



Mood reactivity to daily events in patients with remitted bipolar disorder

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ABSTRACT

Information about mood reactions to naturally occurring stress in remitted bipolar patients may help elucidate the mechanism by which stressors influence the propensity to manic or depressive relapse in these patients. Using the experience sampling method (ESM), we therefore investigated negative and positive mood states and their reactivity to daily hassles and uplifts in 38 outpatients with remitted bipolar disorder and 38 healthy volunteers. Multilevel regression analyses confirmed that mean levels of negative affect (NA) were higher and positive affect (PA) lower in bipolar patients. Reactivity of NA and PA to hassles and uplifts in bipolar patients was similar to controls and was unrelated to the number of previous episodes. Bipolar patients with subsyndromal depressive symptoms, however, showed particularly large NA responses to daily hassles, which they also rated as more stressful. Subsyndromal depressive symptoms in patients with remitted bipolar disorder thus appear to increase sensitivity to everyday stressors.

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1. Introduction

Bipolar disorder is characterized by profound, episodic disturbances in mood, and there is now substantial evidence that life events increase the risk of episode recurrence and impede recovery in patients with bipolar disorder (Alloy et al., 2005; Johnson, 2005). Information about mood reactions to naturally occurring stress in the daily life of remitted bipolar patients may help elucidate the mechanism through which stressors are linked with symptoms, and can be useful in developing interventions aimed at preventing relapse. Surprisingly little, however, is known about the dynamics of mood in daily life situations during either acute phases or periods of remission (Johnson et al., 2007). The present study was designed to provide a detailed description of mood regulation in patients with remitted bipolar disorder in comparison to a healthy control group. We used an intensive sampling procedure, the experience sampling method (ESM) (Csikszentmihalyi and Larson, 1987; de Vries, 1992), to assess daily events and mood states as close as possible to their time and place of occurrence. In combination with appropriate statistical methods, such daily process designs make it possible to link mood fluctuations to daily experiences and contexts (Marco and Suls, 1993; van Eck et al., 1998; Bolger et al., 2003). Frequently repeated self-assessments may also be less prone to recall biases than retrospective end-of-day diary reports (Eckenrode and Bolger, 1995). ESM has

proved to be a particularly useful tool in the study of psychiatric disorders (Johnson et al., 2009; Myin-Germeys et al., 2009).

Research on the structure of self-rated mood has revealed the presence of two major and fairly independent dimensions: negative affect (NA) and positive affect (PA) (Watson and Tellegen, 1985). High NA subsumes a range of negative mood states such as anger, fear, and sadness. High PA reflects pleasurable engagement with the environment: for example, feelings of enthusiasm, self-confidence, and happiness. The presence of elevated NA in patients with remitted bipolar disorder is supported by studies that reported a higher level of neuroticism compared to healthy controls (Hirschfeld et al., 1986; Solomon et al., 1996), as NA is strongly correlated with neuroticism (Watson, 2000). An ESM study in a nonclinical population of young adults also reported that individuals with cyclothymia as well as individuals with intermittent depression have higher levels of negative affect than subjects with no affective disorder (Lovejoy and Steuerwald, 1995). Levels of PA in cyclothymic individuals were significantly higher than in individual with intermittent depression, but similar to the control subjects. In a recent study, patients with remitted bipolar disorder reported lower scores on various items of a positive mood scale than healthy controls (Gruber et al., 2009). Taken together, these studies consistently show that bipolar patients have higher levels of NA than healthy controls, whereas findings on PA levels are mixed.

Several theories predict that patients with bipolar disorder and healthy controls differ in their mood responses to both negative and positive environmental stimuli. According to the kindling and behavioral sensitization hypothesis of recurrent affective disorders

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(Post, 1992), individuals with bipolar disorder become sensitized to psychosocial stress over the course of early affective episodes and subsequently display heightened affective and neurobiological responses to even minor stressors. An analogous cognitive process could take place if dysfunctional cognitive patterns are reactivated by psychosocial stress during subsyndromal dysphoric states in patients with previous depressive episodes (Segal et al., 1996). On the basis of these theories it is to be expected that remitted bipolar patients show larger NA reactivity to negative daily events than healthy controls, especially in patients with many previous episodes or current depressive symptoms. Nonetheless, previous studies have found no evidence of increased negative mood reactivity in remitted bipolar patients except when depressive symptoms are present (Johnson et al., 2007). For example, two recent studies demonstrated that patients with bipolar disorder in remission and healthy control subjects did not differ in their affective reactions to standardized laboratory stressors (Ruggero and Johnson, 2006; Cuellar et al., 2009). These findings are in line with the results of an earlier study on behavioral and mood changes following naturally occurring daily stressors in relation to affective symptoms in a nonclinical sample of young adults (Goplerud and Depue, 1985). Compared to non-symptomatic controls, cyclothymic and dysthymic participants had similar negative mood responses to stressful events, although they did show delayed mood recovery.

An additional hypothesis follows from neurobehavioral theory of affective and behavioural response tendencies. As originally formulated by Gray (1973), the behavioral activation system (BAS) regulates approach behavior and PA in response to cues of potential rewards. In bipolar disorder, the BAS is thought to be inadequately regulated, making the individual vulnerable to extreme states of BAS activity: deficient in the presence of depressive symptoms and excessively high in the presence of hypomanic/manic symptoms (Depue and Iacono, 1989; Depue and Zald, 1993). Studies using a self-report BAS scale have provided some support for this theory (Meyer et al., 2001; Kasch et al., 2002). Further support comes from studies indicating that people with remitted bipolar disorder and those at risk for bipolar disorder show elevated reactivity of PA to specific positive stimuli involving potential reward (Johnson et al., 2007). Other studies, however, demonstrated elevated mood reactivity to several kinds of positive and even neutral stimuli in these groups (Gruber et al., 2008; M'Bailara et al., 2009).

Extending previous research to a clinical sample of patients with remitted bipolar sampled during their normal daily lives, the current study assessed mood states in terms of NA and PA dimensions and measured responses of these dimensions to both negative and positive daily events. In addition, we explored the contributions of selected clinical characteristics in the bipolar group to individual differences in mood reactivity. Bipolar disorder is known to be an extremely heterogeneous diagnostic category, with pronounced inter- and intra-individual variability in functioning and symptom expression, also in individuals receiving prophylactic treatment. Although untangling possible sources of individual differences in mood reactivity would require a much larger sample, the current study explores the influences of the number of previous episodes and the severity of subsyndromal symptoms, as these features of the disorder are highly variable and associated with increased risk of episode recurrence (Keller et al., 1992; Coryell et al., 1998; Kessing et al., 1998). We predicted that current subclinical hypomanic symptoms would be associated with increased PA reactivity to positive events, whereas a large number of previous episodes and the presence of current subclinical depressive symptoms would be associated with increased NA reactivity to negative events. Finally we explored whether the effects of bipolar disorder and clinical characteristics on mood reactivity could be explained by differences in how individuals experience events in terms of stressfulness. The appraised stressfulness of daily situations has been shown to influence mood responses

(van Eck et al., 1998; Gunthert et al., 1999). As prior episodes and subclinical depressive symptoms may both reinforce negative cognitive schema and erode confidence in the ability to cope with daily events, they may increase the subjective stressfulness of events. We therefore expected that clinical characteristics might exert their effects on mood responses indirectly, through the appraised stressfulness of events.

2. Methods

2.1. Participants

Thirty-nine bipolar patients were recruited from lithium clinics in Maastricht and Sittard, The Netherlands. The main inclusion criterion was a primary diagnosis of bipolar I or bipolar II disorder, without rapid cycling, as assessed with the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) (First et al., 1996) by a trained research psychiatrist (R.H.). Additional inclusion criteria were age between 18 and 65 years, in a state of partial or full remission for more than 2 months, and under regular treatment including pharmacotherapy in accordance with standard clinical practice for more than 4 months. Because the study also focused on salivary cortisol patterns (reported separately) the following exclusion criteria were applied: substance abuse in the last year, pregnancy, weight loss exceeding 15% in the previous 6 months, endocrine disorders, and insufficient fluency in Dutch. On study entry, 16 patients received monotherapy with lithium; the others used various combinations of psychotropic drugs as follows: lithium ($n=20$), carbamazepine ($n=4$), valproate ($n=2$), antidepressants ($n=4$), neuroleptics ($n=7$) and benzodiazepines ($n=6$). A control group of 39 healthy subjects in the same age range was recruited from available research pools and through a local newspaper advertisement. Additional exclusion criteria for the control group were current use of psychotropic drugs, any personal history of Axis I disorders, and any inpatient treatment for Axis I disorder in a first-degree relatives. One patient and one healthy control were later excluded from the analysis because they failed to meet ESM compliance criteria (see below). The local medical ethics committee approved the protocol, and all participants gave written informed consent.

2.2. Experience sampling procedure and measures

The ESM was used to assess daily events and mood states during everyday activities. In response to signals ("beeps") from a wristwatch, participants completed self-report forms 10 times a day for 6 days, including a weekend. The beeps were programmed to occur between 7:30 a.m. and 10:30 p.m., at semi-random intervals within each 90-min time block. Reports completed within 20 min after the beep were considered valid. Patients completed fewer valid ESM reports than controls (78% versus 87%; Mann-Whitney U test, $P=0.002$). Subjects with fewer than 20 valid responses (one patient and one control) were excluded from the analyses. On average, bipolar patients took somewhat longer to complete their valid ESM reports than control subjects (5:53 min, S.D. = 2:48 min versus 4:34 min, S.D. = 2:00 min.; $P=0.02$, two-tailed t -test).

2.2.1. Event assessments

Participants who responded affirmatively to the ESM question "Did you experience a positive event or situation since the previous beep?" were asked briefly to describe the event in their ESM booklet and to rate the event on several appraisal dimensions, including stressfulness (1 not at all to 7 extremely). These questions were repeated with respect to "a negative event or situation." Although subjects were instructed to report only external events or situations that actually took place in their daily environment in the preceding interval, some event reports clearly referred to internal states (e.g., ruminations about past events or anticipated events, personal health concerns). Following pre-established criteria, the research team identified such internal events by consensus and omitted them from subsequent analyses, to avoid confounding of event and mood measures. In the bipolar group, 3.7% of the event reports referred to internal states, compared to 5.1% in the healthy control group. Altogether, participants reported 1317 external positive events (on 35% of all valid ESM reports) and 618 external negative events (on 16% of all valid ESM reports).

2.2.2. Mood assessments

Momentary mood states were assessed with 17 adjectives rated on seven-point Likert scales (1 not at all, 7 very). We chose to include items typical of pleasantness–unpleasantness as well as activation or arousal dimensions, because these captured clinically relevant aspects of daily mood in bipolar disorder and have previously been used by our research group in different populations (e.g. (Peeters et al., 2003)). Both factor analyses (principal components analysis with oblique rotation) on subject mean scores and within-subject z -scores identified two mood factors. These factors accounted for 74% of the total variance in subject mean scores and 40% of the total variance in within-subject z -scores. Ratings on the items cheerful, enthusiastic, strong, energetic, satisfied, self-assured, happy, and talkative were averaged to form a PA scale. Ratings on the items tense, agitated, edgy, irritated, restless, sad, anxious, distractable, and guilty were averaged to form a negative affect (NA) scale. Pearson's correlations between PA and NA, calculated over all responses using within-subject z -scores, were

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