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# Increased affective reactivity to neutral stimuli and decreased maintenance of affective responses in bipolar disorder

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## ABSTRACT

**Background:** Affective dysregulation is a core feature of bipolar disorder (BD) and a significant predictor of clinical and functional outcome. Affective dysregulation can arise from abnormalities in multiple processes. This study addresses the knowledge gap regarding the precise nature of the processes that may be dysregulated in BD and their relationship to the clinical expression of the disorder.

**Methods:** Patients with BD ( $n = 45$ ) who were either in remission or in a depressive or manic state and healthy individuals ( $n = 101$ ) were compared in terms of the intensity, duration and physiological response (measured using inter-beat intervals and skin conductance) to affective and neutral pictures during passive viewing and during experiential suppression.

**Results:** Compared to healthy individuals, patients with BD evidenced increased affective reactivity to neutral pictures and reduced maintenance of subjective affective responses to all pictures. This pattern was present irrespective of clinical state but was more pronounced in symptomatic patients, regardless of polarity. Patients, regardless of symptomatic status, were comparable to healthy individuals in terms of physiological arousal and voluntary control of affective responses.

**Conclusion:** Our study demonstrates that increased affective reactivity to neutral stimuli and decreased maintenance of affective responses are key dimensions of affective dysregulation in BD.

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## 1. Introduction

Affective dysregulation is considered a core feature of psychiatric disorders and a significant predictor of psychiatric morbidity in the general population [9,54]. Affective dysregulation can arise from abnormalities in (i) affective intensity, (ii) affective reactivity to environmental cues, (iii) maintenance of affective response, (iv) physiological arousal, and (v) voluntary control of affect [42,61].

The present study focuses on affective dysregulation in the context of bipolar disorder (BD). BD typically presents with episodes of abnormal mood, dominated by manic or depressive symptoms, and variable inter-episode remission. A significant proportion of patients experience mixed episodes characterized by the co-existence and rapid alterations of manic and depressive states [66]. BD is associated with substantial functional impairment [55],

which has been most convincingly linked to inter-episode affective dysregulation [25,53,65]. Moreover, affective dysregulation has emerged as a significant predictor of syndromal conversion to BD [3]. Affective dysregulation is therefore a core feature of the disorder and a significant prognostic predictor.

Despite general agreement that affective dysregulation is present in BD, information about the precise nature of the processes implicated is limited and at times inconsistent. For example, some studies report increased affective intensity in BD only in response to positive [30], or negative [35] or neutral [26,51] stimuli. Others report increased affective intensity for both positive and negative stimuli [25,36] or no abnormalities [41,47]. With regards to affective reactivity, patients show increased reactivity to negative stimuli in ecological studies [32,35] and to neutral stimuli in experimental studies [26,51,62]. There is also evidence of rapid affective shifts (lability) in BD, which suggests that affective responses are likely to be shorter in patients compared to healthy individuals [36,65]. With regards to physiological arousal in BD, it may be increased in symptomatic but not in remitted patients [16,26,30,47]. Finally, voluntary control of affective responses in remitted patients with BD

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is described as more effortful [31–33] but similar to that of the general population [67].

In sum, previous studies in BD demonstrate abnormalities in different dimensions of affective regulation. There is however insufficient information regarding the processes involved and particularly how they relate to each other and to the clinical symptoms of BD.

The aim of the present study was to conduct a multidimensional examination of affective dysregulation in patients who were either in remission or in a depressive or manic state. Patients ( $n = 45$ ) and healthy individuals ( $n = 101$ ) were compared in terms of the intensity, duration and physiological arousal in response to positive, negative and neutral pictures during passive viewing and during experiential suppression. Our hypotheses were that patients would show abnormalities in multiple dimensions of affective dysregulation, and that the degree of deviance would increase with the severity of affective symptoms.

## 2. Methods

### 2.1. Participants

Patients were recruited through local outpatient clinics and assessed via personal interview to confirm their diagnosis using the patient version of the Structured Clinical Interview (SCID) for Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) Axis I disorders [18]. The level of psychopathology was assessed with the Hamilton Depression Rating Scale (HDRS) [34] and the Young Mania Rating Scale (YMRS) [69]. They were included if they:

- fulfilled diagnostic criteria DSM-IV-TR criteria for BD;
- had been on the same medication regime for at least one month prior to assessment;
- did not have any medical, neurological or cardiovascular problems;
- did not have concurrent or previous alcohol or substance abuse or dependence as defined by the DSM-IV-TR;
- their total HDRS and YMRS scores were respectively below 18 and 21 to avoid recruiting highly symptomatic patients that may not have been able to engage in the tasks.

Following their assessment, patients were divided in three groups according to symptomatic status. Patients were considered:

- remitted if their HDRS and YMRS scores were below 7;
- moderately depressed if their HDRS score was between 14 and 18 and their YMRS score was below 10;
- moderately manic if their YMRS score was between 15 and 21 and their HDRS score was below 10.

Normal comparison data derived from a cohort of 101 healthy individuals, aged 25–65 years, who had been recruited for the purpose of examining the effect of experiential suppression during affective picture presentation in a healthy community sample [48]. In this study, we found that experiential suppression was associated with decreased duration of the emotional response and reduced autonomic reactivity, independent of age, picture valence, personality traits, hedonic capacity, and anxiety [48]. Healthy individuals were recruited from the local community through advertisements and assessed with the non-patient version of the SCID [19]. They were excluded if they had:

- lifetime history of Axis I disorder or substance abuse as defined by the DSM-IV-TR;

- regularly prescribed medication excluding contraceptives;
- concurrent medical or neurological conditions or history of head injury;
- family history of hereditary central nervous system disorders;
- verbal intelligence quotient (IQ) < 75 based on the vocabulary subscale of Wechsler Adult Intelligence Scale-Revised [68].

The study was approved by the local ethics committee and written informed consent was obtained from all participants.

### 2.2. Experimental design

Patients and healthy individuals were recruited contemporaneously. Data collection for healthy individuals and patients followed exactly the same procedures. Participants were tested individually in a single session that comprised a familiarization phase, and two experimental conditions (passive viewing and experiential suppression). A schematic representation of the experimental conditions is shown in Fig. 1. Participants were told that during the experiment, pictures of emotional content would be presented on the screen and that each picture should be viewed for the entire presentation time. Skin conductance and electrocardiogram (ECG) were recorded throughout the session using SONY CONTACT PSYLAB Stand Alone Monitor unit ([www.psyllab.com](http://www.psyllab.com)) programmed to be compatible with Visual Basic Software (Visual Basic 6.0). Prior to testing, six pictures (four neutral, one positive, and one negative), not shown later in the experiment, were used to familiarize participants with the procedure. Data from these pictures were not included in the analyses. The State-Trait Anxiety Inventory (STAI) [63] was administered to all participants before and after testing to assess potential group differences induced by the testing process itself.

#### 2.2.1. Affective stimuli

Positive, negative, and neutral pictures ( $n = 108$ ) were selected from the International Affective Picture System (IAPS) on the basis of normative subjective ratings of valence and arousal [46]. Valence ratings above 7 or below 3 were, respectively, used to identify positive and negative pictures while an average valence rating of 5 ( $\pm 0.5$ ) was used for neutral pictures. Regardless of positive or negative valence, pictures were also selected on the basis of high ( $\geq 6$ ) normative arousal ratings (Supplemental Table S1). Positive images depicted adventure scenes (e.g. cliff diving, mountain climbing), negative images portrayed scenes of violence (e.g. aggression, physical brutality, and combat) or threatening figures or weapons (e.g. pointed guns, looming attackers). Neutral pictures showed buildings and household objects. Normative arousal ratings did not differ between negative and positive pictures ( $P > 0.05$ ). To confirm the relevance of the normative valence ratings to this study, we asked all participants to rate all stimuli they had viewed at the end of the experimental procedures (Supplemental Table S1).

#### 2.2.2. Affective intensity

Participants were asked to rate the subjective intensity of their emotional response to each IAPS picture using a bar chart ranging from 1 (minima) to 10 (extreme).

#### 2.2.3. Duration of affective response

Participants were asked to indicate by button press the end of their emotional response to each IAPS picture.

#### 2.2.4. Physiological arousal

**2.2.4.1. Skin conductance.** Skin conductance (SC) was constantly acquired by a SC5 digital amplifier (24 bit resolution) using a constant voltage (0.5 V) method from the index and middle fingers

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