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Increased rates of events that activate or deactivate the Behavioral Approach System, but not events related to goal attainment, in bipolar spectrum disorders

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Abstract

Research indicates that life events involving goal-attainment and goal-striving trigger hypomania/mania and negative life events trigger bipolar depression. These findings are consistent with the behavioral approach system (BAS) dysregulation model of bipolar disorders, which suggests that individuals with bipolar disorders are hypersensitive to cues signaling opportunity for reward and cues signaling failure and loss of rewards. However, no studies to date have investigated whether individuals with bipolar spectrum disorders experience increased rates of these BAS-relevant life events, which would place them at double-risk for developing bipolar episodes. The present study found that individuals with bipolar II disorder and cyclothymia experience increased rates of BAS-activating and BAS-deactivating, but not Goal-attainment, life events. Finally, for bipolar spectrum individuals only, BAS-activating events predicted BAS-deactivating events' rates.

Keywords

Behavioral Approach System; Bipolar Disorder; Life Events

Introduction

It has been hypothesized that what is inherited in bipolar spectrum disorders¹ are "... affectively dysregulated temperaments and that the progression to full-blown bipolar illness is due to environment" (Akiskal, 1986). Recent reviews emphasize the importance of psychosocial factors in predicting the bipolar course (e.g., Miklowitz & Johnson, 2006). Thus, a search for life events that trigger relapse into hypomania/mania and bipolar depression has received increased attention (for a review see Alloy et al., 2005). Both negative and positive life events, especially behavioral approach system (BAS)-relevant life events, have been found to predict hypomanic/manic episode relapse and symptom increase. For example, events involving goal-attainment, but not positive life events in general, predicted increases in manic symptoms in a two-month prospective period for individuals with bipolar I disorder (Johnson et al., 2000). Goal-attainment events also predicted prospective changes in manic symptoms over 27 months among bipolar I disorder individuals (Johnson et al., 2008). Furthermore, in individuals with bipolar II disorder and

¹In this article, the term bipolar spectrum disorders refers to bipolar I disorder, bipolar II disorder, bipolar disorder NOS, and cyclothymia. For a criticism of the bipolar spectrum concept see Patten and Paris (2008).

cyclothymia, a goal-striving event related to a pertinent goal (i.e., final examination period for university students) predicted onset of hypomanic, but not depressive, episodes (Nusslock et al., 2007). Similarly, hypomanic personality traits predicted greater goal pursuit in everyday life among healthy adolescents (Krumm-Merabet & Meyer, 2005).

Empirical evidence also supports, although not unequivocally, that negative life events trigger relapse into bipolar depression (see for review Alloy et al., 2005). For example, studies have found negative life events to predict onset of, and prolonged recovery from, bipolar depression episodes (e.g., Hammen & Gitlin, 1997; Johnson & Miller, 1997; Kulhara et al., 1999; Swendsen et al., 1995). Data on the relationship between negative life events and mania/hypomania is less consistent. Whereas some studies found support for negative life events predicting increased hypomanic symptoms in bipolar II disorder and cyclothymia, especially in interaction with negative cognitive style (e.g., Reilly-Harrington et al., 1999), others have not (e.g., Johnson et al., 2008).

Overall, these findings are consistent with the behavioral approach system (BAS) dysregulation model of bipolar disorders (Urošević et al., 2008; Alloy et al., 2009). The BAS dysregulation model postulates that individuals with bipolar spectrum disorders are hyperresponsive to reward-relevant environmental cues. Accordingly, in individuals with bipolar disorders, life events involving opportunities to obtain goals/rewards and opportunities to remove obstacles to goals/rewards (i.e., BAS-activating events) lead to BAS hyperactivation, which is reflected in hypomania/mania. In other words, only a subtype of positive life events involving goal-striving is defined as BAS-activating, which is consistent with prior research (Johnson et al., 2000; Nusslock et al., 2007). Also, the BAS dysregulation model proposes that only negative life events involving obstacles to rewards/goals with opportunity for active coping trigger mania/hypomania and are BAS-activating (Urošević et al., 2008). In other words, frustrative non-reward without opportunity for active coping will lead to BAS deactivation, as suggested by a recent study (Wright, Lam, & Brown, 2009). Moreover, the BAS dysregulation model postulates that negative life events that involve failure to obtain or loss of goals/rewards (i.e., BAS-deactivating events) lead to cessation of approach behaviors and trigger depression in individuals with bipolar disorders (Urošević et al., 2008). It is less clear whether the actual attainment of goals/rewards is BAS-activating or BAS-deactivating (i.e., whether it leads to satiation and cessation of approach or to increased motivation to pursue other rewards).

In addition to research on BAS-relevant events and bipolar symptomatology, studies have found individuals with bipolar disorders to exhibit BAS hypersensitivity on self-report measures and in experimental paradigms. Individuals with bipolar I disorder (Meyer, Johnson, & Winters, 2001; Salavert et al., 2007), with bipolar II disorder and cyclothymia (Urošević et al., 2010), and individuals prone to bipolar symptoms (Meyer, Johnson, & Carver, 1999) exhibited BAS hypersensitivity on self-report measures. In a laboratory experiment, opportunities for challenging goal-striving (i.e., solving difficult anagrams for money) led to exaggerated approach motivation, as indexed by increased relative left frontal asymmetry assessed by electroencephalography, in bipolar II disorder and cyclothymia (Harmon-Jones et al., 2008). Furthermore, proneness to hypomania has been linked to greater left frontal asymmetry in response to experimentally manipulated obstacles to goals with potential for active coping (Harmon-Jones et al., 2002). Finally, BAS hypersensitivity also predicted prospective bipolar episodes and history of bipolar diagnoses (Alloy et al., 2006; Alloy et al., 2008; Meyer et al., 2001).

In summary, research suggests that individuals with bipolar disorders exhibit both BAS hypersensitivity and an increase in bipolar symptomatology in response to BAS-relevant life events. However, no study to date has explored whether individuals with bipolar disorders

also experience greater rates of BAS-relevant life events compared to individuals with no psychopathology. This is an important clinical and empirical question. Clinically, if individuals with bipolar disorders are both hypersensitive to BAS-relevant life events and experience greater rates of these events, then they will be at increased risk for relapse of manic/hypomanic and depressive episodes. Empirically, increased rates of BAS-relevant events would suggest a potential stress-generation mechanism in bipolar disorders, akin to the one hypothesized in unipolar depression (Hammen, 1991), with significant implications for the mechanisms of psychopathology in bipolar disorder. The present study tests this empirical question by comparing rates of BAS-activating, BAS-deactivating, and goal-attainment life events for individuals with bipolar II disorder and cyclothymia and individuals without psychopathology.

Method

Participants

Participants were drawn from the Wisconsin sample of the Longitudinal Investigation of Bipolar Spectrum Disorders (LIBS) Project. In the LIBS Project, participants were selected by a two-stage screening procedure. In Stage I, university students completed the General Behavior Inventory (GBI; Depue, Krauss, Spont, & Arbisi, 1989), in order to identify individuals prone to bipolar symptomatology. Participants who met the GBI cut off criteria: 1) for high risk for bipolar spectrum ($n = 658$), or 2) for the absence of affective psychopathology (i.e., low-risk, $n = 388$), as specified by Depue et al. (1989), were identified.

In Stage II, these participants were administered an expanded Schedule for Affective Disorders and Schizophrenia--Lifetime diagnostic interview (exp-SADS-L; Endicott & Spitzer, 1978)². The exp-SADS-L interviews were conducted by seven extensively trained interviewers (i.e., completed over 200 hours of didactics, training on case vignettes and audiotaped interviews, role-playing, and regular exams with feedback) with least a bachelor's degree. Diagnostic interviewers were blind to participants' Stage I group status. Consensus DSM-IV-TR and RDC diagnoses were determined by a 3-tiered standardized diagnostic review procedure involving senior diagnosticians and an expert diagnostic consultant, Dr. Alan Gruenberg. Participants were excluded from the longitudinal study due to: a) bipolar I diagnosis at the Stage II since the project investigated "soft" bipolar conditions; b) history of a primary psychiatric disorder other than bipolar disorders; and c) bipolar disorder secondary to a physical illness (e.g., endocrinopathies)³. An interrater reliability, based on 105 jointly rated exp-SADS-L interviews, yielded kappas $\geq .96$ for bipolar spectrum diagnoses.

Based on this screening procedure, two groups of individuals were identified and invited to participate in the longitudinal project: 1) individuals who were high risk for bipolar spectrum on the GBI and met DSM-IV and/or RDC criteria for cyclothymia or bipolar II disorder (i.e., the bipolar spectrum group); and 2) individuals who were low-risk on the GBI and met DSM-IV and/or RDC criteria for absence of psychopathology (i.e., control group; for additional information on the project sample see Alloy et al. 2008). Of the GBI high-risk group, 22.5% met criteria for bipolar spectrum participants; of the GBI low-risk group, 46.6% met criteria for control participants. Of individuals who met the Stage I and Stage II

²The exp-SADS-L interview was modified to derive both DSM-IV-TR (2000) and Research Diagnostic Criteria (RDC; Spitzer, Endicott, & Robins, 1978) diagnoses. For detailed information on the GBI and the expanded-SADS-L, please see Depue et al. (1989) and Nusslock et al. (2007) respectively.

³However, for the bipolar spectrum group, individuals with non-primary comorbid disorder (e.g., alcohol abuse) and, for the control group, individuals with only Specific Phobia diagnoses were included.

criteria, 66.9% agreed to participate in the longitudinal project and did not differ on demographics from the individuals not recruited.

The present sample consisted of 115 participants (55 men, 60 women) with complete data for the present analyses—55 in the bipolar spectrum group (13 cyclothymia and 42 bipolar II disorder) and 60 in the control group. At the time of the present study, participants were on average 24.6 years of age ($SD = 1.70$) and predominantly Caucasian (89.6%; 5.2% Asian; 3.5% Hispanic; and 1.7% African-American).

Procedure

Life events were assessed using the Life Events Scale (LES; Francis-Raniere, Alloy, & Abramson, 2006), and a semi-structured interview, the Life Events Interview (LEI; Francis-Raniere et al., 2006) for a mean interval of 142.85 days ($SD = 25.48$; ranging from 69 to 168 days). Following the LEI, each participant was assessed using the expanded SADS—Change (SADS-C; Spitzer & Endicott, 1978) for presence of bipolar episodes by an interviewer blind to the participant's LES and LEI information. The present study was conducted at one of the regularly scheduled prospective assessments for the larger longitudinal project. Participants were at least 3.5 years into their longitudinal follow-up at the time these data were collected. In order to improve accuracy of recall, participants were provided with printed calendars containing anchor dates (e.g., national holidays, community events).

Measures

Life Events Scale (LES; Francis-Raniere et al., 2006)—The LES assesses 193 a priori defined life event categories spanning various domains (e.g., employment, academic, romantic relationships, family). The LES assessed both positive and negative events, minor hassles and major life events, as well as chronic situations. Finally, the 193-item LES included a wide array of BAS-activating events, like events involving goal-striving (e.g., working on a significant work/school/hobby project), or goal obstruction (e.g., blocked in pursuit of a goal by bureaucracy/red tape).

Life Events Interview (LEI; Francis-Raniere et al., 2006)—Researchers have promoted the interview-based approach to the assessment of life events in mood disorders (e.g., Monroe & Hadjiyannakis, 2002; Monroe & Roberts, 1990). Consistently, the LEI was designed to complement the LES assessment. The LEI is accompanied by the Event Specific Criteria and Probes manual (ESCP) that provides clear definitions for the event categories and probes for determining whether the participant's reported events meet the criteria. Interviewers were extensively trained (e.g., review of audio-taped interviews, live observation, role-playing) and tested on their knowledge of the ESCP manual (i.e., written exam and mock interview). Interviewers made final decisions about each participant's event categorization according to the ESCP manual and regular consultations with the senior interviewers, which were recorded on the Life Event Interview Rating Form, one per each event category for each participant. The LEI standardized event definitions and procedures reduced inaccuracies in determination of timing of events, as well as double-reporting and omission of events (see Francis-Raniere et al., 2006 for reliability and other information about the LES and LEI).

BAS Activation, BAS Deactivation, and Goal-Attainment ratings—Each of the LES event categories was a priori rated by three authors (LYA, SU, & RN) on three dimensions—BAS Activation (i.e., the extent the life event category involves goal-striving, opportunity to obtain goals/rewards, or opportunity to remove obstacles to these goals/rewards), BAS Deactivation (i.e., the extent the life event category triggers cessation of

approach and/or involves failure to obtain rewards/goals), and Goal Attainment (i.e., the extent the life event category involves actually obtaining rewards/goals), using a 4-point Likert scale (with anchors of not at all, somewhat, very, and extremely). Only life event categories deemed to not involve Goal Attainment to any extent were rated independently on BAS Activation and BAS Deactivation dimensions. Three independent raters had good reliability on all three dimensions' ratings—Cronbach's alpha = .79 for BAS Activation, .94 for BAS Deactivation, and .91 for Goal Attainment. Furthermore, any discrepancies in ratings of “0” (i.e., “not at all”) on the Goal-attainment dimension were resolved by consensus and, in ambiguous situations, erred towards inclusion in the Goal-attainment category. Consequently, the Goal-attainment events category consisted of a unique set of the LES life events categories and was separate from BAS-relevant life event categories. Finally, each life event category had three scores averaged across three raters indicating intensity on BAS Activation, BAS Deactivation, and Goal Attainment dimensions.

Average daily sums of life events were calculated for each participant in the study, one for each group of life events—BAS-activating, BAS-deactivating, and Goal-attainment events. All three of the dependent variables were weighted by severity on relevant dimensions (e.g., average daily sum of BAS-activating events was calculated by first adding intensity ratings on the BAS-activation dimension for each life event experienced by a participant and then dividing by that participant's interval length in days). Average daily rates were considered a better measure than a total sum of relevant life event ratings because they accounted for individual differences in the assessment interval length⁴.

The expanded SADS-C (Endicott & Spitzer, 1978) was expanded in a similar manner as the SADS-L. Interviewers completed the above-described diagnostic training and were blind to the SADS-L information. An interrater correlation was computed for each bipolar symptom, yielding an average interrater correlation of .93 for both depressive and hypomanic symptoms. Based on the expanded SADS-C, DSM-IV diagnoses of major depressive episodes, both subsyndromal (i.e., all criteria met but duration only one week, or all DSM-IV criteria met but only four depressive symptoms) and syndromal, and of syndromal hypomanic episodes were made. During the assessment interval, 32.7% of bipolar spectrum participants experienced at least one major depressive episode, whereas 83.6% experienced at least one hypomanic episode.

Results

Table 1 summarizes descriptive data for BAS-activating, BAS-deactivating and Goal-attainment events. Two separate hierarchical regression analyses were conducted with BAS-activating events as the outcome variable. In one regression analysis, diagnostic group (control vs. bipolar spectrum) was entered in Step 1, BAS-deactivating events in Step 2, and a cross-product interaction term of Diagnostic Group $\times$ BAS-deactivating Events in Step 3. In the second regression analysis, Goal-attainment events were substituted for BAS-deactivating events in Step 2 and the cross-product term in Step 3 was Diagnostic Group $\times$ Goal-attainment Events. There was a significant effect of diagnostic group ($b = .90$, $t = 2.50$, $p = .014$), with bipolar spectrum participants exhibiting higher rates of BAS-activating events. There were significant main effects of BAS-deactivating events ($b = .68$, $t = 11.22$, $p < .001$) and of Goal-attainment events ($b = 1.08$, $t = 2.86$, $p = .005$) on BAS-activating events rates. There were no significant interactions with diagnostic group (p 's $> .40$).

⁴For an approach to deriving life events measures not based on the BAS dysregulation theory, please see Bender et al. (2010), based on data from the Temple University sample of the LIBS project. Bender et al. (2010) examine rates of independent vs. dependent and interpersonal vs. achievement life events and their relationship to bipolar symptoms.

Two analogous hierarchical regression analyses were conducted for BAS-deactivating events as the outcome variable and diagnostic group, BAS-activating or Goal-attainment events, and cross-product interaction terms of diagnostic group with BAS-activating or Goal-attainment events as predictors. There was a significant main effect of diagnostic group ($b = 1.69, t = 4.37, p < .001$), with bipolar spectrum participants exhibiting higher rates of BAS-deactivating events compared to controls. There was also a main effect of BAS-activating events ($b = .78, t = 11.22, p < .001$) on BAS-deactivating events. In addition, there was a significant interaction of Diagnostic Group $\times$ BAS-activating Events, with bipolar participants exhibiting higher rates of BAS-deactivating events for each increase in BAS-activating events ($b = .31, t = 2.27, p = .025$). There were no significant main or interaction effects of Goal-attainment events on BAS-deactivating events (p 's $> .13$).

Two analogous hierarchical regression analyses were conducted with Goal-attainment events as the outcome variable and diagnostic group, BAS-deactivating or BAS-activating events, and cross-product terms of Diagnostic Group $\times$ BAS-deactivating or BAS-activating Events as predictors. There was no significant main effect of diagnostic group ($p = .643$) or significant interactions.

The bipolar spectrum and control groups did not significantly differ in average daily rates of life events overall ($p = 0.48$). Both bipolar spectrum and control individuals experienced approximately one life event every three days. In addition, there were no significant differences ($p = 0.13$) in the mean length of the assessment interval between the bipolar spectrum ($M = 146.64$ days, $SD = 23.97$ days) and control groups ($M = 139.38$ days, $SD = 26.51$ days). In sum, the diagnostic group differences in rates of BAS-activating and BAS-deactivating life events were not due to differences in overall rates of life events or assessment interval length. There were also no significant differences in rates of BAS-deactivating, BAS-activating, or Goal-attainment events, between individuals with bipolar II disorder and individuals with cyclothymia (p 's $> .10$). Repeating the hierarchical regression analyses with only bipolar II disorder vs. control participants yielded the same pattern of results.

Finally, among bipolar spectrum participants, there were no significant differences in rates of BAS-activating, BAS-deactivating, and Goal-attainment events based on the presence vs. absence of major depressive episodes (p 's $> .29$) or presence vs. absence of hypomanic episodes (p 's $> .11$). Rates of all three types of events were not significantly related to percentage of interval days spent in major depressive episode or in hypomanic episode (all p 's $\geq .10$).

Discussion

The present study is the first to investigate and find increased rates of BAS-relevant life events in individuals with bipolar II disorder and cyclothymia compared to individuals with no psychopathology. Prior research has found similar BAS-relevant life events to trigger manic, hypomanic, and depressive episodes (for review see Urošević et al., 2008). Given studies supporting BAS hypersensitivity of bipolar spectrum disorders (e.g., Alloy et al., 2006, 2008; Harmon-Jones et al., 2008; Meyer et al., 2001), it appears that individuals with bipolar spectrum disorders are at double-risk for developing bipolar episodes. They are both hypersensitive to these BAS-relevant environmental cues, to the point of developing bipolar symptoms in response, and they experience higher rates of the BAS-relevant events.

It is less clear whether goal-attainment events (i.e., actually obtaining a reward or goal) are cues for activation of approach towards new rewards/goals or BAS deactivation due to satiation. However, life events involving goal-attainment have been found to predict

increased manic symptoms in bipolar I disorder (Johnson et al., 2000, 2008). The present study shows that individuals with 'soft' bipolar disorders do not experience greater rates of Goal-attainment events, thus, there appears to be no double-risk for development of bipolar symptoms. Future studies are needed to differentiate the effect of goal-attainment from goal-striving (i.e., BAS-activating events) on prospective manic and hypomanic episodes.

In the present study, there were no differences in rates of either type of life events between bipolar spectrum individuals who experienced a depressive or hypomanic episode versus bipolar individuals who did not experience an episode during the assessment interval. This pattern of results suggests that increased rates of BAS-activating and BAS-deactivating events are independent of concurrent clinical state, but additional replications are needed. Also, this finding does not contradict prior research linking BAS-relevant life events to prospective relapse of bipolar episodes. The present study's approach of calculating BAS-relevant life events' average daily rates over multiple months is optimal for measuring trait levels of environmental influences in an individual's life. However, to test the ability of BAS-relevant events to predict bipolar episode relapse, assessment of these events in a discrete time period with prospective follow up is needed (for an example, see Nusslock et al., 2007). Both types of studies provide valuable but distinct types of information about risk for bipolar episode relapse.

Finally, we found a significant interaction of diagnostic group by BAS-activating events' rate on the BAS-deactivating events' rate. In other words, in the bipolar spectrum group, there was a significant increase in rate of BAS-deactivating events for every increase in the rate of BAS-activating events, whereas the reverse relationship was not found. This pattern of results suggests that a potential pursuit of unrealistic goals and rewards often leads to loss and failure for individuals with bipolar disorders. This is consistent with prior findings of unrealistically optimistic outcome expectancies, in both everyday life (e.g., Meyer & Krum-Merabet, 2003) and experimental paradigms (e.g., Ruggero & Johnson, 2006), for individuals with bipolar spectrum disorders.

Limitations and Future Directions

The present study has several limitations. The study's sample consisted of individuals with bipolar II disorder and cyclothymia drawn from a community. Thus, a replication in bipolar I sample is needed, in order to determine whether the same pattern of results holds in more severe bipolar conditions. As our sample of cyclothymia individuals was small, larger samples are needed to more powerfully test differences in BAS-relevant life events between cyclothymia, bipolar II, and bipolar I disorders. In interpreting the present findings, it is important to note that the use of independent ratings on BAS Activation and BAS Deactivation dimensions allows life events to be rated highly on both dimensions. However, this measurement strategy cannot account for the crucial finding of group differences in a priori ratings of life events, nor the interaction of BAS-activating events by diagnostic group on the BAS-deactivating events rate.

In future research, it will be crucial to examine the ability of BAS-activating vs. Goal-attainment events to predict relapse of hypomania/mania. The optimal window for therapeutic intervention may differ depending on whether the actual attainment of reward or initiation of reward/goal pursuit triggers hypomania/mania. Similarly, future studies should assess the effects of frustrative non-reward, with and without opportunity for active coping, on prospective bipolar symptoms. Additional research is also needed to investigate the link between goal-pursuit (i.e., BAS-activating events) and negative BAS-deactivating events, which could potentially describe a mechanism for switching from hypomania/mania (i.e., high BAS activation state) into depression (i.e., a state of BAS shut-down). Examination of other types of environmental stressors, such as independent and dependent life events based

on the classical stress generation theory (Bender et al., 2010), are also necessary to further explore the specificity of the present findings.

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Table 1

Means and Standard Deviations of Average Daily Rates of BAS-Activating, BAS-Deactivating, and Goal-Attainment Events, Weighted by Severity on the Relevant Dimension

	Bipolar Spectrum Group		Control Group
	Bipolar II Disorder	Cyclothymia	
BAS-Activating Events	3.66 (2.07)	2.63 (1.85)	2.52 (1.81)
BAS-Deactivating Events	4.24 (2.40)	3.01 (1.98)	2.27 (1.76)
Goal-attainment Events	0.40 (0.45)	.42 (.48)	0.36 (0.48)