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Inhibitory Control for Emotional and Neutral Scenes in Competition: An Eye-Tracking Study in Bipolar Disorder

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ABSTRACT

This study examined the inhibitory control of attention to social scenes in manic, depressive, and euthymic episodes of bipolar disorder (BD). Two scenes were simultaneously presented (happy/threatening/neutral [target] versus control). Participants were asked either to look at the emotional pictures (i.e., attend-to-emotional block) or to avoid looking at the emotional pictures (i.e., attend-to-neutral block) while their eye movements were recorded. The initial orienting (latency and percentage of first fixation) and subsequent attentional engagement (gaze duration) were computed. Manic patients showed a higher percentage of initial fixations on happy scenes than on the other scenes, regardless of the instructions. However, in the attend-to-neutral block, their gaze durations were longest for threatening scenes. Inhibitory control was not modulated by the scene's emotional salience in the other groups. Thus, manic patients had difficulties voluntarily ignoring emotional information – this was characterized by a happy-related bias during initial orienting, but a threat-related bias during attentional engagement.

Bipolar disorder (BD) is a mood disorder characterized by episodes of abnormal, persistent high mood (mania) and, at times, low mood (depression), together with remission episodes (euthymia) (Goodwin and Jamison, 2007). While the last publication of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) includes mood dysregulation as a new clinical entity for BD, the underpinnings of how mood dysregulation occurs in BD is still under discussion (Brotman et al., 2007).

To understand what emotion dysregulation entails in BD, it is fundamental to assess whether individuals are able to voluntarily control emotional responses in terms of directing attention to emotionally relevant stimuli (Gratz and Roemer, 2004; Phillips, Ladouceur, & Drevets, 2008). In this experiment, we do so by simultaneously presenting two images (i.e., target [happy, threatening, or neutral] versus control [neutral]) to which BD patients in their different episodes (mania, depression, and euthymia) have to respond according to specific instructions (i.e., pay attention *only* to the emotional picture versus pay attention *only* to the neutral picture) while their eye movements are recorded – note that the recording of the participants' eye movements is an excellent procedure to assess the temporal (duration) and spatial (location) measures of attentional capture (see Rayner, 2009, for a review on cognitive processes and eye movements).

Recent eye-tracking research in our laboratory has examined how the inhibitory control of attention is captured by emotional stimuli as a function of the BD patients' mood (e.g., García-Blanco, Perea, & Salmerón, 2013). Specifically, García-Blanco, Perea, & Salmerón (2013) conducted an emotional antisaccade experiment with happy, sad, and neutral faces in BD patients (during mania, depression, and euthymia episodes). A group of healthy individuals served as controls. Participants had to inhibit the automatic prosaccade and voluntarily generate an antisaccade to the opposite location. Results showed that manic and depressed BD patients committed more antisaccade errors than control individuals – this difference was absent in euthymic BD patients. Importantly, manic BD patients committed more antisaccade errors with happy faces, whereas depressed BD patients showed a non-significant trend to commit more antisaccade errors with sad faces. Neither euthymic BD patients nor control individuals showed differences across conditions. García-Blanco et al. (2013) concluded that BD patients had an impaired ability to inhibit their attentional orienting toward mood-congruent stimuli during abnormal mood states, especially during manic episodes. This pattern provides some support to the Beck's Cognitive Model (1976) for BD: negative schemata would characterize depression and positive schemata would

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characterize mania.

Clearly, antisaccade tasks offer valuable information with respect to the initial orienting of attention. However, in addition to initial orienting, attentional capture involves other attentional processes such as the engagement of attention paid to a particular image when looking at it for the first time before looking away from it (Posner and Petersen, 1990). Another potential limitation of the García-Blanco et al. (2013) experiment is that they only used happy and sad images as emotional stimuli. Freeman, Garety, Kuipers, Fowler, and Bebbington (2002) showed that BD patients have difficulties ignoring threatening stimuli. Indeed, threat-related schemata may underline psychotic states and paranoid traits in BD, especially during manic episodes (Mansell, Morrison, Reid, Lowens, & Tai, 2007). To overcome these difficulties, García-Blanco, Salmerón, & Perea (2015) simultaneously displayed a target scene (happy, threatening, neutral) and a neutral control scene for 3 s in a free-viewing task with BD patients – a group of healthy individuals was included as a control. Participants' initial orienting of gaze (i.e., the location of the first fixation) was directed more frequently toward emotional images (both happy and threatening) than toward neutral images in all groups. However, unlike healthy individuals, BD patients (regardless of their episode) showed greater attentional engagement (i.e., sum of fixation durations before leaving the item [gaze duration]) to threatening scenes relative to neutral ones (see also García-Blanco, Salmerón, Perea, & Livianos, 2014, for similar evidence in a free viewing task with four simultaneously presented images). This threat-related bias is consistent with the idea that threat-related information is highly salient in BD (Freeman, Garety, Kuipers, Fowler, & Bebbington, 2002). Importantly, these biases occurred during attentional engagement but not during initial orienting.

Of particular interest here is examining whether BD patients can modify their attentional biases and ignore distracting information that attracts attention. The idea is that a deficit to control attention that overrides voluntarily dominant responses may induce abnormal emotional reactions that entail difficulties in emotional self-regulation. However, free-viewing tasks such as the task used by García-Blanco et al. (2015) do not provide a measure of inhibitory control of attention per se. In the present experiment, we modified the instructions given in the García-Blanco et al. (2015) experiment so that we could directly obtain a direct measure of inhibitory control: in one block, participants were instructed to *only* attend to the emotional image, whereas in the other block participants were instructed to *only* attend to the neutral image (Nummenmaa, Hyönä, & Calvo, 2006, for a similar procedure with healthy individuals). To be able to look at only one of the two images, participants need to: (i) recognize the correct scene by means of peripheral vision; (ii) fixate on this scene; and (iii) keep fixating on this scene until the completion of the trial. As healthy individuals in free-viewing tasks tend to orient their attention more frequently toward emotional images than neutral ones (Nummenmaa, Hyönä, & Calvo, 2006), the attend-to-neutral block involves a controlled inhibition: participants are required to inhibit the automatic response to emotional images and voluntarily direct their gaze to neutral pictures. With healthy individuals in the attend-to-neutral block, Nummenmaa et al. (2006) found that the percent of first fixations was higher and the gaze duration was longer for emotional than for neutral images – this pattern was not modulated by stimulus valence (happy versus threatening). That is, in attend-to-neutral blocks, healthy individuals have difficulty in ignoring emotional information in terms of both initial orienting (i.e., emotional images received a higher percent of first fixations than neutral images) and attentional engagement (i.e., emotional images received longer gaze durations than neutral images).

To sum up, the main goal of the present experiment was to examine inhibitory control across the three BD states (manic, euthymic, depressed) as a function of the type of target scene (happy, threatening, and neutral). The two main research questions were: (i) whether manic BD individuals would show higher deficit in inhibitory control for happy pictures than for neutral or threatening images (i.e., a mood-congruent bias), as Beck's (1976) theory would predict or (ii) whether BD individuals – regardless of their episode – would show higher deficit in inhibitory control for threatening images than for happy and neutral ones (i.e., a bias toward threatening information), as Freeman et al.'s (2002) cognitive model would predict). To shed some light on these two questions, we examined two attentional components (see also Nummenmaa et al., 2006, for a similar approach): (1) initial orienting of attentional capture (i.e., the latency of the first fixation and the percentage of the first fixation); and (2) attentional engagement (i.e., the gaze duration).

1. Method

1.1. Participants

Eighty-four BD patients from the Psychiatry Department at the "La Fe" University and Polytechnic Hospital (Valencia, Spain) and 27 healthy individuals recruited through advertising in the community took part in the experiment. Patients fulfilled the DSM-IV-TR criteria for BD and were included in the manic (n = 29), depressed (n = 27), or euthymic (n = 28) group at the time of assessment. BD patients were recruited from inpatient wards (n = 40) and from Bipolar Disorders Unit for outpatients (n = 44). Four patients in manic episodes refused to cooperate. The ethics committee of the "La Fe" Health Research Institute authorized this study. Demographic and clinical details are presented in Table 1.

No participant showed difficulty in obtaining stable eye tracking (e.g., eye diseases, interference from glasses, or frequent crying) or major medical disorders, neurological history, or use of non-psychotropic medication that could influence cognition (e.g., treatment with corticosteroids). No healthy control reported any kind of psychiatric history. Additional exclusion criteria for patients were (i) other psychiatric diagnoses based on the DSM-IV-TR criteria (American Psychiatric Association [APA], 2000) and (ii) having received electroconvulsive therapy within the previous 3 months. All patients were referred by psychiatrists in the Bipolar Disorders Unit who diagnosed the BD patients following the DSM-IV-TR criteria. The responsible psychiatrist together with a postgraduate clinical psychology intern corroborated the BD diagnosis via a clinical interview and case note review. Every BD patient had to present at least one manic episode. The Young Mania Rating Scale (YMRS; Young, Biggs, Ziegler, & Meyer, 1978) and the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996) were used to control the presence of affective symptoms in healthy participants and in euthymic patients and to exclude mixed states (BDI-II scores < 9, except in the depressed

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

	Control (N = 27)	Euthymic (N = 28)	Depressed (N = 27)	Manic (N = 29)	p value
% Female	48.1	39.3	44.4	44.8	0.93
Age	42.0 (12.6)	41.1 (10.3)	49.4 (9.8)	44.4 (12.0)	0.05
SASS	43.8 (6.0)	40.1 (5.3)	40.8 (6.8)	39.5 (6.2)	0.07
No. of episodes	–	6.1 (5.3)	7.6 (4.5)	7.1 (5.6)	0.56
BAI	11.2 (7.0)	6.3 (5.0)	24.9 (90)	11.5 (7.3)	**0.000**
BDI	5.9 (6.0)	3.4 (41)	25.8 (7.9)	5.1 (3.6)	**0.000**
YMRS	–	1.2 (2.2)	1.8 (2.4)	23.7 (5.5)	**0.000**
Medication (% of patients)					
Lithium (%)	–	89.3	70.4	72.4	0.18
Antiepileptic	–	46.4	66.7	41.4	0.14
Antipsychotic	–	39.3	48.1	96.6	**0.000**
Antidepressive	–	7.1	55.6	6.9	**0.000**
Anxiolytic	–	42.9	81.5	89.7	**0.000**

Note: The p-values correspond to the omnibus test for all groups. Bold values indicate significant differences between groups.

group > 18; YMRS scores < 6, except in the manic group > 20). Additionally, every participant filled out: (i) the Social Adaptation Self-Evaluation Scale (SASS; Bosc, Dubini, & Polin, 1997) to assess social functioning and (ii) the Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988) to measure anxiety. Six of the 117 participants in the original sample (89 patients and 28 healthy controls) were excluded based on these criteria, resulting in a final sample of 111 participants.

1.2. Apparatus

The participants' eye movements were monitored using a remote eye-tracking system (SMI RED250). This system allows the participant free head movements across a wide range. The sampling rate of gaze-point position was 250 Hz. Areas of interest (AOIs) were also identified for each trial and corresponded to the total area for each of the target images.

1.3. Materials

We used the same images employed by Nummenmaa et al. (2006) in their Experiment 2. The stimuli were 128 pictures taken from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2005). A total of 16 happy and 16 threatening target scenes together with 16 neutral scenes and 80 control images were employed. The control pictures illustrated various inanimate images and non-living objects, whereas the neutral images represented animate scenes with people in non-emotional activities or aspects of daily life. The happy target scenes represented people showing positive affect or taking pleasure in something. The threatening target scenes depicted aggressive people or people suffering from serious threat or harm.

In each trial, two pictures appeared, namely, a target scene (happy, threatening, or neutral) and a control picture, where the emotional scene and control images were randomly paired. Each trial began with a centrally presented fixation cross located in the middle of the screen, followed by simultaneous presentation of two images for 3000 ms. There were three types of experimental trials – 16 happy-control, 16 threatening-control, and 16 neutral-control. In addition, 16 pairs of control–control trials were used as filler trials to mask the nature of the task. Each trial was displayed two times. Overall, the experimental session comprised a total of 128 trials (96 experimental + 32 filler). For each trial, the images were displayed in two opposing corners of the screen (top right/bottom left or top left/bottom right). The horizontal and vertical locations of the target pictures were balanced across trials, keeping in mind that each stimulus category had to appear in each of the four positions four times across 16 trials. The presentation order of the scenes was randomized across participants. The participants were not able to use any predetermined scanning strategy due to the variation in the picture positions and the randomization of trials (Fig. 1).

1.4. Procedure

After signing an informed consent form, all participants completed a demographic interview and the SSAS, BAI and BDI rating scales. Additionally, patients completed a clinical interview and the YMRS. In the same session, participants carried out the experiment in a dimly lit room. They were tested individually and were seated in a height adjustable chair approximately 60 cm from the screen. The experimental session began once the eye-tracker was successfully calibrated (i.e. average error was < 1.5° of visual angle for each calibration point) and six practice trials were completed.

The 128 trials were divided into two blocks. Each participant performed the task with both blocks, which were counterbalanced across participants. Before each block, the participant was instructed to either (i) "direct your gaze to an emotional image and keep it there as long as the images are presented" (attend-to-emotional block) or (ii) "direct your gaze to a neutral image and keep it there as long as the images are presented" (attend-to-neutral block). Each stimulus pair appeared only once in the attend-to-emotional and once in the attend-to-neutral condition.

1.5. Data analyses

We measured the following eye-movement measures: (a) the latency of the first fixation (i.e., the time taken to fixate on a target picture); (b) the percentage of first fixations (i.e. the percentage of trials in which the first fixation was on a target picture); (c) the gaze duration (i.e. the sum of fixation durations on a target picture when it is looked at for the first time and before leaving it); and (d) the total fixation time (i.e. the overall gaze duration with possible re-fixations on a target picture during the 3 s exposure period). Initial orienting was assessed through the latency of the first fixation and the percentage of first fixation on a target picture. The gaze duration assessed subsequent attentional engagement. Finally, the total fixation time assessed allocation of attention – this measure was included in order to verify that the participants followed the instructions appropriately for each block.

2. Results

The descriptive statistics (means and standard errors) on the eye-movement measures for the different target types are displayed in Table 2. Eye-movement measures were analyzed in a 4 (Group: control, euthymic, depressed, manic) × 3 (Valence of image: happy, threatening, neutral) × 2 (Block: attend to neutral, attend to emotional) analysis of variance (ANOVA) in which Group was a between-subjects factor and Valence and Block were within-subject factors. In the case of significant interactions, Bonferroni corrections were employed in the simple effect tests.

2.1. Initial orienting

2.1.1. Latencies of the first fixation

The ANOVA showed a main effect of Group, $F(3,107) = 9.59$, $p < 0.001$, $\eta^2 = 0.21$: on average, latencies of the first fixation were longer in the manic (708 ms) and depressed (717 ms) groups than in the control (556 ms) and euthymic (575 ms) groups (all $ps < 0.005$). The main effects of Block, $F(1,107) = 11.34$, $p = 0.001$, $\eta^2 = 0.10$, and Valence, $F(2,107) = 11.34$, $p < 0.001$, $\eta^2 = 0.10$ were also significant. Only the Block × Valence interaction was significant, $F(2, 107) = 3.18$, $p = 0.043$, $\eta^2 = 0.03$ – all other interactions had $ps > 0.41$.

To analyze the Block × Valence interaction, we tested the effect of Valence in each Block. We found an effect of Valence in the attend-to-neutral block, $F(2, 220) = 11.50$, $p < 0.001$, $\eta^2 = 0.10$, but not in the attend-to-emotional block, $F(2, 220) = 1.95$, $p = 0.14$. Further analyses on the attend-to-neutral block showed that latencies were shorter for happy pictures (617 ms) than for neutral (717 ms) and threatening (665 ms) pictures (both $ps < 0.04$) – these two conditions did not differ significantly ($p = 0.07$).

2.1.2. Percentage of the first fixations

The ANOVA showed a main effect of Block, $F(1, 107) = 61.38$, $p < 0.001$, $\eta^2 = 0.37$, Valence, $F(2, 214) = 10.39$, $p < 0.001$, $\eta^2 = 0.09$, and Group, $F(3, 107) = 2.98$, $p = 0.03$, $\eta^2 = 0.08$. Importantly, the Group × Valence interaction, $F(6,107) = 4.03$, $p = 0.001$, $\eta^2 = 0.10$, and the Group × Block interaction, $F(3,107) = 7.48$, $p < 0.001$, $\eta^2 = 0.17$ were significant. The other interactions were not significant, all $Fs < 1$.

To analyze the Group × Valence interaction, we examined the effect of Valence in each group (Fig. 2). The effect of Valence was significant in the control ($F(2, 52) = 10.96$, $p < 0.001$, $\eta^2 = 0.30$), euthymic ($F(2, 54) = 3.33$, $p = 0.043$, $\eta^2 = 0.11$), and manic ($F(2, 56)$

Fig. 1. Stimulus sequence of two experimental trials with a threatening and happy target scene.

= 12.22, $p < 0.001$, $\eta^2 = 0.30$) groups, but not in the depressed group ($F < 1$). For the control group, threatening images received a higher percentage of initial fixations than neutral images (69.91 versus 58.50%, respectively) ($p < 0.001$), and none of them differs significantly from the happy images (65.89%) (all $ps > 0.06$). For the euthymic group, even though the main effect was significant, there were no significant differences across levels of Valence (happy: 56.09%, threatening: 64.36%, neutral: 59.00%; all $ps > 0.10$). For the manic group, happy images received a higher percentage of initial fixations (65.15%) than threatening (59.05%) and neutral images (53.05%) (both $ps < 0.03$) – these two condition did not differ significantly ($p = 0.09$).

To analyze the Group × Block interaction, the effect of Block was examined for each group. The effect of Block was significant in the control ($F(1, 26) = 31.80$, $p < 0.001$, $\eta^2 = 0.55$), euthymic ($F(1, 27) = 13.88$, $p = 0.001$, $\eta^2 = 0.34$), and manic ($F(1, 28) = 15.25$, $p = 0.001$, $\eta^2 = 0.35$) groups, but not in the depressed group, $F(1, 26) = 2.76$, $p = 0.11$. The percentage of initial fixations on the target picture was higher in the attend-to-emotional blocks (control: 76.29%, euthymic: 65.18%, manic: 63.33%) than in the attend-to-neutral blocks (control: 53.24%, euthymic: 65.18%, manic: 63.33%) in all groups except for the depressed group (attend-to-emotional: 62.37% and attend-to-neutral: 58.42%).

2.2. Attentional engagement

2.2.1. Gaze duration

The ANOVA revealed significant main effects of Block ($F(1,107) = 427.22$, $p < 0.001$, $\eta^2 = 0.80$), Valence ($F(2,214) = 7.76$, $p < 0.001$, $\eta^2 = 0.07$), but not of Group ($F(1,107) = 1.26$, $p < 0.29$). Importantly, these effects were qualified by the Block × Valencia × Group interaction ($F(6,214) = 2.47$, $p = 0.025$, $\eta^2 = 0.06$). To analyze this three-way interaction, we examined the Valence × Group interaction in each level of the factor Block (Fig. 3).

In the attend-to-emotional block, the main effects of Valence ($F(2, 214) = 60.41$, $p < 0.001$, $\eta^2 = 0.36$) and Group ($F(3, 107) = 7.32$, $p < 0.001$, $\eta^2 = 0.17$) were qualified by a significant Valence × Group interaction ($F(6, 214) = 2.16$, $p = 0.048$, $\eta^2 = 0.06$). To examine this interaction, the effect of Valence was analyzed in each group. The effect of Valence was significant in all groups (control: $F(2, 52)$

Table 2
Mean (standard deviation) for the latency of first fixation, the percentage of first fixation, the gaze duration, and the total fixation duration for each stimulus category for the control (C), euthymic (E), depressed (D), and manic (M) groups.

Stimulus category		Latency of first fixation (ms)				Percent first fixation (%)				Gaze duration (ms)				Total fixation duration (ms)			
		C	E	D	M	C	E	D	M	C	E	D	M	C	E	D	M
Emotional	Happy	518	553	681	657	80.4	61.6	62.4	69.0	1629	1618	1312	1278	1703	1835	1397	1451
		(168)	(144)	(224)	(209)	(18.4)	(19.5)	(16.6)	(18.2)	(520)	(460)	(428)	(452)	(521)	(367)	(488)	(444)
	Threatening	549	513	686	665	80.5	70.5	64.4	64.7	1571	1474	1252	1065	1721	1774	1387	1286
		(195)	(107)	(209)	(173)	(14.8)	(18.7)	(16.8)	(15.7)	(552)	(341)	(373)	(394)	(546)	(292)	(442)	(380)
	Neutral	575	570	681	706	67.9	63.4	60.3	56.4	1364	1100	883	945	1575	1471	1127	1092
		(205)	(120)	(265)	(154)	(9.1)	(14.4)	(13.5)	(14.0)	(607)	(467)	(370)	(366)	(535)	(419)	(461)	(339)
Neutral	Happy	541	563	693	670	51.4	50.6	59.8	61.3	276	335	522	483	231	282	519	488
		(156)	(161)	(309)	(197)	(22.3)	(19.2)	(20.0)	(16.3)	(228)	(140)	(281)	(280)	(211)	(161)	(315)	(325)
	Threatening	561	619	731	746	59.3	58.2	57.6	53.4	315	359	504	640	283	328	494	664
		(195)	(184)	(287)	(177)	(19.8)	(16.3)	(16.2)	(14.9)	(181)	(148)	(230)	(275)	(236)	(179)	(288)	(349)
	Neutral	593	633	832	807	49.1	54.6	57.8	49.7	597	541	649	691	588	569	721	725
		(144)	(193)	(376)	(177)	(15.1)	(17.4)	(11.3)	(12.4)	(338)	(278)	(333)	(279)	(311)	(306)	(328)	(292)

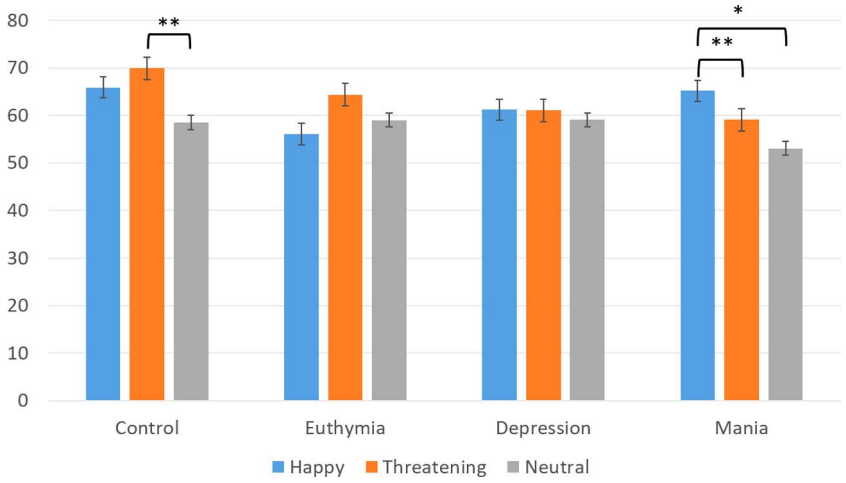

Fig. 2. Percentage of initial fixation (%) for Valence and Group. Data shown are means and standard errors.

= 5.68, $p = 0.006$, $\eta^2 = 0.18$; euthymic: $F(2, 54) = 29.52$, $p < 0.001$, $\eta^2 = 0.52$; manic: $F(2, 56) = 10.60$, $p < 0.001$, $\eta^2 = 0.28$; depressed: $F(2, 52) = 29.86$, $p < 0.001$, $\eta^2 = 0.53$). As shown in Table 2, the pattern of data was similar in the control, euthymic, and depressed groups: gaze durations were shorter on neutral targets than on happy and threatening targets (all $ps < 0.02$) – there were no significant differences between these two conditions (all $ps > 0.13$). In contrast, manic patients showed a different pattern: gaze durations were longer on happy targets than on threatening or neutral targets (both $ps < 0.01$) – there were no significant differences between these two conditions ($p = 0.25$).

In the attend-to-neutral bock, the main effects of Valence ($F(2, 214) = 37.87$, $p < 0.001$, $\eta^2 = 0.26$) and Group ($F(3, 107) = 7.38$, $p < 0.001$, $\eta^2 = 0.17$) were also qualified by a significant Valence × Group interaction ($F(6, 214) = 2.66$, $p = 0.02$, $\eta^2 = 0.07$). To analyze this interaction, we examined the effect of Valence in each group. The effect of Valence was significant in all groups (control: $F(2, 52) = 18.46$, $p < 0.001$, $\eta^2 = 0.42$; euthymic: $F(2, 54) = 10.82$, $p < 0.001$, $\eta^2 = 0.29$; manic: $F(2, 56) = 8.46$, $p < 0.001$, $\eta^2 = 0.23$; depressed: $F(2, 52) = 5.67$, $p = 0.006$, $\eta^2 = 0.18$). There was a common pattern in the control, euthymic, and depressed groups: gaze durations were longer on neutral targets than on happy or threatening targets (both $ps < 0.05$) – there was no significant difference between happy and threatening pictures ($p > 0.90$). Again, manic patients showed a different pattern: gaze durations were longer on threatening and neutral images than on happy pictures (both $ps < 0.003$), whereas there was no significant difference between threatening and neutral pictures ($p > 0.90$).

2.3. Overall allocation of attention

2.3.1. Total fixation time

The ANOVA of the total fixation time showed a significant main effect of Block ($F(1,107) = 708.76$, $p < 0.001$, $\eta^2 = 0.87$), but not of Valence or Group (both $Fs < 1$). Importantly, these effects were qualified by a significant Valence × Group × Instruction interaction ($F(6, 214) = 2.31$, $p = 0.03$, $\eta^2 = 0.06$). To further analyze this interaction, we tested the Valence × Group interaction in each Block.

In the attend-to-emotional block, we found main effects of Valence ($F(2, 214) = 46.77$, $p < 0.001$, $\eta^2 = 0.30$) and Group ($F(3, 107) = 8.88$, $p < 0.001$, $\eta^2 = 0.20$). The Valence × Group interaction did not reach statistical significance ($F(6, 214) = 2.04$, $p = 0.06$, $\eta^2 = 0.05$). With respect to the effect of Valence, total fixation times were shorter on neutral targets that on happy and threatening targets

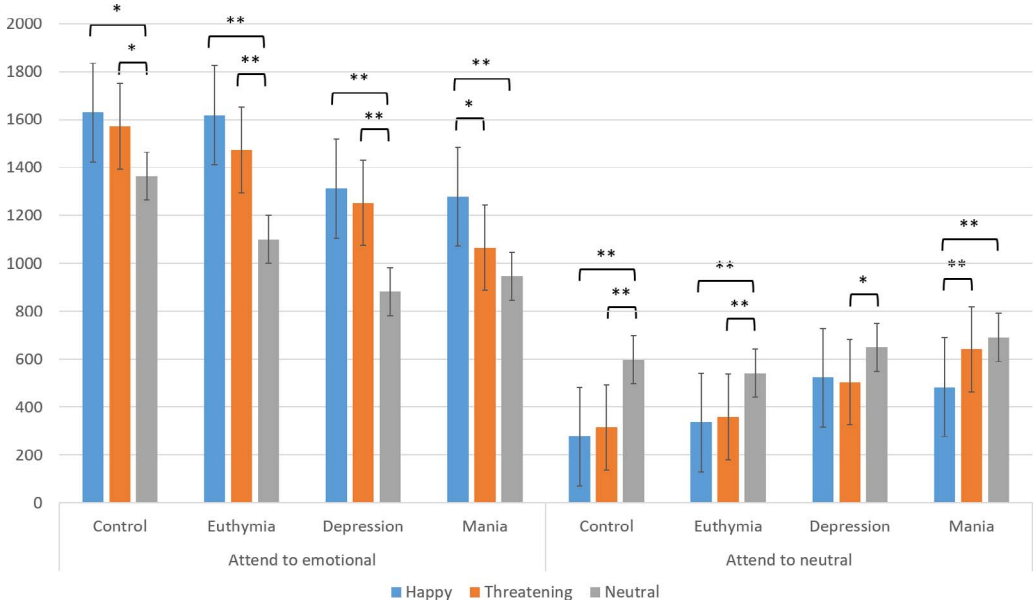

Fig. 3. Gaze duration (ms) for Block, Valence, and Group. Data shown are means and standard errors.

(both $ps < 0.001$) –there was no significant difference between these two conditions ($p = 0.24$). With respect to the effect of Group, total fixation times were similar in the control and euthymic groups ($p > 0.90$), which in turn were longer than those in the manic and depressed groups (all $ps < 0.001$). Finally, the total fixation times were similar in the manic and depressed groups ($p > 0.90$).

In the attend-to-neutral block, the main effects of Valence ($F(2, 214) = 56.84$, $p < 0.001$, $\eta^2 = 0.35$) and Group ($F(3, 107) = 8.74$, $p < 0.001$, $\eta^2 = 0.20$) were qualified by a significant interaction between these two factors ($F(6, 214) = 2.70$, $p = 0.01$, $\eta^2 = 0.07$). To analyze this interaction, the effect of Valence was examined in each group. The effect of Valence was significant in all groups (control: $F(2, 52) = 22.00$, $p < 0.001$, $\eta^2 = .46$; euthymic: $F(2, 54) = 26.14$, $p < 0.001$, $\eta^2 = 0.49$; manic: $F(2, 56) = 11.45$, $p < 0.001$, $\eta^2 = 0.29$; depressed $F(2, 52) = 8.93$, $p < 0.001$, $\eta^2 = 0.26$). We found a similar pattern in the control, euthymic, and depressed groups: total fixation durations were longer on neutral images than on happy and threatening images (all $ps < 0.001$) – these two conditions did not differ significantly ($p > 0.31$). In contrast, for manic patients, total fixation durations were longer on threatening and neutral images than on happy images (all $ps < 0.002$) – total fixation times on threatening and neutral pictures did not differ significantly ($p = 0.99$).

3. Discussion

The present eye-movement experiment was designed to examine how the emotional valence of images (happy, threatening, and neutral) affects the inhibitory control of attentional capture (initial orienting and attentional engagement) in the different episodes of BD patients (mania, euthymia, and depression). First, we had initially hypothesized – following Beck's (1976) theory, that manic BD individuals would show a deficit in inhibitory control for happy pictures. In the initial orienting, we found that manic BD patients showed a higher percentage of initial fixations on happy scenes than on the other scenes, regardless of the instructions. Second, we had hypothesized – in terms of Freeman's et al. (2002) theory – that BD patients (regardless of their episode) would show difficulties ignoring threatening stimuli. Our findings on attentional engagement partially support this hypothesis, but it was restricted to manic BD patients: in the attend-to-neutral block, manic BD patients had longer gaze duration for threatening and neutral scenes than for happy scenes. Therefore, manic patients show a deficit in inhibitory control for happy scenes in initial orienting, whereas they show a deficit in inhibitory control for threatening scenes in attentional engagement. In the following paragraphs, we discuss the implication of these findings for Beck's (1976) cognitive theory on mania and Freeman et al.'s (2002) cognitive model.

Regarding the inhibitory control of initial orienting to emotional stimuli, manic and depressive individuals showed slower latencies of the first fixation than euthymic and control individuals. In addition, when the percentage of the first fixation was analyzed, manic BD patients showed an initial orienting bias toward happy scenes, regardless of the instructions. This pattern resembles that found in the García-Blanco et al. (2013) experiment with manic patients in which there were more antisaccade errors (i.e., a deficit to inhibit an automatic prosaccade) to happy stimuli than to sad or neutral faces. The happy-related bias during initial orienting in manic BD patients is consistent with Beck's Cognitive theory on mania (1976): mania involves positive biases in information processing. In the present experiment, the stimulus valence modulation of initial orienting was absent in depressed BD patients (see García-Blanco et al., 2013 for a similar finding with an antisaccade task). Thus, depressive BD patients showed an "anhedonic bias" rather than a negative bias as Beck's cognitive theory (1976) postulates. The lack of emotional bias in bipolar depression may be explained by the distinctive feature of BD relative to major depressive disorder (Mansell, Morrison, Reid, Lowens, & Tai, 2007) because melancholic symptoms (e.g., loss of pleasure in activities or lack of reactivity to emotional stimuli) are more characteristic of bipolar than unipolar depression. Finally, healthy participants showed a threat-related bias during initial orienting, regardless of the instructions. As indicated earlier, previous eye-tracking studies reported preferential initial orienting toward threatening scenes (Santos et al., 2012). This bias has been interpreted as an adaptive threat-detection advantage that may represent an evolutionary advantage for survival (Öhman, 2009). Therefore, vigilance concerning threatening stimuli, despite the instructions to ignore them, may be a survival function that is conserved in healthy individuals.

With respect to the inhibitory control of attentional engagement, we found that gaze durations were longer on neutral than on emotional images in all groups, except in the manic group. Specifically, manic BD patients showed longer gaze durations on threatening and neutral scenes than on happy scenes. That is, manic BD patients showed a threat-related bias. This finding is consistent with theoretical proposals that emphasize the relevance of threat-related schemata in BD (Freeman et al., 2002). Importantly, unlike free-viewing tasks (García-Blanco, Salmerón, Perea, & Livianos, 2014; García-Blanco et al., 2015), this threat-related bias did not occur in depressed or euthymic BD patients. That is, depressed and euthymic BD patients can inhibit the attentional engagement to threatening scenes and voluntarily direct their gaze to neutral pictures. This finding suggests that threatening scenes are especially salient in manic states. One explanation for this pattern is that threat-related schemata are more prominent during mania than other mood episodes (Mansell et al., 2007). Indeed, we found that severity of manic symptomatology had a modulating role in threat-related bias formation.[1] Taken together, the present data suggest a dissociation between initial orienting and attentional engagement in mania when the participant's task is to attend to neutral information: whereas manic BD patients are initially oriented to positive information, subsequently their attention is engaged in threat-related information. This difficulty to disengage attention from threatening images may contribute to threat-related rumination (Koster, De Lissnyder, Derakshan, & De Raedt, 2011). Therefore, the impairment for inhibiting the automatic initial orienting of attention toward happy stimuli and the impairment for disengaging attention from threatening stimuli could be a key component of emotion dysregulation observed in mania (Alloy, Abramson, Walshaw, & Neeren, 2006).

The current experiment also examined the blocks in which participants were instructed to attend to emotional information. Except for the individuals in the manic group, who showed the highest attentional capture for happy images, the other groups showed an attentional capture for emotional stimuli (both happy and threatening scenes received a higher percentage of first fixation than neutral images) (see García-Blanco et al., 2013, 2015, for similar findings with a prosaccade task and a free-viewing task, respectively). Therefore, all groups of participants were able to recognize which was the correct target scene during early stages of processing – note that – while non-significant – the attentional capture of manic patients was higher for threatening than for neutral images.

Finally, the current eye-tracking experiment comes with certain limitations that are typical in studies with patients. All patients were medicated at the time of testing (Table 1). We acknowledge that medication and other illness variables (i.e., number of previous episodes and age of illness onset) can affect inhibitory control. However, medication or historical illness variables alone cannot explain why attentional capture in each episode was modulated by the emotional salience of stimuli. Nevertheless, manic and depressed individuals had slower latencies of the first fixations than euthymic

[1] We computed the Pearson's coefficient to examine the relationship between attentional engagement to threat-related information (i.e., the gaze duration for threatening scenes) during the attend-to-neutral block and the YMRS scores (i.e. manic symptoms) in BD patients. YMRS scores were significantly correlated with the gaze duration for threatening scenes ($r = 0.418$, $p < 0.001$). That is, the higher the manic symptomatology, the higher the attentional engagement to threatening scenes.

and control individuals. We conducted *post hoc* analyses of covariance that included antipsychotic, antidepressive, and anxiolytic medication as covariates. No medication significantly interacted with any of the main effects or interactions in the analyses ($ps > 0.18$ and $ps > 0.09$, respectively). Thus, medication was not the main cause of the differences across groups in the latencies of the first fixations.

In summary, the current eye-movement experiment adds to previous studies in BD that a manic state posits difficulties in inhibiting happy information during initial orienting and in inhibiting threatening information during attentional engagement. Therefore, despite the fact that threatening information is salient for all BD mood episodes when it is free-viewed, only manic patients had difficulties ignoring it voluntarily. Thus, our findings revealed an impaired inhibitory control in mania, which was modulated both by stimulus valence (happy versus threatening) and by the component of attentional capture (initial orienting versus attentional engagement). That is, inhibitory control when processing emotional information is impaired in BD, and this is especially so during manic episodes. This impairment may play an important role in an individual's emotion regulation. Indeed, a potential line of research at the applied level is the examination of whether attention training with emotional stimuli is a useful treatment target for BD individuals (see Wells and Beevers, 2010, for evidence with major depression).

Conflict of Interest

The authors declare that they have no conflict of interest.

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