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Attentional biases for emotional facial stimuli in currently depressed patients with bipolar disorder[1]

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ABSTRACT. Compared to the extensive research focussing on cognitive vulnerability factors underlying the onset and maintenance of major depressive disorder, studies investigating dysfunctional processing of emotional information in bipolar depression remain scarce. Therefore, this experimental study examined the nature and time course of attentional biases for emotional information in depressive patients with bipolar disorder. Fourteen currently depressed patients with Bipolar I Disorder (BD) and 14 nondepressed control participants (NC), matched for age, gender and education level, performed an emotional modification of the spatial cueing task. Cues consisted of angry, positive and neutral facial expressions presented for 200 and 1,000 ms. BD patients showed an enhanced cue validity effect for angry faces and had more difficulties in disengaging attention away from angry as well as happy facial expressions compared to NC participants, who conversely demonstrated a «protective bias» away from negative information. This pattern of differential attentional processing was only found within the early stage of information processing at a presentation duration of 200 ms. These results provide evidence for deficits at the early stages of attentive processing of emotional information in depressed bipolar patients compared to healthy controls.

KEYWORDS. Bipolar depression. Attention. Facial expressions. Spatial cueing. Experiment.

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RESUMEN. En comparación con las numerosas investigaciones centradas en los factores de vulnerabilidad cognitiva que subyacen en el inicio y el desarrollo del trastorno depresivo mayor, los estudios que investigan el procesamiento disfuncional de la información emocional en el trastorno bipolar siguen siendo escasos. Por ello, el presente estudio experimental ha analizado la naturaleza y el curso temporal de los sesgos atencionales en pacientes depresivos con trastorno bipolar. Un total de catorce pacientes deprimidos con Trastorno Bipolar I (TB) y catorce participantes controles no deprimidos (CN), emparejados en edad, sexo y nivel educativo, realizaron una modificación emocional de la tarea de señalización espacial. Las señales consistían en expresiones faciales de enfado, neutrales y positivas presentadas durante 200 y 1.000 ms. Los pacientes con TB mostraron un mayor efecto de validación de las señales en las caras de enfado y presentaron más dificultades a la hora de desvincular la atención de las expresiones faciales de enfado y de alegría en comparación con los participantes CN, que por el contrario, demostraron un «sesgo protector» distanciado de la información negativa. Este patrón diferenciado de procesamiento atencional solo se halló en la fase inicial del procesamiento de la información en una presentación de 200 ms de duración. Estos resultados demuestran la existencia de déficits en las fases iniciales del procesamiento atencional de la información emocional en pacientes deprimidos bipolares en comparación con los controles sanos.

KEYWORDS. Experimento. Depresión bipolar. Atención. Expresiones faciales. Claves espaciales.

An increasing amount of empirical evidence has demonstrated the presence of general information processing deficits underlying the onset and endurance of bipolar disorder (Green, Cahill, and Mahli, 2007; Quraishi and Frangou, 2002). Patients with bipolar I and bipolar II disorder show significant deficits on a variety of conventional neuropsychological tests with disturbances on measures of working memory (*e.g.* Glahn *et al.,* 2006), selective and sustained attention (*e.g.* Clark, Iversen, and Goodwin, 2002; Nehra, Chakrabarti, Pradhan, and Khehra, 2006), mental flexibility (*e.g.* Frangou, Donaldson, Hadjulis, Landau, and Goldstein, 2005; Krabbendam, Arts, Van Os, and Aleman, 2005), and verbal fluency (*e.g.* Martinez-Aran *et al.*, 2002; Martinez-Aran, Vieta, Reinares *et al.,* 2004). These information-processing deficits are not restricted to symptomatic bipolar patients in the depressed or manic state of the illness, but also seem to persist during remission as stable vulnerability factors. Importantly, these deficits have been associated with longer illness duration, more affective episodes and frequent hospitalisations (*e.g.* Cavanagh, Van Beck, Muir, and Blackwood, 2002; Ferrier, Stanton, Kelly, and Scott, 1999; Kolur, Reddy, John, Kandavel, and Jain, 2006; Martinez-Aran *et al.,* 2005; Martinez-Aran, Vieta, Colom *et al.,* 2004; Simonsen *et al.,* 2008).

Apart from the investigation of general processing deficits or disturbances in the processing neutral information, in recent years, research has been extended to the examination of cognitive impairments in the processing of emotional information (Scott and Pope, 2003). This research pathway may offer new insights that are of high clinical importance because potential disturbances in the processing of emotional and social relevant information in bipolar disorder may interfere with their psychosocial functioning and therefore increase the risk of future relapse.

Studies evaluating attentional processing in bipolar disorder have provided mixed findings. Bentall and Thompson (1990) and French, Richards, and Scholfield (1996) demonstrated that both manic and hypomanic bipolar patients show an attentional bias for negative information, evidenced by a slowing down in colour naming on an emotional Stroop task, specifically for negative valenced words but not euphoria-related words. Lyon, Startup, and Bentall (1999) replicated these findings and additionally demonstrated that patients in the depressive state of the illness also exhibited this slower colour naming for negative valenced words. However, two recent emotional Stroop studies (Kerr, Scott, and Phillips, 2005; Malhi, Lagopoulos, Sachdev, Ivanoviski, and Shnier, 2005) could not replicate these findings and only established a significant slowdown in colour naming for all emotional stimuli in euthymic, depressed and manic bipolar participants.

The above mentioned emotional Stroop studies only provided a general measure of attentional interference, by presenting both task-relevant (the colour of the stimulus) and task irrelevant information (the emotional content of the stimulus) within one stimulus display (Fox, Russo, and Dutton, 2002; Mogg and Bradley, 2005). As a consequence, using this task it is not possible to examine difficulties within different components of attention, such as problems in engaging toward and disengaging away from emotional information (Posner and Peterson, 1990). Moreover, in some of the above studies, measures of attentional interference were not computerized, causing potential inaccuracies in response registration (Kerr *et al.,* 2005).

Given these limitations, attentional functioning in bipolar disorder has recently been investigated by using computerized tasks that allow a more elegant examination of attentional shifting and spatial orienting processes. Using an affective shifting task, Murphy *et al.* (1999) reported significant impairments in the ability to shift the focus of attention away from negative material in major depressive patients and for positive material in manic participants. An inability to disengage attention was also found in a more recent study by Jongen, Smulders, Ranson, Arst, and Krabbendam (2007), who demonstrated, using a modified dot-probe task, that deficits in general reorienting were positively associated with measures of depressed mood in bipolar patients. However, related to the attentional processing of affective information, these authors revealed a bias away from depressive and positive words in their bipolar depressed patient group. Finally, using an affective go/no-go task, Rubinsztein, Michael, Underwood, Tempest, and Sahakian (2006) were not able to demonstrate a differential response to sad target words within a sample of bipolar depressed patients.

In light of the inconsistency in current research, the main goal of the present study was to further elucidate the nature of emotion-specific attentional biases in bipolar disorder while taking into account three important considerations.

First, it must be noted that heterogeneities in clinical samples used in previous research might have complicated the examination of potential biases in the attentional processing of emotional information in bipolar disorder. Therefore, this study aimed at investigating a carefully selected sample of only currently depressed bipolar I patients. A sample of bipolar I patients was selected, because recent research (Simonsen *et al.,* 2008) has indicated that the magnitude of cognitive dysfunction is greater in bipolar I compared to bipolar II patients. Moreover, we were particularly interested in investigating patients during the depressive episode of their illness, because with longer duration of

illness, depressive episodes tend to dominate the course of bipolar disorder relative to manic episodes (Di Marzo *et al*., 2006; Mansell, 2005; Rubinsztein *et al.,* 2006) and a greater number of depressive episodes seems to be correlated with greater cognitive decline (Bearden, Hoffman, and Cannon, 2001).

Secondly, to date, no attentional studies have used facial stimuli to investigate emotion-related biases of selective attention in bipolar disorder. Compared to verbal stimuli used in previous research, facial expressions might be more relevant in evaluating attentional processing because they convey information concerning interpersonal evaluation that is of high relevance to mood disorders (Bradley, Mogg, and Miller, 2000; McClure, Pope, Hoberman, Pine, and Liebenluft, 2003). Previous research has demonstrated that bipolar individuals show high levels of social conformism and interpersonal dependency, related to their underlying cognitive schema of low self-worth (Scott and Pope, 2003). Because of their high need of social approval, the present study aimed at comparing differential attentional responding to displays of social approval and disapproval (happy versus angry facial expressions) compared to the mood-congruent information presented in previous research. More specifically, we predicted that depressed patients with bipolar I disorder will show biases specifically emerging for negative, socially rejecting information.

Finally, while a number of studies have already indicated the presence of attentional biases in bipolar affective disorder, few have taken into account the time course of attentional processing. In other words, no research to date has explored whether bipolar I patients are characterized by a hypervigilant orienting toward emotional information at early stages of information processing or rather show increased sustained attention at later stages of information processing. Because longer stimulus presentations (1000 ms or more) are likely to evoke ruminative responses – a characteristic feature of bipolar disorder (Thomas, Knowles, Tai, and Bentall, 2007) – it may be expected that in depressive patients with bipolar disorder the focus of attention will maintain on the negative, socially rejecting information. This assumption corresponds with previous findings in major depressive disorder in which biases in attention where only found at later stages of information processing (*e.g.* Leyman, De Raedt, Schacht, and Koster, 2007). On the other hand, because bipolar I disorder is also characterized by a disinhibited emotional style, it is possible that these patients will manifest a hypervigilant orienting response toward negatively valenced, socio-emotional cues when presenting stimuli for short durations (< 500 ms). This assumption was supported by recent research demonstrating attentional dysfunctions in the early and automatic stages of social information processing in hypomania (Putman, Saevarsson, and van Honk, 2007). Because, to our knowledge, no study to date has focussed on the examination of both early and late attentional processing in bipolar I disorder, the present experimental study (Montero and Léon, 2007; Ramos-Alvarez, Moreno-Fernandez, Valdes-Conroy, and Catena, 2008) aimed at addressing the above assumptions.

To examine the above predictions, attentional processing was measured using an emotional modification of the Exogenous Cueing task (Posner, 1980). In this task, a target appears (either for 200 or 1000 ms) at one of two spatial locations, preceded by a cue at the same ('valid trial') or opposite location ('invalid trial'). Faster response to

valid compared to invalid trials at short intervals between cue and target onset (Stimulus Onset Asynchrony: SOA < 300 ms) is usually referred to as 'the Cue Validity effect'. In the present study it was hypothesised that depressed bipolar I patients would demonstrate a stronger and more prolonged cue validity effect when presented with socially rejecting stimuli compared to neutral information *(i.e.* 'enhanced cue validity'; Fox *et al.,* 2002). Second, comparing the speed of responding on valid and invalid emotional versus neutral trials, we hypothesized that in depressed bipolar I patients angry cues may a) facilitate attentional engagement, leading to response benefits on valid trials and/or b) delay the disengagement of attention, leading to delayed responding on invalid trials (Fox, Russo, Bowles, and Dutton, 2001; Koster, Crombez, Van Damme, Verschuere, and De Houwer, 2004).

Method

Participants

Two groups of participants volunteered to take part in this study: DSM-IV bipolar I disorder patients in the depressive phase of their illness (n = 14) and non-psychiatric control participants (n = 14) matched as adequate as possible with the patient group on age, gender and education level. Participants included in the patient group were selected from a larger pool of ambulant patients (n = 66) recruited from support groups associated with the Flemish Association for Manic-Depression[3]. Non-psychiatric control participants were recruited using a snowball procedure.

In order to obtain a reliable diagnosis of bipolar I disorder, participants were screened using different clinical measures. First, all participants were interviewed using the Dutch version of the Mini International Neuropsychiatric Interview (MINI; Pinninti, Madison, Musser, and Rissmiller, 2003); a structured clinical interview designed to assess current and lifetime psychiatric disorders based on DSM-IV criteria, shown to have good test-retest reliability (Sheenan *et al.,* 1998). The BD patient sample consisted of individuals with diagnosis of bipolar disorder who all met criteria for a current depressive episode or dysthymia. Exclusion criteria were current substance abuse, current and past psychotic symptoms (unrelated to the mood disorder) and neurological or medical diseases requiring treatment. The NC group had no diagnosis of a current or past Axis I disorder and no family history of affective illness in a first-degree relative. NC participants were also excluded when taking psychotropic medication. For additional confirmation of diagnoses and assessment of symptom severity, all participants completed the Beck Depression Inventory-II (Beck, Steer, and Brown, 1996) and the Altman Self-Rating Mania Scale (ASRM; Altman, Heedecker, Peterson, and Davis, 1997). Based on cut-off score guidelines (Van der Does, 2002), participants included in the BD group all scored above 19 on the BDI-II. The ASRM cut-off score was set at a maximum of 6 for all participants, indicating the absence of a current manic episode. In addition, to screen for past depressive and manic episodes, participants completed the Inventory to Diagnose

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Depression Lifetime (IDDL; Zimmerman and Coryell, 1987) and the Mood Disorder Questionnaire (MDQ; Hirschfeld *et al.,* 2000). Participants within the BD group all scored above a cut-off score of 40 on the IDDL and reported scores on the MDQ above a standard cut-off of 7, both indicative of severe and intrusive depressive and manic episodes in the past. Finally, we also administered the Dutch trait version of the State-Trait Anxiety Inventory (STAI-T; Spielberger, Gorsuch, Lushene, Vagg, and Jacobs, 1983; Van der Ploeg, Defares, and Spielberger., 2000) in order to check for co-morbidity of anxiety symptoms.

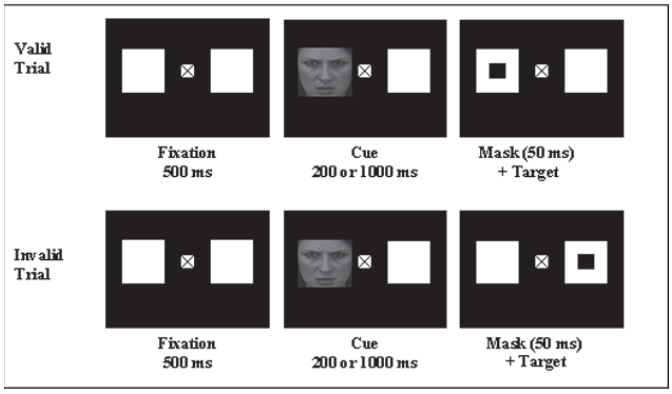
Procedure

At the beginning of the experiment (Montero and Léon, 2007), written informed consent of all participants was obtained. Participants first completed the clinical interview. Thereafter, they were instructed to perform the spatial cueing task while seated at +/- 50 cm in front of an IBM-compatible laptop with a 60-HZ, 15-inch colour monitor.

In the spatial cueing task participants were instructed to attend to a central fixation cross and determine as quickly and accurately as possible the location of a target (a black square of 1.1 by 1.1 cm) that appeared on the left or right side of the computer screen by pressing a corresponding left or right keypad (*i.e.* 'q' and 'm') on a standard keyboard. Before the target appeared, a picture of an angry, neutral or happy face was presented. In the present study, the location of the picture cued the spatial location of the target on 50% of the trials (valid trial) and incorrectly cued the location of the target on the other 50% of the trials (invalid trial).

Each trial started with the presentation of a fixation cross in the middle of the screen flanked by 2 white frames (8.5 cm high by 7 cm wide) located on both sides of a black background. These remained on the screen throughout the entire trial. After 500 ms, a pictorial cue was presented for either 1000 or 200 ms, replacing one of the white frames. Next, after a mask of 50 ms, the target appeared. Upon responding the next trial started immediately (see also Figure 1). In order to assure that the subjects' gaze

FIGURE 1. Stimulus presentation on valid and invalid trials.



returned to the centre of the screen at the beginning of each trail, digit trials were randomly introduced. On these trials the fixation cross was replaced by a digit going from 1 up to 4 which had to be reported as quickly as possible by pressing the corresponding number on the numeric keyboard.

Participants first completed 16 practice trials, followed by two blocks of 192 test trials presenting cues for either 200 or 1000 ms. The order of blocks was randomized across subjects. Within practice trials four digit trials were presented, within each test block 12 digit trials were randomly introduced. Pictures of facial affect were presented at random, and neutral, angry and happy faces appeared equally often on the left and right side of the screen. Valid and invalid trails were also presented randomly.

Pictures of Facial Affect were taken from The Karolinska Directed Emotional Faces (KDEF) database (Lundqvist, Flykt, and Öhman, 1998). Before selection, all pictures were adjusted to exclude interference of background stimuli (hair, clothing) and were adjusted to the same size (326 x 326 pixels). A total of 19 neutral, angry and happy faces were selected based on a prior validation study of the KDEF picture set (Goeleven, De Raedt, Leyman, and Verscheure, *in press*). Four neutral, angry and happy faces were presented in the practice phase; the remaining pictures of 15 neutral, angry and happy faces were presented in the test blocks. Inquisit software (De Clercq, Crombez, Roeyers, and Buysse, 2003; Inquisit 1.33, 2001) was used to control experiment presentation and response recording.

At the end of the experiment, all participants filled out the BDI-II, ASRM, STAI-T, IDDL, and MDQ. The study was approved by the local ethics committee and all participants were fully debriefed.

Design

A mixed Analysis of Variance (ANOVA) with group (BD, NC) as a between-subjects factor and cue validity (valid, invalid), cue valence (neutral, angry and happy) and presentation duration (200 and 1000 ms) as within-subjects factors was used on the response latencies. In order to examine our hypotheses, index scores for cue validity, attentional engagement and disengagement were calculated using the following formulas:

- Cue validity: RT invalid cue – RT valid cue (a high score indicates enhanced attention for that cue).
- Attentional Engagement: RT valid/neutral cue – RT valid/emotional cue (a positive score indicates attentional capture by emotional faces).
- Attentional Disengagement: RT invalid/emotional cue – RT invalid/neutral cue (a positive score indicates difficulties to detract attention from emotional faces).

On these index scores, two-tailed *t*-tests were performed to examine our research question within groups and between the depressed bipolar and non-depressed group. The significance level was set at $p \leq 0.05$ for all analyses.

Results

Group characteristics

Demographics of the two participant groups are summarized in Table 1. The two groups did not differ with respect to age ($p > .90$) and education level ($p > .10$). All BD participants were currently taking psychotropic medication. At the time of testing all but one patient were on mood stabilizing medications such as lithium, valproate and carbamazepine. Nine of these patients were also taking antidepressant medication. One patient was only taking antidepressants. The mean duration of the illness from diagnosis in the BD group was 16.50 years with an average history of depressive ($M = 3.86$) and manic episodes ($M = 2.36$). More specifically, two BD participants (14%) reported two previous depressive episodes, the remaining BD participants reported three (7%), four (43%) or more previous depressive episodes (36%). Four BD participants (29%) reported 1 previous manic episode, whereas the remaining participants reported two (29%), three (21%) and four (21%) previous manic episodes.

TABLE 1. Demographic variables for bipolar depressive and control participants.

Variable	*Bipolar disorder (n = 14) M (SD)*	*Normal controls (n = 14) M (SD)*
Age	46.36 (8.21)	46 (7.33)
Gender ratio (Female/Male)	6/8	6/8
Level of education	2.71 (.82)	2.29 (.47)
% currently on psychotropic medication	100%	0%
Beck Depression Inventory (BDI-II)*	30.14 (7.32)	5.79 (3.24)
Altman Self Rating Mania Scale (ASRM)	1.50 (1.40)	.86 (1.29)
State-Trait Anxiety Inventory (STAI- Trait)*	61.46 (11.11)	32.21 (5.03)
Inventory to Diagnose Depression Lifetime (IDDL)*	59.31 (9.58)	3.93 (10.51)
Mood Disorder Questionnaire (MDQ)*	11.69 (1.44)	.21 (.80)
Duration of illness from diagnosis (years)	16.50 (8.39)	-
Number of depressive episodes	3.86 (1.03)	-
Number of manic episodes	2.36 (1.15)	-

Note. Level of education was coded as follows: 1 = did not finish high school, 2 = high school, 3 = master's degree, 4 = advanced degree.

* Means are significantly different at $p < 0.0001$ based on independent t-tests.

By design, significant differences were found between groups on the clinical measures. BD patients scored significantly higher on measures of current and past depression (BDI-II: $t_{(26)} = 11.86$, $p < .001$; IDDL: $t_{(26)} = 14.27$, $p < .001$) than matched controls. The BD patients also had significant higher trait anxiety levels than the non-psychiatric control participants (STAI-T: $t_{(26)} = 8.92$, $p < .001$). Finally, BD patients scored significantly higher on the MDQ, indicating severe past manic symptomatology (MDQ: $t_{(26)} = 25.89$, $p < .001$), but did not differ from the controls in their report of current manic symptoms (ASRM: $t_{(26)} = 1.26$, $p = .22$).

Attentional effects - Preparation of the data

Before analysis of the data, practice trials and digit trials were discarded from analyses. On digit trials, participants made few errors (M = 1.86). Both groups did not differ in terms of errors on digit trials ($t_{(26)}$ = 1.58, p = .13). Second, all trials with errors were omitted. Across groups, few errors were made (1.38%) and erroneous responding did not differ between groups ($t_{(26)}$ = 1.75, p = .09). Next, responses shorter than 200 ms and longer than 750 ms were considered as outliers, reflecting anticipatory and delayed responding, and were also removed from analyses (Koster, Crombez, Van Damme, Verscheure, and De Houwer, 2005; Leyman *et al.,* 2007). Data analyses were performed on a remaining 93.70% of the original data.

Overall effects

A 2 (Presentation duration: 200 ms, 1000 ms) *x* 2 (Cue Validity: valid, invalid) *x* 3 (Valence: angry, neutral, positive) *x* 2 (Group: BD, NC) mixed ANOVA design revealed a marginally significant main effect of Cue Validity ($F_{(1, 26)}$ = 3.57, p = .07, η_p^2 = .12), due to faster responding on valid (M = 436 ms) compared to invalid trails (M = 443 ms). We also could establish a significant two-way interaction between Cue Validity and Group ($F_{(1, 26)}$ = 4.79, p < .05, η_p^2 = .16). This two-way interaction can be subsumed under the four-way interaction that was marginally significant ($F_{(2,25)}$ = 2.75, p = .08, η_p^2 = .18). No other effects reached significance. Mean reaction times and standard deviations for this interaction are shown in Table 2. In order to further explore this four-way interaction

TABLE 2. Mean reaction times (in ms) and standard deviations (shown in parentheses) as function of presentation duration, cue valence, trial validity and group.

Presentation duration	*Cue valence*	*Trial validity*	*Bipolar disorder (n = 14) M (SD)*	*Normal controls (n = 14) M (SD)*
200 ms	Anger	Valid	438 (59)	431 (58.40)
		Invalid	455 (60.50)	424 (58)
	Happy	Valid	440 (56.40)	425 (52.30)
		Invalid	456 (65.50)	431 (56.60)
	Neutral	Valid	440 (62.10)	431 (55.20)
		Invalid	448 (60.40)	438 (59.90)
1000 ms	Anger	Valid	442 (78.20)	433 (58.60)
		Invalid	452 (65.60)	431 (55.20)
	Happy	Valid	434 (73.50)	447 (59.40)
		Invalid	453 (63.60)	436 (52.10)
	Neutral	Valid	439 (76.20)	436 (72.90)
		Invalid	460 (69.40)	435 (56.80)

effect, separate Cue Validity (CV) indices for angry, neutral and positive cues and for each Presentation Duration were calculated for each participant group. Next, within each Presentation Duration, we also calculated attentional engagement and disengagement indices for the angry and positive facial expressions.

– 200 ms condition. A 3 (Valence: angry, neutral, positive) *x* 2 (Group: BD, NC) ANOVA with Cue Validity indices as dependent variables revealed a near significant two-way interaction effect ($F_{(2, 25)} = 3.07$, $p = .06$, $\eta_p^2 = .20$). Mean Cue Validity Indices and standard errors for this interaction are presented in Figure 2. Independent *t*-tests indicated that bipolar depressive participants showed a significant larger Cue Validity effect for angry faces compared to the control participants ($M = 16$ ms *versus* $M = -7$ ms; $t_{(26)} = 2.20$, $p < .05$, $d = .81$). No significant differences were found comparing Cue Validity indices for neutral or positive facial expressions between groups (t's < 1, all d's $< .36$). However, comparing Cue Validity indices for angry and neutral faces ($M = 7$ ms) within the bipolar depressed group, no significant differences where found ($t_{(13)} = 1.47$, $p = .17$, $d = .35$). Yet, comparing Cue Validity indices for angry and neutral faces ($M = 7$ ms) within the control group, we did establish a near significant difference ($t_{(13)} = 2.07$, $p = .06$, $d = .51$). Comparing Cue Validity indices for positive and neutral faces within both groups, no significant differences were found (t's < 1.1, d's $< .34$). Next, we investigated differences between participant groups in attentional engagement and disengagement indices for angry and positive faces (see Figure 3). No significant differences were found between participant groups in attentional engagement for positive and negative information (t's < 1, d's $< .24$). However, independent *t*-tests indicated that participant groups differed significantly in attentional disengagement for angry facial expressions ($t_{(26)} = 3.56$, $p < .05$, $d = 1.40$). More specifically, bipolar depressive participants showed significant more difficulties in disengaging attention from angry faces ($M = 7$ ms) as compared to the control group ($M = -14$ ms). Within the bipolar depressive group, mean attentional disengagement for angry faces did not differ significantly from zero, ($t_{(13)} = 1.70$, $p = .11$). Conversely, the negative disengagement score for angry faces within the control group significantly differed from zero ($t_{(13)} = 3.30$, $p < .01$), indicating a faster shifting of attention away from negative material. Independent *t*-tests also indicated a near significant difference between groups in attentional disengagement for positive facial expressions, ($t_{(26)} = 1.96$, $p = .06$, $d = .77$). More specifically, bipolar depressed participants showed a significant larger attentional disengagement score for happy faces ($M = 8$ ms) as compared to the non-psychiatric control group ($M = -7$ ms). However, within both groups mean attentional disengagement scores for positive faces did not differ significantly from zero (BD: $t_{(13)} = 1.40$, $p = .18$; NC: $t_{(13)} = 1.38$, $p = .19$).

FIGURE 2. Mean cue validity indices (RT invalid cue – RT valid cue) and standard errors as function of group and cue valence within the 200 ms presentation duration.

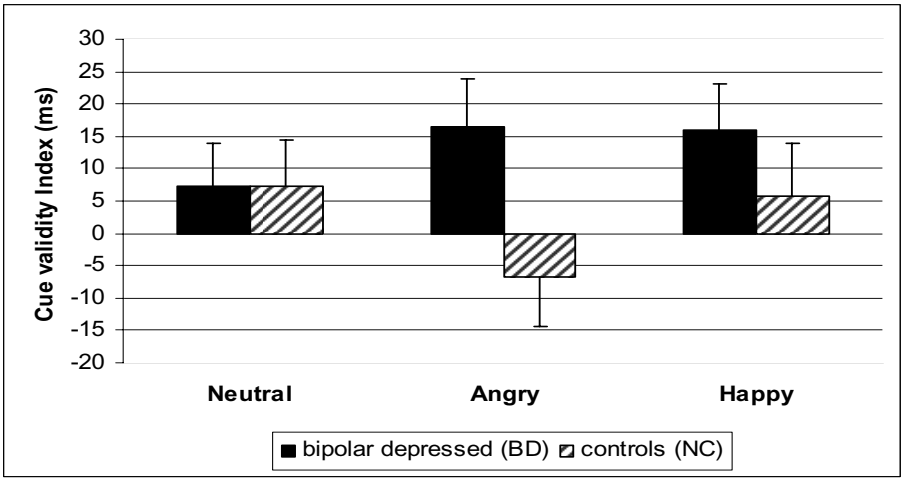
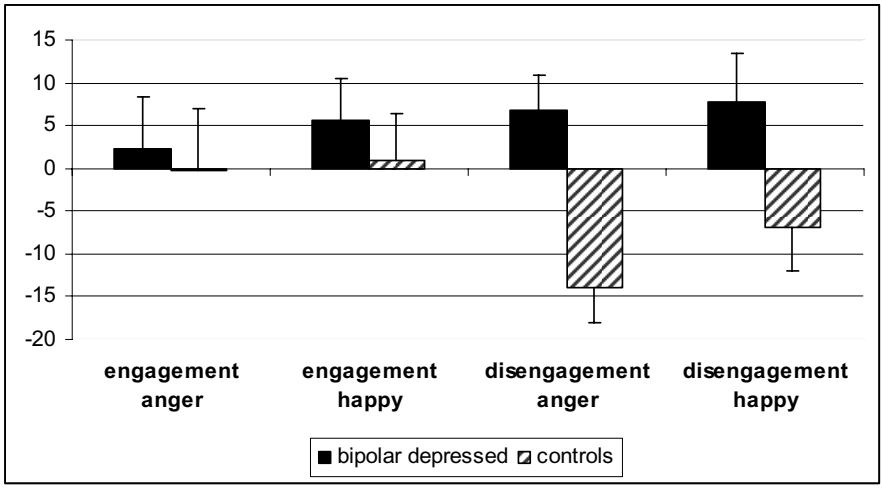


FIGURE 3. Mean attentional engagement, disengagement scores and standard errors as function of group and cue valence within the 200 ms presentation duration.



– 1000 ms condition. The 3 (Valence: angry, neutral, positive) x 2 (Group: BD, NC) ANOVA design with Cue Validity indices as dependent variables revealed no significant main or interaction effects (all F´s < 1, η_p^2's < .07). Comparing attentional engagement and disengagement indices between participant groups also revealed no significant differences (all t´s < 1.5, d's < .55).

Discussion

In the present study the nature and time course of dysfunctional attentional processing of emotional information was examined in a carefully selected sample of currently depressed bipolar I patients using a pictorial spatial cueing task. Findings indicated a differential pattern of responding between bipolar patients and healthy controls within the early stages of information processing. The bipolar depressed group was characterized by enhanced attention for angry faces and experienced more difficulties disengaging attention away from angry and positive facial expressions as compared to healthy controls. Healthy participants were more efficient in detracting their attention away from negative information.

The results found within our patient sample replicate those of Lyon *et al.* (1999), demonstrating the presence of an attentional bias for negative information in bipolar patients during the depressive phase of their illness. Yet, the present study is the first to observe these effects with emotional facial expressions, which provides an interesting link with recent reports of neural disturbances in the brain circuitry involved in affective processing in bipolar disorder (*e.g.* Pavuluri, O'Conner, Harral, and Sweeney, 2007). Moreover, using these ecological valid stimuli, we were able to demonstrate that a bias in attentional processing of emotional stimuli is not merely restricted to mood-congruent, negative information, but also seems to be present for stimuli that are of social relevance. The bias in attentional responding to displays of social disapproval might be in line with a previously reported tendency in bipolar disorder to misinterpret nonverbal facial cues as angry or sad (McClure *et al.,* 2003). Because both biases may be related to the social difficulties bipolar disordered patients experience, future longitudinal research should attempt to clarify their causal relationship.

Apart from differences in the attentional processing of socially disapproving information, the present study also demonstrated differences in disengaging attention away from positive facial expressions when comparing the bipolar depressed patient group with the healthy control participants. These results do not correspond with the mood-congruency hypothesis (Beck, 1976) and are also different from findings in major depressive disorder (*e.g.* Koster, De raedt, Goeleven, Franck, and Crombez, 2005; Leyman *et al.,* 2007). However, findings of attentional biases for negative as well as positive emotional stimuli in bipolar depressed patients have also been reported in two recent studies by Kerr *et al.* (2005) and Malhi *et al.* (2005). Some explanations for these findings are possible.

First, the selected patients in this study were bipolar I patients who all reported history of mania. Therefore, vulnerability factors, such as affective biases for positive material found in previous studies investigating mania (Murphy *et al*., 1999), can remain present during the depressive episode of the illness (Cuellar, Johnson, and Winters, 2005, Di Marzo *et al.,* 2006). Secondly, it might be possible that attentional processing in bipolar depressed patients is characterized by a global impairment of attentional shifting away from emotional information, caused by underlying fronto-subcortical pathway dysfunctions (Pavuluri *et al.,* 2007; Yurgelun-Todd *et al.,* 2000). As already mentioned before, neuroimaging studies have shown neural abnormalities during the processing of emotion-relevant stimuli in bipolar disorder – with reductions in blood flow and glucose metabolism in prefrontal areas and abnormal activation patterns within areas of the

limbic system (Adler, DelBello, and Strakowski, 2006). Although these neural abnormalities have also been demonstrated within major depressive disorder (Drevets *et al.,* 1997), recent fMRI findings have indicated that bipolar depressed patients show even stronger activation patterns in subcortical and ventral prefrontal cortical regions during the processing of all categories of emotional expressions (Lawrence *et al.,* 2004). Moreover, these increased activation patterns in the 'fast' subcortical network were associated with a disconnection in the transfer of information within frontostriatal networks (Lagopoulos and Mahli, 2007), providing a potential explanation for the established deficits in implementing attentional control.

Apart from attentional biases found within the bipolar depressed group, this study also provided evidence for the existence of what is called a 'protective bias' for negative information in healthy individuals. Contrary to the bipolar depressed patients, healthy participants were faster in directing attention away from angry facial expressions compared to neutral faces. Findings of a protective bias in healthy persons have been frequently reported in previous research (Koster, De Raedt *et al.,* 2005; Leyman *et al.,* 2007; McCabe, Gotlib, and Martin, 2000).

To our knowledge, this study is the first to provide information concerning the time course of attentional biases in bipolar affective disorder. In contrast with findings of attentional biases present at long stimulus presentations (1000 ms or more) in major depressive disorder, the present study showed deficits in the early attentional component, whereas information processing at later, elaborative stages did not differ between control and bipolar depressed patients. A dysfunctional attentional processing at the early stages of information processing has frequently been reported within studies examining attentional processing in anxiety disorders, demonstrating automatic allocation of attentional resources to threat-related stimuli (*e.g.,* Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, and van Ijendoorn, 2007). Results found within the present study may to some extend be explained by anxiety symptoms, based on the high correlations found between anxiety and depression scores ($r = .85$, $p < .001$) and a co-morbid diagnosis of anxiety disorders in 9 of the 14 BD patients. These findings confirm the high prevalence of comorbidity of anxiety amongst recurrent bipolar patients as reported in previous studies, specifically when the cast is predominantly depressive (MacKinnon, Zandi, Gershon, Nurnberger, and DePaulo, 2003; Mitchell, Mahli, and Ball, 2004). Therefore, the present study provides important insights into the dysfunctional processing of emotional information in bipolar disorder that can be generalized to more prevalent patient samples, which is not possible when selecting a depressed sample free of co-morbidity.

Although the present study offered evidence of differences in attentional responding between bipolar depressed patients and healthy individuals, some important limitations have to be taken into account. First, results might have been confounded by the impact of psychotropic medication use within the bipolar group. Some authors suggested that mood stabilizers such as lithium may influence cognitive performance (Bearden *et al*., 2001; Honig, Arts, Ponds, and Riedel, 1999; Kocsis *et al.,* 1993), recommending the examination of cognitive performance in a drug-free cohort of patients. However, while medication may cause some degree of cognitive slowing, other researchers have reported

no cognitive deficits as a primary effect of medication treatment (Stip, Dufresne, Lussier, and Yatham, 2000). Moreover, withdrawing medication treatment is ethically unjustifiable and would reduce the generalizability of our results to the general bipolar population.

Another methodological limitation concerns the limited sample size of our patient group, partially due to the stringent selection criteria used in this study. This might have caused some results to be only marginally significant possibly due to little power to detect differences. Thirdly, all patients in this study were recruited from a larger pool of bipolar patients joining support groups. Because our sample consisted of ambulant patients, a larger degree of impairment could arise in hospitalized patients.

Taking these shortcomings into account, the results of the present study should be regarded as an initial demonstration of potential disruptions in the attentional processing of social relevant information in bipolar depressive disorder. Future research should therefore aim at replicating this study within a larger, hospitalized sample of bipolar patients at different stages of their illness, also examining whether attentional biases for emotional facial expressions remain present during remission. Using cross-sectional designs, like the present study, potential vulnerability factors can be proposed, but these designs remain inadequate to answer whether differences in attentional processing are causally related to the development and maintenance of mood disorders. Therefore, future longitudinal research seems indispensable.

To conclude, this study was the first to examine the nature of attentional impairment in a carefully selected sample of depressed bipolar patients during the time course of attentional processing of interpersonal relevant emotional information. This study thereby offers new insights into the current knowledge on attentional biases in bipolar disorder.

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