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Attentional Processing of Threat in Bipolar Disorder: Going Beyond Mood-Congruency

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Abstract

Emotional processing in bipolar disorder (BD) entails a complex attentional pattern not merely restricted to happy or sad biases, but also directed towards threatening information. This study examined threat-related bias on attentional orienting when participants were not instructed about the presentation of emotional stimuli (i.e., implicit instructions). An emotional dot-probe task in which an emotional face (i.e., threat, sad, happy) is simultaneously displayed with a neutral face was applied to BD individuals in their different episodes: mania (n = 26), depression (n = 24), and euthymia (n = 28) as well as to a group of healthy controls (n = 28). Symptomatic BD patients (i.e., in a manic or depressive episode) showed an attentional orienting bias toward threatening faces but not for happy or sad faces, while euthymic BD patients did not exhibit any attentional bias for emotional stimuli. A bias toward happy faces was found in the control group. Threat-related bias was not related to the severity of affective and anxiety symptoms in BD. When attention is not explicitly directed to emotional information, threat-related bias may characterize attentional orienting during mania and depression, but may be attenuated during euthymia.

Keywords Attentional bias · Threat · Mood-congruency · Dot-probe task · Bipolar disorder

Introduction

Bipolar disorder (BD) is a chronic and severe psychiatric disorder characterized by impaired emotional processing (Leppänen, 2006). One of key factors in the origin and the maintenance of BD are the biases when attending emotional information (MacLeod et al., 2002). Typically, attentional biases in BD have been explored by means of cognitive tasks in which participants are instructed about how to attend to emotional stimuli. Even in free-viewing tasks, participants are asked to pay attention to several emotional images as if they would be watching TV (see García-Blanco et al., 2014, 2015). A limitation of these tasks, however, is that, in a natural environment, attention is not explicitly directed to any information.

A potentially better measure of attentional biases in BD would be obtained if patients were not given any instructions about what to focus on from the stimuli. The Emotional Dot Probe (EDP) task allows to do just that with a valid measure in distinguishing between clinical and non-clinical groups (e.g., see Bar-Haim et al., 2007, for meta-analytic evidence using EDP in anxiety disorders, and Winer & Salem, 2016, for meta-analytic evidence using EDP in depression). In an EDP task, two cue stimuli (e.g., words, facial expressions, or pictures), one emotional (e.g., happy, threatening, sad or neutral) and one neutral, are simultaneously presented to participants in different locations of a computer monitor (top vs. bottom or left vs. right). Then, a neutral probe appears in the spatial location of either the emotional cue (emotional trial) or the neutral cue (neutral trial). Participants are asked to respond to probe location, not to cue stimuli (Posner et al.,

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1980). The EDP task allows to measure orienting attentional bias toward or away from the emotional stimulus, namely: ii) faster reaction times for emotional than for non-emotional trials would be interpreted as an attentional bias toward emotional information; ii) faster reaction times for neutral trials would involve an attentional bias away from emotion. Due to the high relevance of social and emotion-focused processing in mood disorders (Leyman et al., 2009), emotional facial expressions represent valid ecological stimuli in the examination of attentional biases in BD. In the current experiment, we administered an EDP task with two faces (i.e., target [happy, threatening, or sad] versus control [neutral]) to BD individuals in their different episodes (mania, depression, and euthymia) and to healthy controls.

Biases in attentional processing in BD have been traditionally enclosed within Beck's (1976) cognitive model, which asserted biased information processing as the core explanatory factor of affective BD symptoms. In this framework, attentional biases were restricted to the congruency with the pathological mood state: happy-biased attention during mania and sad-biased attention during depression. However, BD presents other distinctive emotional, cognitive, and behavioral features, which would have important implications in terms of attentional preferences. Notably, BD acute patients usually manifest psychotic and paranoid features (Mansell et al., 2007), melancholic symptoms typically accompany bipolar depression (García-Blanco et al., 2015), and irritability states are also included in the altered emotional reactivity during mania (Gruber et al., 2008; Meyer et al., 2001). Thus, in line with complex clinical manifestations, attentional patterns in BD are not merely restricted to happy or sad biases. Indeed, empirical evidence in BD has found that during depression, there is an avoidance of positive stimuli rather than an approach to negative information (García-Blanco et al., 2014; Jabben et al., 2012), whereas that during mania the approach to happy information is not always exhibited (Garcia-Blanco et al., 2015).

Critically, a number of recent studies have consistently reported a bias toward threatening information in BD (García-Blanco et al., 2014, 2015; Leyman et al., 2009). However, it is yet unclear whether this threat-related bias in BD is a trait or a state. When BD patients are asked to voluntarily ignore a threatening stimulus, threat-related bias only occurs in symptomatic episodes (i.e., a state; García-Blanco et al., 2017). In contrast, when BD patients are asked to look at several emotional stimuli displayed simultaneously as if they would be watching TV, threat-related biases are maintained even during euthymia (i.e., a trait; García-Blanco et al., 2014, 2015).

A plausible explanation for these controversial findings would be the type of attentional mechanism examined by the task (Posner & Raichle, 1994). When attentional inhibitory control is examined, as in attend-to tasks, threat-related bias is exhibited by the difficult in intentionally ignoring threatening stimuli, as occurs in BD individuals in acute episodes (García-Blanco et al., 2017). In contrast, when attentional orienting is examined, as in free-viewing tasks, threat-related bias is exhibited by the priority attentional selection of threatening stimuli, and this occur in BD regardless the episode (García-Blanco et al., 2014, 2015). Note that, as indicated earlier, attentional orienting to threatening stimuli in BD only has been examined by means of tasks with explicit instructions. In the present study, we aimed to focus on a condition not yet explored: whether when participants had not been instructed about the presentation of emotional stimuli (i.e., implicit instructions) as occurs in EDP task, threat-related bias in attentional orienting is maintained across the different episodes in BD.

Prior evidence with EDP tasks in BD has mainly focused in the examination of mood-congruent bias including positive and negative stimuli as the emotional cue. Jongen et al. (2007) used an EDP task by presenting pairs of words (one neutral and the other either positive or negative) to euthymic and depressed BD patients and healthy controls. Depressed BD patients compared to controls exhibited an attentional bias away from negative words, whereas no biases were found in euthymic BD patients (note that a weak biased effect away from positive words was found in euthymic group without getting significance). Jabben et al. (2012) applied a similar experiment but including healthy first-degree relatives as an additional group for comparison. Depressed BD patients compared to controls exhibited an attentional bias away from positive words, whereas no bias was found in euthymic patients and relatives. More recently, Peckham et al. (2016) administered an EDP task presenting pairs of faces (one neutral and the other either happy or sad) to euthymic BD patients and healthy controls under a positive mood induction. No attentional biases were found towards happy or sad faces.

Other studies have used the EDP task in BD pediatric patients; however, as subclinical symptoms were not controlled, their results have to be interpreted with caution. Brotman et al. (2007) presented pairs of faces (one neutral and the other either threatening or happy) to children with BD with and without a lifetime anxiety disorder diagnosis and healthy controls. Only children with BD and anxiety disorder exhibited a bias toward threatening faces compared to healthy controls, suggesting that anxiety symptoms could determine the bias toward threatening information in BD. In addition, Whitney et al. (2012) administered the EDP task displaying pairs of faces (one neutral and the other either happy or sad) to adolescents with BD (who only had a manic episode in the last year) and healthy controls. No significant effects in terms of group or valence were found.

In sum, there are certain limitations in prior empirical evidence with the EDP paradigm in BD, such as the differences in the sample characteristics (e.g., clinical state or age) or in some procedural aspects of the task (e.g., type of visual stimuli [words vs. faces] and emotional valence [positive vs. negative]), which would not allow to conclusively determine how emotional-related bias condition attentional orienting across the different episodes in BD. In our study, we aim to overcome these limitations by including one group per each episode in BD (mania, euthymia, and depression) for comparison, and four different emotional faces (i.e., emotional [happy, threatening, or sad] versus neutral) as cue stimuli. Furthermore, we measured anxiety symptoms (Brotman et al., 2007) and controlled the severity of affective symptoms in order to exclude mixed states in BD individuals and subclinical affective symptoms in euthymic BD patients and healthy participants.

The predictions are as follows. First, if the processing of social relevant stimuli in BD is mainly modulated by stimuli with paranoid-related features (McClure et al., 2003), one would expect a threat-related bias for both symptomatic and non-symptomatic BD individuals (i.e., a trait). This finding would suggest that threat-related biases affect attentional orienting in BD not only when attention to emotional stimuli is directed by explicit instructions (García-Blanco et al., 2014, 2015), but also under subtle conditions (i.e., implicit instructions). Alternatively, if paranoid features in BD are closely associated to the psychotic symptoms usually manifested during depression and mania, one would expect threat-related bias only in symptomatic BD patients (see García-Blanco et al., 2017, for evidence with an eye-tracking paradigm) (i.e., a state). Second, we examined whether attentional orienting biases during mania and depression would be determined by the congruence with the pathological mood state, as Beck's (1976) model would predict, or whether it would be rather defined by specific clinical features (see Mansell et al., 2007). Indeed, on the basis of prior research in EDP (Jabben et al., 2012; Jongen et al., 2007), we expected to confirm an anhedonic bias as a differential source of altered processing in BD with regard to major depression (Gotlib & Joorman, 2010). In relation to mania, we examined whether, under subtle conditions, attentional orienting is mostly biased to threatening or to happy information (see García-Blanco et al., 2017).

Method

Participants

The participants were 85 BD patients from the Psychiatry Department (53 from in-patient wards and 32 from the out-patient Bipolar Disorder Unit) at the Hospital La Fe (Valencia, Spain) and 28 healthy individuals. Patients fulfilled the DSM-5 criteria (American Psychiatric Association, 2013) for BD type I and were included in the manic (n = 28), depressed (n = 29), or euthymic (n = 28) group at the time of assessment. This study was authorized by the Ethics Committee at the Health Research Institute La Fe. Demographic and clinical details are presented in Table 1.

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

	Control (N = 25)	Euthymic (N = 26)	Depressed (N = 23)	Manic (N = 25)	P
% Female	52	39	35	40	.22
Age	36.1 (12.4)	43.2 (11.1)	49.0 (9.3)	41.7 (16.1)	.07
SASS[a]	46.2 (4.5)	40.5 (6.2)	28.8 (8.1)	34.0 (10.8)	.00
# of episodes	-	7.2 (5.7)	6.8 (5.7)	4.8 (3.5)	.35
BAI[b]	1.0 (1.8)	9.5 (10.3)	17.4 (10.2)	9.8 (8.9)	.00
BDI-II[c]	0.3 (0.8)	5.7 (3.3)	29.9 (7.8)	2.9 (3.2)	.00
YMRS[d]	-	0.5 (0.95)	0.6 (1.8)	28.2 (6.1)	.00
Medication (% of patients)					
% Lithium	-	73.1	50.0	45.0	.00
% Antiepileptic	-	53.9	31.9	20.0	.05
% Antipsychotic	-	50.0	59.1	95.0	.11
% Antidepressive	-	23.1	68.2	00.0	.00
% Anxiolytic	-	50.0	86.4	95.0	.00

[a]SASS: Social Adaptation Self-Evaluation Scale

[b]BAI: Beck Anxiety Inventor

[c]BDI-II: Beck Depression Inventory-II

[d]YMRS: Young Mania Rating Scale

No participant reported neurological history or major medical disorders likely to affect cognition. Additional exclusionary criteria for the patients were as follows: use of non-psychotropic medication that could affect cognition; other psychiatric diagnoses based on DSM-5 criteria; and having undergone electroconvulsive therapy in the previous three months. Eight participants were excluded from the original sample (six patients; two controls) on the basis of these criteria.

All patients were referred by psychiatrists in the department. DSM-5 diagnoses were established with a clinical interview and case note review. The responsible psychiatrist of the unit and a clinical psychology intern corroborated the diagnoses. 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, and the Social Adaptation Self-Evaluation Scale (SASS; Bosc et al., 1997) to measure social functioning. Five participants (four patients; one control) were excluded based on these criteria, resulting in a final sample of ninety-nine participants (see Fig. 1 for the selection process of the final sample).

Materials

The emotional stimuli, which served as cues, were 84 photographs in color of facial expressions (half male) taken from the FACES database (Ebner et al., 2010). These faces represented young, middle-aged, and older people. Two faces appeared as cues in each trial, namely an emotional face (happy, threatening, or sad) and a neutral face. We selected a total of 12 happy, 12 threatening, and 12 sad faces and 48 neutral images (36 for control and 12 for practice trials). Each emotional face was matched with the neutral control faces of the same actor. Each participant was presented with three types of experimental trials: 12 happy–neutral, 12 threatening–neutral, and 12 sad–neutral cues. Each pair of cued faces was presented four times during the experiment (i.e., 48 trials per condition). In addition, 6 pairs of neutral faces were presented before the experimental trials as a practice block.

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, BD patients completed a clinical interview and the YMRS. Afterwards, the dot-probe task was administered. Presentation of stimuli and recording of responses were controlled by DMDX software (Forster

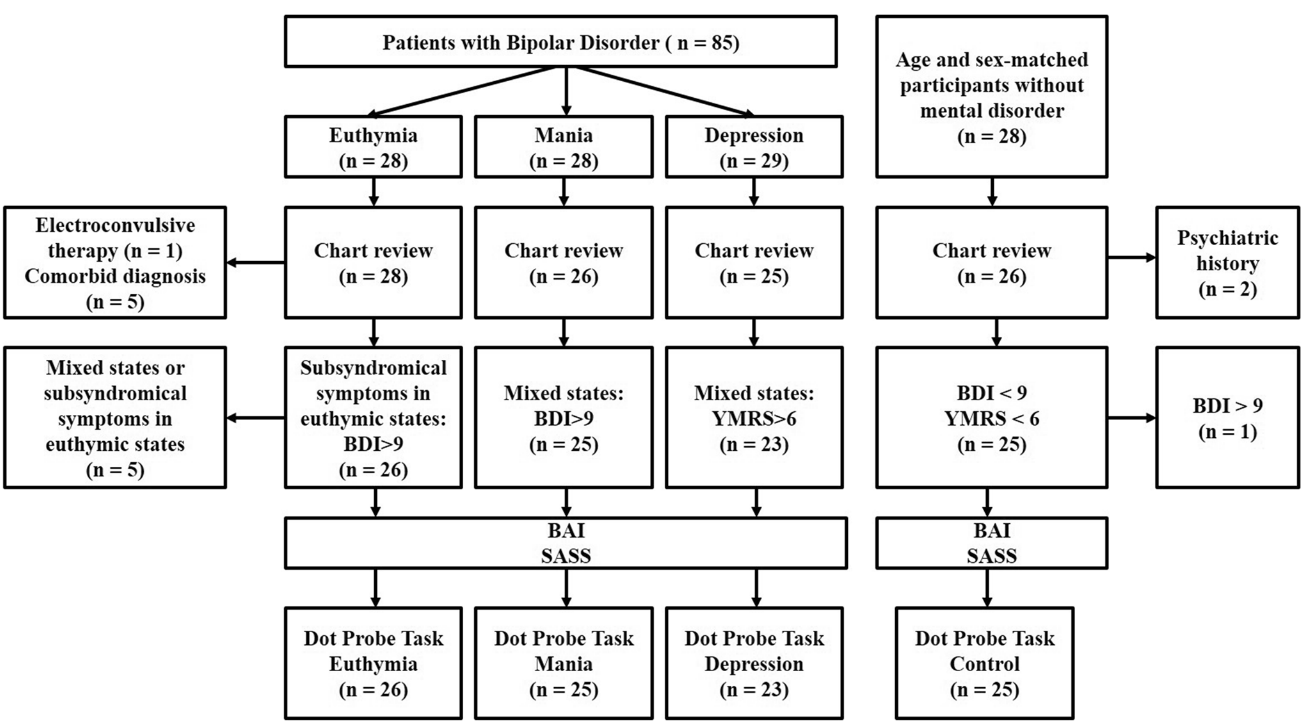

Fig. 1 Selection process of the final sample

& Forster, 2003). Participants were seated approximately 60 cm in front of the monitor. The experimenter monitored the stimulus presentation.

In each trial participants were instructed to look at a fixation point (+) in the screen center, which was presented for 1500 ms. Then, two images were presented simultaneously at different screen locations (up and down), which were two cued stimuli with different emotional valences (one neutral and one emotional) displayed for 1250 ms. Then, these images disappeared and a green or red square replaced one of the two pictures—either emotional (emotion trial) or neutral (neutral trial). Participants were told to press a button to indicate the color of the square as quickly and as accurately as possible (see Fig. 2).

The task comprised one practice block followed by three test blocks composed of 48 experimental trials. Each block corresponded to a different emotional valence (i.e., happy, sad and threatening blocks). The presentation order of the blocks was randomized across participants. Thus, a total of 150 trials (144 study + 6 filler) were presented. The vertical location and the type of face (emotional or neutral) replaced by the square were balanced across trials, with the constraint that each type of face appeared in each two positions on half of the trials and the square replaced the emotional cues on the other half. The variation in the image locations and the randomization of trials guaranteed that the participants were not able to use any predetermined scanning strategy. The session lasted 35–40 min.

Data Analyses

Probe response times (RTs) were calculated for correct responses (i.e., errors responses were excluded from further latency analyses). Preliminary analyses showed that all groups showed very low error rates (less than 5%) and that there were no differences between groups and conditions (all Fs < 1). Before examining the bias scores, very short RTs (less than 200 ms) or those exceeding 2.5 standard deviations above the participants' means in each experimental condition were excluded to ensure that the latencies were based on actual responses to the probe locations. For each participant, the mean RT in each condition (for happy, threatening, and sad faces at 1250 ms) was calculated. The difference in proportion between the emotional (i.e., where the probe replaced an emotional face) and neutral trials (i.e., where the probe replaced a neutral face) was calculated to estimate the bias scores [(mean RT neutral trials/mean RT emotional trials*100)-100)] to control for the RT differences between the BD patients (in each episode) and the healthy participants. Positive bias scores indicate an attentional bias toward a particular emotional face, whereas negative bias scores indicate an attentional bias away from an emotional face.

First, the bias score was analyzed in a 4 (Group: depression, mania, euthymia, and control) × 3 (Valence: happy, threatening, sad) omnibus analysis of variance (ANOVA), in which Group was a between-subjects factor and Valence was a within-subject factor. Second, one-sample t-tests were used to determine whether the bias score was different from zero. Third, bivariate correlations were conducted to examine the relation between dot-probe bias scores (i.e., those different from zero) and BDI-II, YMRS, and BAI symptoms in BD patients. Data were analyzed using SPSS 25.0.

Results

The RT mean for each condition is shown in Table 2. The mean (and standard deviation) in bias scores is shown in Fig. 3.

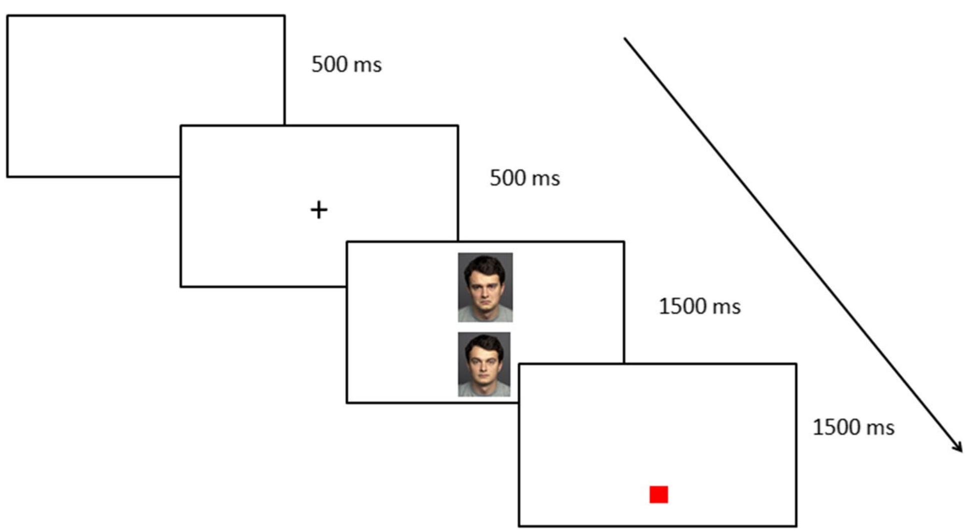

Fig. 2 The stimulus presentation sequence in a neutral trial

Table 2 The mean Response Time (with standard deviation) for each condition in the control and the bipolar patients groups

	Control		Euthymic		Depressed		Mania	
	Emotional trial	Neutral trial	Emotional trial	Neutral trial	Emotional trial	Neutral trial	Emotional trial	Neutral trial
Happy	571 (159)	590 (166)	660 (168)	658 (162)	1048 (347)	1058 (317)	848 (291)	843 (304)
Threat	577 (178)	570 (172)	643 (155)	653 (169)	1017 (308)	1073 (394)	818 (261)	860 (320)
Sad	581 (164)	576 (156)	636 (149)	637 (158)	1069 (389)	1037 (368)	855 (388)	849 (317)

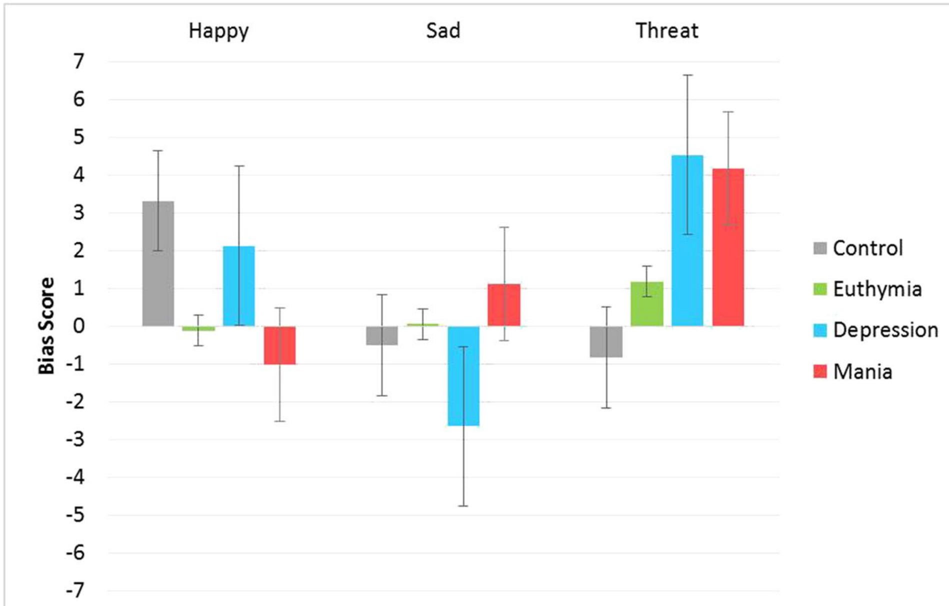

Fig. 3 Attentional bias for happy, sad and threatening faces per group

Omnibus ANOVA

The ANOVA for the bias score showed a main effect of Valence [$F(2,188)=4.058$, $p=0.019$, $\eta^2=0.04$], whereas the main effect of Group did not approach significance [$F<1$]. Importantly, the Valence x Group interaction was significant, $F(6,188)=2.948$, $p=0.009$, $\eta^2=0.09$. To examine this interaction, we conducted an ANOVA for each level of Valence with Group as a factor.

For threatening faces, we found an effect of Group [$F(3,94)=3.394$, $p=0.021$, $\eta^2=0.10$]. To examine these differences, Dunnett t-tests showed higher bias scores to threatening faces for the manic and the depressive group when compared with the control group ($p=0.024$ and $p=0.030$, respectively), while the euthymic group behaved similarly as the control group ($p=0.63$). For sad and happy faces, we did not find an effect of group ($F(3,94)=1.077$, $p=0.36$; $F(3,94)=2.035$, $p=0.12$, respectively).

Analyses of Bias Scores

One-sample t-tests were used to determine whether the bias score was different from zero for each group. For the depressive group, the bias score was higher than zero for threatening faces [$t(22)=2.465$, $p=0.02$], but not for sad or happy faces (both $ps>0.13$). For the manic group, the bias score was also higher than zero for threatening faces [$t(23)=2.264$, $p=0.03$], but not for happy or for sad faces (all $ps>0.53$). For the euthymic group, we found no significant bias scores (all $ps>0.17$). Finally, for the control group, the bias score was higher than zero for happy faces [$t(24)=3.044$, $p=0.006$], but not for threatening or sad faces (all $ps>0.29$).

Correlation Analyses

None of the Pearson coefficients between the bias scores for threatening faces and BDI-II, YMRS, or BAI symptoms in BD patients approached significant (all $ps>0.27$). Similarly, we found no significant Pearson coefficients when the analyses were conducted separately for each BD group (all $ps>0.29$ for the depressive group; all $ps>0.47$ for the manic group; all $ps>0.07$ for the euthymic group.

Discussion

We examined emotion-related biases in attentional orienting across the different episodes in BD by using a task with implicit instructions (an EDP task) in which an emotional face (threat, sad, or happy) is displayed next to a neutral face. The main finding was that symptomatic BD patients (i.e., in their depressive or manic episodes) showed a bias in attentional orienting for threatening faces but not for happy or sad faces, whereas euthymic BD patients did not exhibit any attentional bias for emotional stimuli. Additionally, we only found a bias toward happy faces in the control group. We now discuss how these findings help shed light on how BD patients process emotional stimuli.

Symptomatic BD patients showed faster reaction times in the location of the probe when it was preceded in the same spatial location by a threatening face than a neutral one (i.e., an attentional bias toward threatening faces). Thus, these patients oriented their attention to threatening stimuli even when attention was not explicitly directed to emotional information. This pattern is consistent with prior evidence showing a threat-related bias in the early processing of visual stimuli during bipolar depression (Leyman et al., 2009) and mania (García-Blanco et al., 2017). Thus, threat-related bias in attentional orienting in BD would be especially salient in affective episodes and loose strength during euthymia. Together with previous research, these findings suggest a dissociation in threat-related bias in attentional orienting in BD: when patients are required to attend to emotional stimuli, threat-related bias is a trait (García-Blanco et al., 2014, 2015), whereas when they are not instructed to attend to any stimuli, threat-related bias is a state. An explanation for this pattern is that threat-related schemata are mainly associated with the increasing paranoid and psychotic features during symptomatic episodes (Mansell et al., 2007), and significantly affect the interpretation of interpersonal stimuli (Leyman et al., 2009).

We also examined whether threat-related bias would be explained by the severity of affective symptoms (depression and mania) as well as anxiety levels. We failed to find any clear signs of an association between these variables in any BD episode. We believe that the reason for these null correlation indexes is that the clinical scales that assess the severity of affective symptoms in BD do not include any particular items for the rating of psychotic symptoms: BDI-II does not explore congruent-depressed psychotic symptoms and YMRS includes a single item for assessing paranoid symptoms during mania. In this sense, the impact of psychotic symptomatology should be considered as a relevant factor as underlying mechanism of emotional processing in BD (Depp et al., 2010; Levy et al., 2013). In relation to anxiety symptoms, and unlike Brotman et al. (2007), we did not find any association to threat-related bias. Plausible clinical differences between both clinical samples could explain the divergence in results—note that Brotman et al. (2007) applied EDP task to pediatric BD patients without the assessment of current affective symptoms.

With respect to the issue of attentional biases toward happy or sad faces in attentional orienting with the EDP task, we only found a bias toward happy faces in healthy participants. This replicates earlier research showing a 'protective bias' for emotional processing in healthy individuals (Joormann & Gotlib, 2007; Leyman et al., 2009; Tamir & Robinson, 2007). However, unlike prior studies (Jabben et al., 2012; Jongen et al., 2007), we did not find a bias away from happy faces (i.e., an anhedonic bias) during bipolar depression. We believe that some procedural aspects of the task could explain the seemingly discrepant results—note that our experiment presented simultaneously the emotional + neutral face during 1250 ms. First, happy-related biases in BD have been reported for words (Jabben et al., 2012; Jongen et al., 2007), but not for faces (Peckham et al., 2016; Whitney et al., 2012). Second, anhedonic bias has been only exhibited using shorter presentation rate of stimuli (Jongen et al., 2007, [800 ms]; Jabben et al., 2012, [500 ms]), but not at longer presentation times (Peckham et al., 2016, [1000 and 3000 ms]), suggesting that this bias may be attenuated at longer stages of processing (see García-Blanco et al., 2015, for a similar finding in a free-viewing task). Third, anhedonic bias in BD has been reported by research using other different tasks than the EDP which did not include stimulus in competition (see Leyman et al., 2009, with a simple-cueing task) or displayed several emotional competitors with the neutral one (see García-Blanco et al., 2014, with a free-viewing task). These apparent discrepancies could have been caused by the severity of affective symptoms—compare the mild depressive symptoms in previous EDP experiments (BDI mean score = 17.1 in Jabben et al., 2012; Hamilton Depressive Rating Scale mean score = 12.1 in Jongen et al., 2007) with the severe levels of depression in our sample (BDI mean score = 29.9).

Finally, the current EDP experiment comes with certain limitations. First, at the time of testing, all BD individuals were medicated, including those in a euthymic state. While medication could explain some between-group differences, this cannot explain why attentional orienting was modulated by the emotional salience of stimuli in symptomatic BD patients—we controlled the effect of meditation by means of intra-group comparisons. Second, the EDP task does not allow distinguishing the components of attentional orienting: initial capture, engagement, and disengagement. Thus, we cannot establish firm conclusions regarding these components of attentional orienting (see Fox et al., 2001). Third, the inclusion of briefer presentations rate of stimuli (e.g., 500 ms) could contribute to clarify the threat-related bias effect in early stages of processing. Fourth, while our findings provided clear evidence of an attentional bias toward threat images in symptomatic BD patients, we are aware that there has been some criticism on the reliability of dot-probe task (Rodebaugh et al., 2016). Additional research should use tasks that measure online processing to better characterize this threat-related bias (e.g., registering the participants' eyes movements).

To sum up, the current EDP experiment with BD patients revealed that when attention is not explicitly directed to emotional information, threat-related bias characterizes the orienting to social relevant stimuli during mania and depression but not in euthymia—this bias may also occur in euthymia under explicit instructions (García-Blanco et al., 2014, 2015). Importantly, the orienting towards threatening faces during acute states suggests that threatening-related schemata would be prominent in the emotional processing in BD (Szmulewicz et al., 2019). This evidence adds support to integrate the processing of threat as a relevant factor in the comprehension of emotional vulnerability factors in BD. Considering that attentional training has demonstrated a positive effect in emotional regulation (Sánchez et al., 2016), future approaches in the treatment of mania and depression should treat threat-related bias as a significant core for intervention.

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Declarations

Ethics Approval This study was performed in line with the principles of the Declaration of Helsinki for studies involving human participants. Approval was granted by the Ethics Committee of at the Health Research Institute La Fe (Date 07/02/2012; Ref: 2011/0502_PP_LIVIANOS).

Consent to Participate Informed consent was obtained from all individual participants included in the study.

Conflict of Interest Belén Gago, Manuel Perea, Lorenzo Livianos, Pilar Sierra and Ana García-Blanco declare that they have no conflict of interest.

Experiment Participants This research involved Human Participants.

References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5thEd ed.). Author.

Bar-Haim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M. J., & van Ijzendoorn, M. H. (2007). Threat-related attentional bias in anxious and non-anxious individuals: A meta-analytic study. *Psychological Bulletin, 133*, 1–24. https://doi.org/10.1037/0033-2909.133.1.1

Beck, A. T. (1976). *Cognitive therapy and the emotional disorders*. International Universities Press.

Beck, A. T., Epstein, N., Brown, G., & Steer, R. A. (1988). An inventory for measuring clinical anxiety: Psychometric properties. *Journal of Consulting and Clinical Psychology, 56*, 893–897. https://doi.org/10.1037/0022-006X.56.6.893

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for the Beck Depression Inventory-II*. Psychological Corporation.

Bosc, M., Dubini, A., & Polin, V. (1997). Development and validation of a social functioning scale, the Social Adaptation Self-Evaluation Scale. *European Neuropsychopharmacology, 7*, 57–70. https://doi.org/10.1016/S0924-977X(97)00420-3

Brotman, M. A., Rich, B. A., Schmajuk, M., Reising, M., Monk, C. S., Dickstein, D. P., … Leibenluft, E. (2007). Attention Bias to Threat Faces in Children with Bipolar Disorder and Comorbid Lifetime Anxiety Disorders. *Biological Psychiatry*, *61*, 819–821. https://doi.org/10.1016/j.biopsych.2006.08.021

Depp, C. A., Mausbach, B. T., Harvey, P. D., Bowie, C. R., Wolyniec, P. S., Thornquist, M. H., … Patterson, T. L. (2010). Social competence and observer-rated social functioning in bipolar disorder. *Bipolar Disorders*, *12*, 843–850. https://doi.org/10.1111/j.1399-5618.2010.00880.x

Ebner, N. C., Riediger, M., & Lindenberger, U. (2010). FACES–a database of facial expressions in young, middle-aged, and older women and men: Development and validation. *Behavior Research Methods, 42*, 351–362. https://doi.org/10.3758/BRM.42.1.351

Forster, K. I., & Forster, J. C. (2003). DMDX: A windows display program with millisecond accuracy. *Behavior Research Methods, Instruments, & Computers, 35*, 116–124. https://doi.org/10.3758/BF03195503

Fox, E., Russo, R., Bowles, R., & Dutton, K. (2001). Do threatening stimuli draw or hold visual attention in subclinical anxiety? *Journal of Experimental Psychology General, 130*, 681–700. https://doi.org/10.1037/0096-3445.130.4.681

Garcia-Blanco, A., Salmerón, L., & Perea, M. (2015). Attentional capture by emotional scenes across episodes in bipolar disorder: Evidence from a free-viewing task. *Biological Psychology, 108*, 36–42. https://doi.org/10.1016/j.biopsycho.2015.03.010

García-Blanco, A., Salmerón, L., & Perea, M. (2017). Inhibitory Control for Emotional and Neutral Scenes in Competition: An Eye-Tracking Study in Bipolar Disorder. *Biological Psychology, 127*, 82–88. https://doi.org/10.1016/j.biopsycho.2017.05.006

García-Blanco, A., Salmerón, L., Perea, M., & Livianos, L. (2014). Attentional biases toward emotional images in the different episodes of bipolar disorder: An eye-tracking study. *Psychiatry Research, 215*, 628–633. https://doi.org/10.1016/j.psychres.2013.12.039

Gotlib, I., & Joorman, J. (2010). Cognition and depression: Current status and future directions. *Revista De Neurología, 27*, 581–584. https://doi.org/10.1146/annurev.clinpsy.121208.131305

Gruber, J., Oveis, C., Keltner, D., & Johnson, S. L. (2008). Risk for mania and positive emotional responding: Too much of a good thing? *Emotion, 8*, 23–33. https://doi.org/10.1037/1528-3542.8.1.23

Jabben, N., Arts, B., Jongen, E. M. M., Smulders, F. T. Y., Van Os, J., & Krabbendam, L. (2012). Cognitive processes and attitudes in bipolar disorder: A study into personality, dysfunctional attitudes and attention bias in patients with bipolar disorder and their relatives. *Journal of Affective Disorders, 143*, 265–268. https://doi.org/10.1016/j.jad.2012.04.022

Jongen, E. M. M., Smulders, F. T. Y., Ranson, S. M. G., Arts, B. M. G., & Krabbendam, L. (2007). Attentional bias and general orienting processes in bipolar disorder. *Journal of Behavior Therapy and Experimental Psychiatry, 38*, 168–183. https://doi.org/10.1016/j.jbtep.2006.10.007

Joormann, J., & Gotlib, I. H. (2007). Selective attention to emotional faces following recovery from depression. *Journal of Abnormal Psychology, 116*, 80–85. https://doi.org/10.1037/0021-843X.116.1.80

Leppänen, J. M. (2006). Emotional information processing in mood disorders: A review of behavioral and neuroimaging findings. *Current Opinion in Psychiatry, 19*, 34–39. https://doi.org/10.1097/01.yco.0000191500.46411.00

Levy, B., Medina, A. M., & Weiss, R. D. (2013). Cognitive and psychosocial functioning in bipolar disorder with and without psychosis during early remission from an acute mood episode: A comparative longitudinal study. *Comprehensive Psychiatry, 54*, 618–626. https://doi.org/10.1016/j.comppsych.2012.12.018

Leyman, L., De Raedt, R., & Koster, E. H. W. (2009). Attentional biases for emotional facial stimuli in currently depressed patients with bipolar disorder. *International Journal of Clinical and Health Psychology, 9*, 393–410. https://doi.org/10.1037/abn0000049

MacLeod, C., Rutherford, E., Campbell, L., Ebsworthy, G., & Holker, L. (2002). Selective attention and emotional vulnerability: Assessing the causal basis of their association through the experimental manipulation of attentional bias. *Journal of Abnormal Psychology, 111*, 107–123. https://doi.org/10.1037/0021-843X.111.1.107

Mansell, W., Morrison, A. P., Reid, G., Lowens, I., & Tai, S. (2007). The interpretation of, and responses to, changes in internal states: An Integrative Cognitive Model of Mood Swings and Bipolar Disorders. *Behavioural and Cognitive Psychotherapy, 35*, 515–539. https://doi.org/10.1017/S1352465807003827

McClure, E. B., Pope, K., Hoberman, A. J., Pine, D. S., & Liebenluft, E. (2003). Facial emotion recognition in adolescents with mood and anxiety disorders. *American Journal of Psychiatry, 160*, 1172–1174. https://doi.org/10.1176/appi.ajp.160.6.1172

Meyer, B., Johnson, S. L., & Winters, R. (2001). Responsiveness to Threat and Incentive in Bipolar Disorder: Relations of the BIS/BAS Scales With Symptoms. *Journal of Psychopathology and Behavioral Assessment, 23*, 29–37. https://doi.org/10.1023/A:1010929402770

Peckham, A. D., Johnson, S. L., & Gotlib, I. H. (2016). Attentional bias in euthymic bipolar I disorder. *Cognition and Emotion, 30*, 472–487. https://doi.org/10.1080/02699931.2015.1014313

Posner, M. I., & Raichle, M. E. (1994). *Images of mind*. Scientific American Library.

Posner, M. I., Snyder, C. R. R., & Davidson, B. J. (1980). *Attention and the Detection of Signals, 109*, 160–174. https://doi.org/10.1037/0096-3445.109.2.160

Rodebaugh, T. L., Scullin, R. B., Langer, J. K., Dixon, D. J., Huppert, J. D., Bernstein, A., ... Lenze, E. J. (2016). Unreliability as a threat to understanding psychopathology: The cautionary tale of attentional bias. *Journal of Abnormal Psychology, 125,* 840–851. https://doi.org/10.1037/abn0000184

Sánchez, A., Everaert, J., & Koster, E. H. W. (2016). Attention training through gaze-contingent feedback: Effects on reappraisal and negative emotions. *Emotion, 16*, 1074–1085. https://doi.org/10.1037/emo0000198

Szmulewicz, A. G., Martino, D. J., & Strejilevich, S. A. (2019). Characterization of Mood Instability through Bipolar Disorders: A cluster-analytic approach using weekly prospective life-chart methodology. *European Psychiatry, 57*, 52–57. https://doi.org/10.1016/j.eurpsy.2018.10.003

Tamir, M., & Robinson, M. D. (2007). The happy spotlight: Positive mood and selective attention to rewarding information. *Personality & Social Psychology Bulletin, 33*, 1124–1136. https://doi.org/10.1177/0146167207301030

Whitney, J., Joormann, J., Gotlib, I. H., Kelley, R. G., Acquaye, T., Howe, M., … Singh, M. K. (2012). Information processing in adolescents with bipolar I disorder. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *53*, 937–945. https://doi.org/10.1111/j.1469-7610.2012.02543.x

Winer, E. S., & Salem, T. (2016). Reward devaluation: Dot-probe meta-analytic evidence of avoidance of positive information in depressed persons. Psychological bulletin, 142, 18-78. https://doi.org/10.1037/bul0000022

Young, R. C., Biggs, J. T., Ziegler, V. E., & Meyer, D. A. (1978). A rating scale for mania: Reliability, validity and sensitivity. *British Journal of Psychiatry, 133*, 429–435. https://doi.org/10.1192/bjp.133.5.429