2.36
Valence		Pre-test	7.13	1.50	6.73	1.48	4.90	2.04	5.61	2.45
		Post-test	7.60	1.40	6.65	1.52	4.97	2.04	6.00	2.18

Table 3
Results from analyses of variances for effects of reward and frustration on performance (in terms of reaction times and error rates).

Effect	df	F value	p value	η^2
Reward (Reaction times)				
Group	3,116	11.93	< .001	.236
Block	3,116	.033	.855	.000
Validity	3,116	50.12	< .001	.302
Group x Block	3,116	4.79	.003	.110
Group x Validity	3,116	3.44	.019	.082
Block x Validity	3,116	2.87	.093	.024
Group x Validity x Block	3,116	.946	.421	.024
Reward (Error rates)				
Group	3,116	8.76	< .001	.185
Block	3,116	7.06	.009	.057
Validity	3,116	1.23	.270	.010
Group x Block	3,116	.280	.840	.007
Group x Validity	3,116	1.41	.242	.035
Block x Validity	3,116	.000	.999	.000
Group x Validity x Block	3,116	.522	.668	.013
Frustration (Reaction times)				
Group	3,116	14.66	< .001	.275
Block	3,116	91.25	< .001	.440
Validity	3,116	43.13	< .001	.271
Group x Block	3,116	1.22	.306	.031
Group x Validity	3,116	2.39	.073	.058
Block x Validity	3,116	1.64	.203	.014
Group x Validity x Block	3,116	.384	.765	.010
Frustration (Error rates)				
Group	3,116	14.71	< .001	.276
Block	3,116	49.10	< .001	.297
Validity	3,116	5.39	.022	.044
Group x Block	3,116	3.69	.014	.087
Group x Validity	3,116	2.11	.103	.052
Block x Validity	3,116	6.43	.013	.053
Group x Validity x Block	3,116	.337	.799	.009

and frustration. Statistically significant interactions or significant main effects (in the case of non-interactive effects) are interpreted below.

Effect of reward

Reaction times

The Group x Block interaction, F(3,116) = 4.79, p = .003, η^2 = .110, was analyzed by examining the Block effect (1 [baseline condition] and 2 [monetary reward]) in each Group (control, euthymia, mania and depression). As Fig. 3 shows, participants in the control and the euthymic groups responded faster when monetary reward was introduced (control group: -31 ms, t(29) = 2.91, p = .007; euthymic group: -34 ms, t (29) = 2.39, p = .023). Instead, the participants in the manic group showed slower reaction times (+41 ms, t(29) = -3.29, p = .003), whereas the participants in the depressed group did not show an effect (+18 ms, t(29) = -.69, p = .493).

Moreover, a Group x Validity interaction [F(3,116) = 3.44, p = .019, η^2 = .082] was found. To examine this interaction, we analyzed the effect of Validity for each group. Repeated measures t-test revealed that, participants had substantially faster reaction times in valid trials than in invalid trials [control group (-15 ms, t(29) = -2.80, p = .009); euthymic group (-66 ms, t(29) = -6.81, p < .001); manic group (-36 ms, t(29) = -2.78, p = .009); and depressed group (-46 ms, t(29) = -2.95, p = .006)].

Error rates

The ANOVA analysis for the examination of the effect of reward with error rates as the outcome measure found significant Group [F(3,116) = 8.76, p < .001, η^2 = .185] and Block [F(1,116) = 7.06, p = .009, η^2 = .057] main effects. The Group effect revealed that the manic (14,62%) and depressive (11.36%) groups significantly committed more errors than the euthymic group (1.47%; p < .001 and p = .013, respectively) and the control group (2.21%; p = .001 and p = .026, respectively). The effect of Block showed that participants committed lower errors in the monetary reward condition (6.39%) than in the social reward condition (8.44%, p = .009). The Group x Block interaction, however, was non-significant [F(3,116) = 0.280, p = .84, η^2 = .007], indicating that, in terms of error rates, patients and control subjects did not respond differently to the introduction of monetary reward.

Effect of frustration

Reaction times

The Group x Block interaction analyzed by examining the Block effect (2 [contingent feedback] and 3 [non-contingent feedback]) in each Group (control, euthymia, mania and depression) was not significant [F(3,116) = 1.22, p = .306, η^2 = .031], indicating that, in terms of reaction times, patients and control subjects did not respond differently to the introduction of frustration. However, a significant main effect of Group, F(3,116) = 14.66, p < .001, η^2 = .275, showed that manic (578 ms) and depressive (645 ms) groups were significantly slower in the frustration-inducing block (Block 3) than the euthymic group (459 ms; p = .046 and p < .001, respectively) and than the control group (361 ms; all ps < .001). Furthermore, the effect of Block, F(3,116) = 91.25, p = .000, η^2 = .440, revealed that participants were faster for the frustration condition (463 ms) than the non-frustration condition (568 ms). Finally, the Validity effect, F(3,116) = 43.13, p = .000, η^2 = .271, indicated that

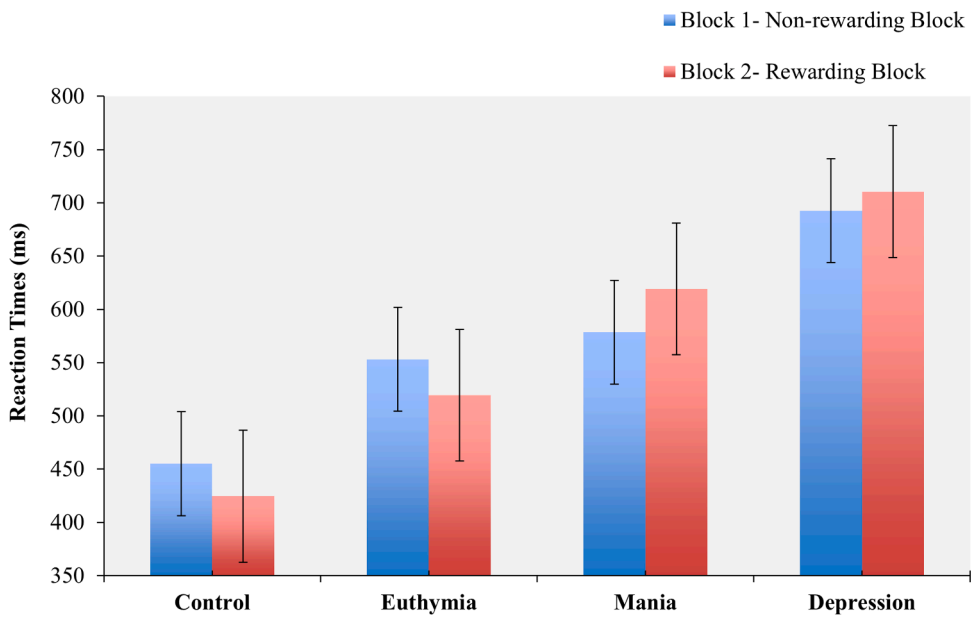

Fig 3. Reaction times in Block 1 (non-rewarding) and Block 2 (rewarding) for BD patients (euthymia, mania and depression) and healthy controls. Error bars show standard errors.

participants were faster for valid trials (497 ms) than for invalid trials (535 ms).

Error rates

The Block x Group interaction, $F(3,116) = 3.69$, $p = .014$, $\eta^2 = .087$, was examined by the analysis of the Block effect for each Group. As Fig. 4 displays, although all groups increased their error rates in the frustrating condition (Block 3), the magnitude of the effect of frustration was larger in patients with BD (euthymic group, +8.19%, $t(29) = 5.48$, $p < .001$; manic group, + 10.75%, $t(29) = 4.74$, $p < .001$, and depressed group, + 6.86, $t(29) = 2.438$, $p = .021$) than in the control group (+ 1.77%, $t(29) = 4.15$, $p < .001$).

Moreover, we found an Block x Validity interaction [$F(3,116) = 6.43$, $p = .013$, $\eta^2 = .053$]. To examine this interaction, we analyzed the effect of Validity for each block. Repeated measures t-test revealed a validity effect in the frustration-inducing block (3.76%, $t(119) = 2.81$, $p = .006$), but not in the non-frustrating block (0.67%, $t(119) = .748$, $p = .456$), indicating that participants committed more errors for invalid trials than valid trials in the frustration condition.

A Self –report mood

Valence

The Group x Time interaction, $F(3,116) = 3.32$, $p = .022$, $\eta^2 = .079$, was analyzed examined the Time effect for each Group. This interaction revealed that individuals in the control group (+0.47, $t(29) = 2.38$, $p = .024$) and the manic group (+ 0.38, $t(29) = 2.48$, $p = .019$) were happier after the task. However, no Time effect was found for the depressed

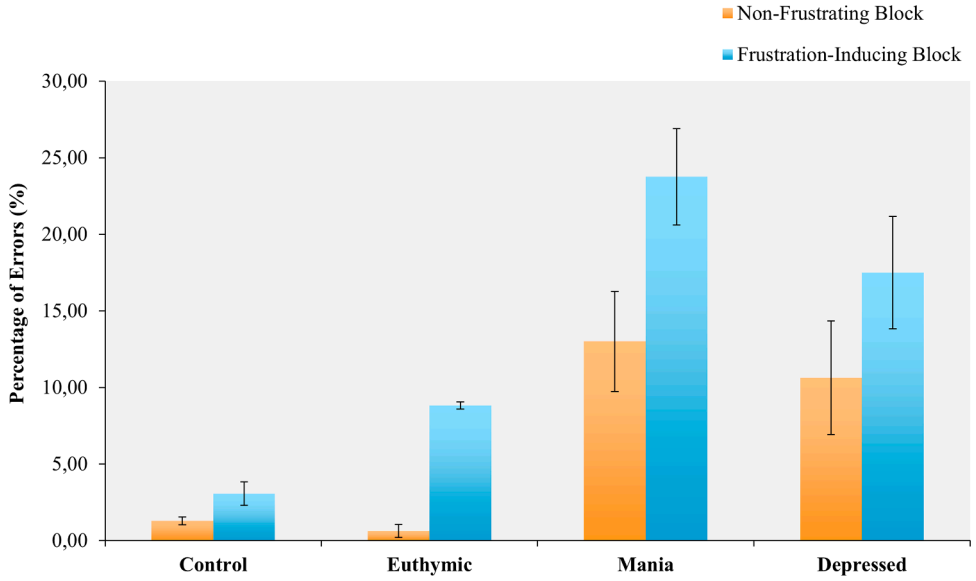

Fig 4. Percentage of errors during Block 2 (non-frustrating block) and Block 3 (frustration-inducing block) for BD patients (euthymia, mania and depression) and healthy controls. Error bars show standard errors.

group (+ 0.06, t(29) = 1.44, $p = .161$) and the euthymic group, (+ 0.08, t(29) = .65, $p = .52$).

Arousal

Although the effect of Group was significant, F(3, 116) = 3.02, $p = .033$, $\eta^2 = .073$), Bonferroni-corrected comparisons did not reveal significant differences among groups (all ps > .05).

Discussion

This is the first study that examined the impact of affective symptoms on the processing of reward and frustration among the affective episodes in BD (e.g., depression, mania and euthymia) using the APT paradigm. Results showed that monetary reward improved performance (in terms of faster response times) in euthymic individuals and healthy controls, whereas it impaired performance in manic individuals and had not significant effect in depressed. In addition, when frustration was induced, we found a higher increase of error rates for all patients with BD regardless of the episode comparing with the non-frustrating condition—this pattern occurred to a much lesser degree for healthy controls. In addition, both manic patients and healthy controls felt unhappier after frustration induction than before the experiment, whereas there were no significant changes in arousal for any of the groups. As we discuss below, these findings may shed light on the underlying psychological mechanisms in the processing of reward and frustration in BD.

These findings extended those reported in prior research with APT in BD (Rich et al., 2005, 2007; Rich et al. 2010; Ross et al., 2020), and added empirical evidence about the processing of reward and frustration in adult patients across mood states. At this point, it must be considered that the previous studies have been mainly centered on the processing of frustration -due to its relevance in the characterization of the bipolar phenotype (Leibenluft, 2011; Perlman et al., 2015)- and they have reported mixed results. Note that, to the best of our knowledge, at least two experiments did not find a significant interference of frustration in BD (see Ross et al. (2020), with the APT in pediatric patients, and Edge et al., 2015, with a videogame in adult patients). Two main factors could explain these divergences. Firstly, the differences in the clinical samples suggest that the affective episode could be relevant in the manifestation of an interference of frustration in task performance. Note that most of the prior studies have been applied in euthymic samples and that, in our study, euthymic individuals with BD executed the task notably better than symptomatic patients in the frustration condition (both in accuracy rate and reaction times). This would suggest that the increased reactivity to frustration in BD would interfere in cognitive performance more notably during symptomatic periods. Secondly, the complexity of the cognitive mechanisms implicated in the execution of the task could condition the frustration effect. In this sense, frustration would impair the task performance when higher cognitive functions are required, whereas this effect would be attenuated in case of tasks with simple cognitive demands. For instance, Ruggero and Johnson (2006) found a significant interference of frustration in the performance of a concept-formation task that implied logical reasoning, whereas Edge et al. (2015) did not find this effect applying a videogame that mainly required attentional vigilance. Future research should examine these hypotheses in order to improve the characterization of the effect to frustration in BD.

Focusing on our findings, and in accordance with the evidence with APT in non-clinical population (Perez-Edgar and Fox, 2005), frustrating condition produced faster reaction times and increased errors in all participants, but in the case of patients with BD, performance was hindered to a larger degree than in controls (that is, frustration notably increased the error rates). Critically, this finding indicates that individuals with BD—regardless of the episode—would exhibit heightened reactivity to frustration in comparison with healthy individuals and supports the view that the effect of frustration is a trait in BD. Interestingly, this finding supports the argument of a high reactivity to frustration as a core factor in the mood dysregulation in BD (Mikita and Stringaris, 2013). Indeed, from a clinical perspective, chronic irritability has been defined as a consistent marker in the onset of BD (see Leibenluft, 2011, for a review), and it is considered as a prime symptom in the diagnosis of pediatric BD (Perlman et al., 2015) and the bipolar spectrum (Angst et al., 2003; Birmaher et al., 2009).

According to the BAS/BIS model in BD (Johnson et. al., 2012), our study suggests that patients would dysregulate their goal-directed behavior when they are in a frustrating context. Indeed, it has been reported that euthymic patients increase their engagement to goal pursuits under frustration (Harmon-Jones et al., 2008), manic patients make decisions in a more fluctuating way when their goals are thwarted (Minassian et al., 2004), and depressed patients inhibit their approach to a goal when it becomes hampered to reach (Winer and Salem, 2016). Thus, despite that the behavioral interference of frustration could be a trait in BD, it would be asked what is the role of the immediate emotional reactions in the dysregulation of goal-directed behavior across the different affective episodes. Note that, as described in the Affective Events Model (Weiss and Cropanzano, 1996), emotional reactions to environmental contingencies play a main role in the management of goal-directed behavior, and this would be especially relevant in BD because of affective symptoms. Even more, the role of emotional reactions has determined the differences in behavioral response to frustration by its relevance in the elicitation of differential motivational underpinnings, namely: anger induces goal approach and helplessness elicits avoidance (Carver and Harmon-Jones, 2009). Thus, the increased reactivity to frustration in BD would be differently conditioned by the mood state, and even more when we consider that the effect of reward is different across the affective episodes. For example, manic patients—who exhibit irritable mood and low frustration tolerance (APA, 2013)—would react with anger to frustrating contingencies, and this would motivate the unyielding approach to reward with the resulting increase of errors. In contrast, depressive patients—who usually react with learned helplessness to punishment (Winer and Salem, 2016)—would feel defeated with frustration and would activate avoidance strategies to potential loss, disengaging from the task and increasing errors. Meanwhile, euthymic patients—who exhibit high approach motivation to reward and increased engagement with frustration (Harmon-Jones et al., 2002; Harmon-Jones et al., 2008)—would become more dysregulated with the increasing frustration and commit more errors than controls. Importantly, note that task performance of euthymic individuals with BD under frustration (in both accuracy rate and reaction times) is notably better than those of symptomatic patients. This suggests that emotional reactions to frustration would be more difficult to regulate during acute affective states, so a more pronounced effect of frustration occur during mania and depression. The exhaustive examination of the effect of frustration as a trait in BD should be explored in future research in order to determine how emotion and motivation modulate behavioral outcomes (Weiss and Cropanzano, 1996), and what is the role of this effect in the onset and the course of BD (Alloy et al., 2012).

Regarding the effect of monetary reward, our findings showed that when participants were motivated with monetary reward, euthymic individuals behaved as healthy controls responded more quickly (but not worse) to the task. In contrast, symptomatic patients behaved differently: manic patients notably increased their reaction times whereas depressive patients showed a slight increase in response times. Importantly, these results revealed two interesting effects: (i) the benefit from monetary rewards in BD only during euthymic states, and (ii) the counterintuitive lower responsiveness to monetary reward during mania. Firstly, the fact that symptomatic patients with BD did not benefit from monetary reward in task performance is consistent with the altered reward-attaining behavior described by the BAS model for affective episodes in BD (Johnson et. al., 2012), and would support that

the effect of monetary reward is a state rather than a trait in BD (see Ernst et al., 2004, and Hayden et al., 2008, for evidence of a state effect of monetary reward in BD using computerized tasks). However, the fact that manic individuals became slower in responding with the addition of monetary rewards suggests that the higher pursuit of reward during mania posited by the BAS model (Gray 1987, 1990) would not be strictly associated to the benefit in the task performance, but this would be rather conditioned by the quality of the reward. In fact, prior empirical evidence using computerized tasks has found increased responsiveness to high-rewarding and immediate monetary incentives in manic individuals (Mason et al., 2012), but lower task engagement with low valuable and delayed monetary reward (Hayden et al., 2008). This pattern could suggest that the immediacy and intensity of monetary rewards in a computerized task would differently modulate goal-directed behavior in manic individuals (Dvorak et al., 2013), in contrast with the generalized lower responsiveness to reward during depression (Alloy et al., 2008; Ernst et al., 2004; Hayden et al., 2008). Future research should examine whether this suggested complexity in the response to reward during affective episodes in BD would be explained by the differentiation of separated elements in the processing of reward (e.g., reward sensitivity, goal striving and effort towards reward), as has been defined in the framework of the BAS model (Johnson et. al., 2012).

With respect to the self-reported experience before vs. after the task, we found a significant increase of happiness in the control and the manic groups after the task, whereas no significant effects occurred in arousal. The increased positive affect in manic individuals after the task could indicate a positive effect of reward on emotional experience during mania but not during euthymia and depression, and the prevalence of the magnitude of this effect over the negative one for the later frustration. This would be consistent with prior research that suggested that positive emotional responses to feedback during mania are modulated by the role of cognitive elements such as the internal attribution of success and the external attribution of error (Meyer et al., 2010). That is, manic patients would devaluate the negative emotional experience after frustration by the attribution of self-confidence in success. However, the assumption of this hypothesis should be taken with caution due to the difficulty in finding consistent evidence about changes in self-affective states after feedback in patients with BD (see (Johnson et. al., 2012), for a review), which could be explained by the altered insight about the own emotional reactions especially during mania (APA; 2013).

We acknowledge that the current APT experiment comes with certain limitations. First, at the time of testing, all patients with BD were mixed medicated, including those in a euthymic state. Although the impact of medication on the obtained effects is controlled by intra-group comparisons, we acknowledge that some specific effects of medication could mildly vary behavioral data. Second, the Blocks in APT were not presented in randomized order, so the lack of counterbalancing leaves open the possibility of an order effect and variability in rate of learning. However, note that APT is designed in this fashion to gradually increase emotionally and to prevent performance in the following blocks from being affected by residual emotions (Pérez-Edgar and Fox, 2005). Thus, our experiment design is in line with the previous experiments using APT (see Deveney et al., 2013; Rich et al., 2005; Tseng et al., 2019). Ultimately, participants' affective experience was self-informed before and after the task by a 5-point Likert scale. Although self-report scales provide valuable information about immediate affective responsivity to the task, some studies have pointed to the later emotional states for the identification of alterations in the affective experience to reward and frustration in patients with BD (Farmer et al., 2006; Wright et al., 2008). In addition, the reliability of the affective experience assessment can be undermined in symptomatic patients with BD because mood lability alters the collection of stable measures and abnormal insight modulates the objectivity of self-reported data. Other measures (e.g., physiological indexes) may provide additional objective data for assessing affective experience using APT in severe mental illness.

In sum, this is the first study to examine the effect of monetary reward and frustration by means of applying immediate and controlled contingent and non-contingent feedback among the different episodes in BD (euthymia, depression and mania), and of controlling affective symptoms. Importantly, we found a dissociated effect of reward and frustration between symptomatic and euthymic episodes: whereas the benefit from the addition of monetary incentives is affected only during symptomatic episodes (i.e., a state), the notably increased interference of frustration is exhibited also during euthymia (i.e., a trait). Following the Affective Events Model (Weiss and Cropanzano, 1996), this would mean that emotional reactions to rewarding and frustrating feedback would differently impact on goal-directed behavior, and this effect in BD would be modulated by affective symptoms. From a clinical perspective, our study highlights that the fluctuations in reward processing and the high reactivity to frustration across mood states in BD could be considered as relevant factors for mood and goal-behavior dysregulation in this disorder. In the light of our findings, the inclusion of reward and frustration management could improve the efficient attainment of the three main goals in current psychological treatments in BD (Geddes and Miklowitz, 2013), namely: (1) for the interventions in early signs of recurrence, we propose the identification of irritability states and sensitivity to environmental rewards as additional factors (e.g., by the registration of anger symptoms or enjoyment in daily activities in self-reports completed by patients); (2) for the approaches based in the management of stress, we suggest strengthening self-control skills in stressful frustrating contexts during symptomatic but also asymptomatic states; (3) for the programs that promote the maintenance of regular lifestyle habits, we recommend to intervene in the self-regulation of goal-directed activities in daily life (e.g., by programming steps to reduce engagement with frustration or by motivate reward-seeking during depression).

Declaration of Competing Interest

No conflict exists: all the co-authors have approved this article and asserted that they have no conflict of interest.

Ethical considerations

All experimental procedures of this study were approved by the Clinical Research Ethic Committee of the Health Research Institute La Fe (Ref: 2011/0502). All procedures were also in conformity to the ethical standards laid down in the 1964 Declaration of Helsinki. All participants signed informed consent.

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