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BRIEF REPORT

Mood-congruent bias and attention shifts in the different episodes of bipolar disorder

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An "affective" go/no-go task was used in the different episodes of bipolar patients (euthymic, depressed, and manic) to examine (1) the presence of a mood-congruent attentional bias; and (2) the patients' ability to inhibit and invert associations between stimuli and responses through blocks. A group of healthy individuals served as controls. Results revealed a mood-congruent attentional bias: patients in the manic episode processed positive information faster, whereas those in the depressive episode processed negative information faster. In contrast, neither euthymic patients nor healthy individuals showed any mood-congruent biases. Furthermore, there was a shift cost across blocks for healthy individuals, but not for the patients. This may reflect a general impairment at selecting relevant information (e.g., in terms of disability to inhibit and invert associations between stimuli and responses) in bipolar participants, regardless of their episode. This state/trait dissociation in an episodic and chronic disorder such as bipolar disorder is important for its appropriate characterisation.

Keywords: Bipolar disorder; Affective go/no-go task; Mood congruent biases; Attention shift.

Bipolar disorder is a chronic, severe, and highly disabling psychiatric disorder that affects approximately 1% of the world population. These individuals experience, mania, abnormally elevated or irritable mood states and, in most cases, depressed mood, abnormally sad or anhedonic mood states—between these extremes, patients can experience symptom-free states of euthymia (see Belmaker, 2004, for a review). Bipolar disorder is usually characterised in terms of deficits in emotional processing (Harmer, Grayson, & Goodwin, 2002) and impaired executive functioning (Bearden, Hoffman, & Cannon, 2001) that persist even in euthymic states. It has been suggested that emotional dysregulation accounts for these cognitive disturbances by reciprocal

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interactions between cognitive and emotional networks in the brain (Strakowski, DelBello, & Adler, 2005). However, studies examining the cognitive disturbances in bipolar patients in every different episode (euthymic, depressed, and manic) are scarce.

In order to analyse the interplay between mood symptoms and cognition in patients with bipolar disorder, we administered an affective shifting task similar to that employed by Murphy et al. (1999). This is a target-detection task that requires participants to respond to relevant targets (e.g., "happy" words) while inhibiting responses to stimuli of the competing affective category ("sad" words). We must bear in mind that this task can be used not only to measure mood-related attentional bias (i.e., faster "happy" responses in patients with mania; faster "sad" responses in patients with depression), but also to assess the ability to shift attention. This is so because some of the blocks are preceded by another block with the same stimulus-to-response associations (e.g., respond to "happy" words in block $K-1$ and respond to "happy" words in block K), whereas other blocks are preceded by a block with the inverse stimulus-to-response associations (e.g., respond to "sad" words in block $K-1$ and respond to "happy" words in block K).

The first goal of the study was to examine whether patients in the different episodes of bipolar disorder show a mood-congruent attentional bias (i.e., faster responses to "happy" words when patients are in a positive mood [mania], faster responses to "sad" words when patients are in a negative mood [depression], and no attentional bias when patients have not experienced major depression or mania for some time [euthymia]). Murphy et al. (1999) compared manic patients and individuals with a unipolar depressive episode. Murphy et al. found that manic patients were faster to respond to positive stimuli (see Elliot et al., 2004, for a similar finding), while unipolar depressed patients were faster to respond to negative stimuli (see Erickson et al., 2005, for a similar finding with unmedicated patients with unipolar depression). However, Rubinsztein, Michael, Underwood, Tempest, and Sahakian (2006) failed to find a mood congruency effect in bipolar depressed individuals. This latter finding casts some doubts on the robustness of the mood-congruent bias for bipolar depression—note that Rubinsztein et al. acknowledged that some manic symptoms could have influenced their results. Thus, it is important to re-examine the existence of a mood-congruent bias in patients with bipolar disorder.

The second goal of the study was to test the ability to shift/reverse attention focus in patients with bipolar disorder. Switching stimulus-to-response associations typically involves a processing cost: response times are longer and/or participants commit more errors in trials that employ the same stimulus-to-response associations as in previous trials than in trials that alternate the associations (e.g., Allport, Styles, & Hsieh, 1994). For instance, in healthy participants, Wager, Jonides, Smith, and Nichols (2005) reported a switching cost in multiple types of attention shifting tasks. Importantly, previous studies with bipolar patients have shown that set-shifting deficits persist across depressed, manic, and euthymic phases (e.g., using the Wisconsin Card Sorting Test, WCST; see Martínez-Arán et al., 2004). Somewhat surprisingly, previous evidence on shift costs with the affective go/no-go task is not particularly consistent. Murphy et al. (1999) failed to find a shift cost in the response time for healthy individuals (545 vs. 542 ms in shift blocks vs. nonshift blocks respectively), although there were more errors in the shift blocks than in the non-shift blocks (7.4 vs. 5.7%). For patients with unipolar depression, Murphy et al. found a significant shifting cost in the response time (570 vs. 556 ms) and a similar trend occurred in errors (6.1 vs. 5.3%). For patients with mania, they found a paradoxical advantage in the response time of shift blocks over non-shift blocks (555 vs. 577 ms), although the opposite trend was found in errors (14.3 vs. 13.1%). In the Erickson et al. (2005) experiment, both healthy participants and patients with unipolar depression made more errors during shift blocks than nonshift blocks (the error data were not provided though), while there were no signs

of a shifting cost in the response time for healthy participants (503 vs. 506 ms) or patients (518 vs. 512 ms). Finally, Rubinsztein et al. (2006) with bipolar depressed patients, and Rubinsztein, Michael, Paykel, and Sahakian (2000) with euthymic bipolar patients also failed to find a shifting cost in the response time and in the errors—they did not provide the mean response times though. The lack of a shifting cost in previous studies with the affective go/no-go task in healthy individuals could be due to the particularities of the task (i.e., it may not be sensitive to reversals of attention) or because of lack of statistical power. Thus, we believe that it is important to re-examine whether there is a shifting cost in this task for healthy individuals (as in other cognitive tasks that require an attention switch), and whether this shifting cost is reduced for patients with bipolar disorder.

In sum, the current state of the research questions seem to be somewhat fragmented because of potential confoundings like mixed states or residual symptoms that may have affected previous studies. In the present study, we overcame the limitations of previous studies by (1) selecting patients with the same disorder, and by (2) comparing groups of these patients who were in distinct mood states. Therefore, the present experiment attempted: (1) to better characterise the interplay between cognition and emotion (in terms of mood-congruent biases) in individuals with bipolar disorder; (2) to confirm whether there is an impaired ability for inhibition and inversion of stimuli-to-responses associations in the different episodes of this disorder.

METHOD

Participants

Eighty patients with bipolar disorder who were in three current mood states, depressive ($n = 22$), euthymic ($n = 28$), and manic ($n = 30$), participated in the experiment. They were recruited from in-patient wards ($n = 32$) and from Bipolar Disorders Unit for out-patients ($n = 58$) in the Psychiatry Department at the Hospital Universitario y Politécnico La Fe (Valencia, Spain). Two patients, both in the depressive episode, refused to participate. An additional (control) group of 23 healthy individuals were recruited by advertisement in the community. Demographic and clinical details are presented in Table 1.

Table 1. *Demographic and clinical data from the control group and the patients (in the depressive, euthymic, and manic episodes)*

	Control (N = 23)	*Depressed (N = 22)*	*Euthymic (N = 28)*	*Manic (N = 30)*	*p*
% Female	52.2	50.0	32.1	33.3	.31
Age	41.9 (10.7)	44.1 (10.5)	42.7 (8.9)	39.1 (13.7)	.42
SASS	43.8 (6.0)	40.8 (6.8)	40.1 (5.3)	39.5 (6.2)	.07
WAIS-III					
Verbal IQ	108.8 (15.3)	101.0 (8.3)	102.3 (12.3)	101.7 (10.0)	.09
Performance IQ	107.0 (14.3)	104.7 (20.1)	99.3 (18.5)	99.6 (19.0)	.35
BDI	4.5 (3.2)	23.5 (7.4)	4.7 (4.5)	4.7 (2.9)	.00
YMRS	—	1.5 (1.7)	1.8 (2.6)	24.9 (4.7)	.00
No. of episodes	—	6.6 (2.5)	5.8 (5.0)	6.9 (5.6)	.65
Age of onset	—	36.4 (9.5)	29.1 (8.8)	32.0 (14.1)	.08
Medication					
Lithium (% patients)	—	72.7	85.7	70.0	.34
Antiepileptic (%)	—	59.1	50.0	36.7	.26
Antipsychotic (%)	—	31.8	39.3	96.7	.00
Antidepressive (%)	—	63.6	7.1	6.7	.00
Anxiolytic (%)	—	86.4	42.9	90.0	.00

Note: The *p*-values correspond to the omnibus test for the four [three] groups.

This study was approved by the research ethics committee from the Health Research Institute "La Fe" and all participants gave written informed consent prior to participation. Patients were excluded from participation on the basis of the following criteria: history of neurological illness or head injury; major medical disorders that are likely to affect cognition; use of non-psychotropic medication which could influence cognition (e.g., treatment with steroids); concurrent comorbid substance dependence or other psychiatric diagnoses based on DSM-IV criteria (American Psychiatric Association, 1994); and ECT in the previous three months. Healthy controls were excluded if there was evidence of psychiatric history, neurological history, psychoactive substance abuse, or use of medication that might potentially influence cognition.

Every participant was given: (1) the Social Adaptation Self-evaluation Scale (SASS; Bosc, Dubini, & Polin, 1997) to measure social functioning; and (2) the Wechsler Adult Intelligence Scale III (WAIS-III; Wechsler, 1997) to assess global intellectual functioning and differentiate between verbal and no-verbal abilities (Verbal IQ and Performance IQ, respectively). Psychiatrists in the department were asked to refer suitable patients for the study. Patients had to fulfil DSM-IV criteria for bipolar affective disorder and be manic, depressed or euthymic, according to experimental group, at the time of screening. Diagnosis was established using clinical interview and case note review (every patient was reported to have a history of at least one manic episode). DSM-IV diagnoses of all patients were confirmed by the responsible psychiatrist and by a postgraduate clinical psychology intern. Furthermore, to ensure the current mood state and the exclusion of mixed states as well as the absence of affective symptoms in euthymic patients and control participants, two clinical scales were applied: (1) the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), to participate in the study, the score had to be less than 9, except in the depressed group, in which case the score had to be over 18; and (2) the Young Mania Rating Scale (YMRS; Young, Biggs, Ziegler, & Meyer, 1978), depressed and euthymic patients could not obtain a score greater than 6, while manic patients' score had to be over 20.

Materials

The stimuli were 90 words with a positive valence and 90 words with a negative valence taken from the Spanish adaptation of the Affective Norms for English Word (ANEW) database (Redondo, Fraga, Padrón, & Comesaña, 2007). The average valence for the positive and negative words was 8.1 and 1.5, respectively, on a 9-point Likert scale (1 = *Very sad*; 9 = *Very happy*). The presented stimuli were carefully controlled for arousal as well as in other potentially relevant lexical/sublexical factors. Specifically, the two sets of words were matched for arousal (6.1 vs. 6.3 for positive and negative words, $p > .15$). We also controlled for the influence of potentially relevant lexical/sublexical factors such as written word frequency (36.6 vs. 28.6 per million words for positive and negative words, respectively, $p > .25$; Davis & Perea, 2005), the number of orthographic "neighbours" (1.2 vs. 1.3 for positive and negative words, $p > .50$), and the number of letters (7.2 vs. 7.1 for positive and negative words, respectively, $p > .50$). The list of stimuli is available at http://www.uv.es/mperea/words_ANEW.pdf.

Procedure

Participants were tested individually in a quiet room. We used an affective go/no task as previously described by Murphy et al. (1999) except that no feedback was provided (note that error rates were very low in our experiment). Presentation of stimuli and recording of responses were controlled by DMDX software (Forster & Forster, 2003). On each trial, a fixation point (+) was presented for 500 ms in the centre of the screen. Then, the target word (in lowercase) was presented centred, in black on a white background until the participant's response or until 2,500 ms had elapsed. The inter-trial interval was 1.5 s. The task comprises two practice blocks followed by eight test blocks of 18 stimuli each (nine Positive

[P] words and nine Negative [N] words). Before each block, either positive or negative words were specified as targets. Thus, there were two types of blocks, in the "positive" blocks, participants were asked to respond only to positive words and in the "negative" blocks, participants were asked to respond only to negative words. As in the Murphy et al. (1999) experiment, targets for the 10 blocks were presented in a PPNNPPNNPP or NNPPNNPPNN order. Due to this arrangement, four test blocks are "shift" blocks, where participants must begin responding to stimuli which were distractors and cease responding to stimuli which were targets in the previous block, and four test blocks are "non-shift" blocks, where participants must continue responding to stimuli which were targets and withholding responses to stimuli which were distractors in the previous block. Each participant received a different order of trials. The whole session lasted approximately 15–20 minutes.

RESULTS

Response times greater than 1,500 ms (less than 1% of trials) and incorrect responses were excluded from the latency analysis. The mean response time, proportion of errors, and proportion of omissions are presented in Table 2. Analyses of variance (ANOVAs) based on the participants' mean correct response times, error rates, and omission rates were conducted based on a 4 (Group: depressed, euthymic, manic, control) $\times$ 2 (Target Valence: positive, negative) $\times$ 2 (Shift: shift block, nonshift block). The number of error and omission rates were very small (.04 and .03, respectively)—given the small number of errors and the binomial nature of the categorical data (i.e., proportion of errors), we employed linear mixed effects models using the Laplace approximation to fit the binomial data. The statistical analyses on the error data failed to reveal any significant effects (all ps $> .18$) and were not further considered.

The ANOVA on the latency data revealed a main effect of Group, $F(3, 99) = 3.15$, $\eta^2 = .09$, $p = .028$; this reflected that healthy individuals responded faster than the patients (784 vs. 882 ms, respectively), $F(1, 99) = 5.02$, $\eta^2 = .07$, $p = .03$. More important, the interaction between Target Valence and Group was significant, $F(3, 99) = 4.59$, $\eta^2 = .12$, $p = .005$. This interaction revealed that patients in the depressive episode showed faster response times for negative words than for positive words (927 vs. 957 ms, respectively), $F(1, 21) = 4.92$, $\eta^2 = .19$, $p = .038$, whereas patients in the manic episode showed faster response times for positive words than for negative words

Table 2. *Mean and standard deviation response times (in ms), error rates, and omission rates for the four groups on the affective shifting task*

	Control	*Depressed*	*Euthymic*	*Manic*
Response times				
Positive-shift	798 (225)	948 (207)	818 (150)	861 (195)
Positive-nonshift	767 (195)	965 (229)	811 (148)	849 (163)
Negative-shift	804 (238)	905 (195)	844 (145)	892 (170)
Negative-nonshift	766 (181)	948 (218)	831 (156)	905 (206)
Error rates				
Positive-shift	0.05 (0.12)	0.02 (0.04)	0.04 (0.05)	0.06 (0.08)
Positive-nonshift	0.03 (0.07)	0.06 (0.12)	0.04 (0.07)	0.04 (0.09)
Negative-shift	0.06 (0.11)	0.04 (0.11)	0.04 (0.07)	0.06 (0.10)
Negative-nonshift	0.03 (0.06)	0.02 (0.05)	0.04 (0.06)	0.04 (0.07)
Omission rates				
Positive-shift	0.03 (0.05)	0.04 (0.02)	0.02 (0.05)	0.06 (0.03)
Positive-nonshift	0.00 (0.07)	0.07 (0.10)	0.03 (0.11)	0.02 (0.06)
Negative-shift	0.02 (0.04)	0.04 (0.06)	0.06 (0.10)	0.04 (0.05)
Negative-nonshift	0.01 (0.11)	0.04 (0.05)	0.03 (0.09)	0.03 (0.05)

(855 vs. 899 ms, respectively), $F(1, 29) = 8.17$, $\eta^2 = .22$, $p = .009$. Neither patients in the euthymic phase nor healthy individuals showed a significant effect of Target Valence—patients in the euthymic phase: 818 vs. 838 ms for positive words and negative words, respectively, $F(1, 27) = 2.39$, $\eta^2 = .09$, $p = .13$; healthy individuals: 783 vs. 785 ms, for positive and negative words, respectively, $F < 1$.

The interaction between Shift and Group was significant, $F(3, 99) = 3.39$, $\eta^2 = .09$, $p = .02$. This interaction revealed a sizeable 34 ms effect of shift cost for healthy individuals (shifting block: 801 ms; non-shifting block: 767 ms), $F(1, 21) = 8.01$, $\eta^2 = .27$, $p = .01$, but not for the patients—patients in the manic phase: 877 and 877 ms in the shift and nonshift blocks, respectively, $F < 1$; patients in the euthymic phase: 831 and 821 ms, in the shift and nonshift blocks, respectively, $F < 1$; patients in the depressive phase: 927 vs. 957 ms in the shift and nonshift blocks, respectively, $F(1, 21) = 2.17$, $\eta^2 = .09$, $p = .16$.

None of the other effects/interactions in the ANOVA were close to significance, all Fs < 1.

DISCUSSION

The present affective go/no-go task experiment has revealed that a mood-congruent attentional bias occurs in the different episodes of the bipolar disorder: patients in the manic phase responded faster to positive information, while patients in the depressive phase responded faster to negative information—note that, similarly to healthy controls, patients in the euthymic phase did not show a mood-congruent bias. Thus, these data extend the findings of Murphy et al. (1999) within a single disorder: type I bipolar disorder. Furthermore, the experiment revealed that the ability to inhibit and invert stimulus-to-responses associations was impaired in the patients, independently of their episode. Specifically, we found a significant shift cost within healthy controls relative to patients, but not within the three groups of bipolar patients. This finding clearly suggests the existence of a deficit in cognitive flexibility—or more specifically a deficit in the ability to inhibit and invert the response across blocks. Finally, the present experiment is a demonstration that a shifting cost can be obtained (with healthy individuals) in an affective go/no-go task (i.e., this task can be used in future studies to examine set-shifting costs).

As in any empirical study, some potential weaknesses of our study merit comment. First, all patients with bipolar disorder in the present study—including those in a euthymic state—were medicated. This may explain why the response times of the patients were, on average, greater than those of the healthy individuals. Nonetheless, leaving aside that there is evidence showing that the mood congruency effect occurs in the same degree for medicated and unmedicated patients (Erickson et al., 2005), the differences in response times between patients and controls cannot explain alone the mood congruency effect, or the differential shifting cost between patients and healthy participants. Second, as a reviewer suggested, it could be argued that the lack of a significant shift-cost effect for the patients could have been due to the fact that the bipolar groups were somewhat heterogeneous (e.g., in terms of medication or disorder severity). However, post hoc analyses on the relationship between the magnitude of shift cost (and the magnitude of the mood-congruent effect) and the dose/type of medication failed to obtain any clear trends—we acknowledge, however, that one should be cautious at interpreting this null effect. Third, even though the employed design (which mimicked the one employed by Murphy et al., 1999) was powerful enough to detect an interaction between mood and valence, and between mood and shift, a more powerful design (e.g., using longer blocks and a greater emphasis on speed) may be necessary to capture the subtleties of attentional effects in bipolar patients. And fourth, in future studies, it may be important to examine in greater detail the intricacies of executive functioning involved in set-shifting with the go/no-go task, and how it relates with a validated test for detecting executive dysfunction, such as the WCST. Indeed, there is empirical evidence that shows mood congruency

effects using mood induction with healthy individuals (e.g., Roiser et al., 2009). Importantly, Roiser et al. also found that mood induction seems to be more effective in individuals with bipolar disorders than healthy controls. Clearly, the study of the differences in top-down control of emotion over attention is an important issue for further research.

What are the implications of the present findings? It has been suggested that cognitive biases play a crucial role in the development, maintenance, and/or remission of affective psychopathology (Clark, Beck, & Alford, 1999). On the one hand, recent work on cognitive bias modification has demonstrated that attentional biases in depression can be trained and this training leads to changes in mood and reduces reactivity to stressful events (MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002; Wadlinger & Isaacowitz, 2008). However, unlike other affective disorders, research on attention biases in bipolar disorder remains scarce. On the other hand, the ability to invert the focus of attention can be a relevant factor to improve executive function in bipolar patients. In this sense, Siegle, Ghinassi, and Thase (2007) have demonstrated that a neurobehavioural "cognitive control training" reduces both physiological mechanisms underlying depression and depressive symptomatology. This is also an important issue for further research with bipolar patients.

To sum up, the present study demonstrated that bipolar patients showed different attentional biases depending on their clinical state, while specific executive deficits (defined as the ability to inhibit and invert the response across blocks) persisted even in asymptomatic patients. This state/trait dissociation in an episodic and chronic disorder such as bipolar disorder is important for an appropriate characterisation of the disorder. Future efforts should be directed toward increasing the translation of basic research into the clinic (e.g., via new treatments which focus on executive function). Our findings provide clear evidence in favour of a mood-congruent bias for individuals with bipolar disorder—note that previous studies did not control for the different affective symptoms in each episode (e.g., Rubinsztein et al., 2006). This finding is consistent with the claim that emotion exerts significant top-down control over attention. Furthermore, our findings on shifting costs are consistent with previous evidence with other tasks (e.g., Martínez-Arán et al., 2004) and reveal that the disability to shift stimulus-to-responses associations may represent an inherent phenotype in mood disorders.

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