Life Events as Predictors of Mania and Depression in Bipolar I Disorder

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To date, few prospective studies of life events and bipolar disorder are available, and even fewer have separately examined the role of life events in depression and mania. The goal of this study was to prospectively examine the role of negative and goal-attainment life events as predictors of the course of bipolar disorder. One hundred twenty-five individuals with bipolar I disorder were interviewed monthly for an average of 27 months. Negative and goal-attainment life events were assessed with the Life Events and Difficulties Schedule. Changes in symptoms were evaluated using the Modified Hamilton Rating Scale for Depression and the Bech-Rafaelsen Mania Scale. The clearest results were obtained for goal-attainment life events, which predicted increases in manic symptoms over time. Negative life events predicted increases in depressive symptoms within regression models but were not predictive within multilevel modeling of changes in depressive symptoms. Given different patterns for goal attainment and negative life events, it appears important to consider specific forms of life events in models of bipolar disorder.

Keywords: life events, bipolar disorder, mania, goal attainment

Many studies have been published regarding life events in bipolar disorder. Most of these have focused on the role of severe negative life events. The more methodologically careful studies have consistently documented a robust influence of negative life events on the course of bipolar disorder (Johnson & Roberts, 1995). For example, severe negative life events have been found to be associated with more than four times the risk of relapse (Elliott, Hammen, Gitlin, Brown, & Jamison, 1990) and a threefold increase in the time until recovery (Johnson & Miller, 1997), and have been found even to predict onset of mood disorder among offspring of persons with bipolar disorder (Hillegers et al., 2004).

In recent years, researchers have begun to consider the influence of psychosocial variables on depression and mania separately (see Johnson & Meyer, 2004). Severe negative life events, such as major losses, appear to specifically predict the course of depression within bipolar disorder (Johnson, Winett, Meyer, Greenhouse, & Miller, 1999). The effects of negative life events on mania are less clear. There are many published case reports of mania occurring after the deaths of close ties (Hollender & Goldin, 1978; Krishnan, Swartz, Larson, & Santoliquido, 1984; Morgan, Beckett, & Zolese, 2001; Rickarby, 1977; Rosenman & Tayler, 1986; Sakamoto, Horikawa, & Yamazaki, 1993; Singh, Jawed, & Wilson, 1988). Nonetheless, the most careful life events studies—those that have analyzed severe negative life events that were independent of or not caused by symptoms—have found mixed support for negative life events in relation to mania. That is, six out of eight studies found that independent severe negative life events were not more common before than after manic episodes (see Johnson, 2006, for a review). Consistent with this null pattern, independent severe negative life events did not predict manic symptoms in one prospective study of bipolar I disorder (Johnson et al., 2000). Nonetheless, each of these studies has relied on very small sample sizes that might not have had sufficient power to detect effects. In one prospective study of undergraduates with bipolar spectrum disorders, Reilly-Harrington, Alloy, Fresco, and Whitehouse (1999) found that life stress predicted hypomanic symptoms among those students with depressogenic cognitive styles. In sum, studies have not provided strong evidence for negative life events as a predictor of mania, but
the null findings could be the consequence of the small sample sizes of these studies.

Beyond negative events, recent studies suggest that other types of life events may be triggers of manic symptoms. Consistent with the idea that sleep loss is a powerful predictor of manic symptoms (Barbini et al., 1998; Eilers, Frank, & Kupfer, 1988), life events that disrupt sleep have been found to precede mania (Malkoff-Schwartz et al., 1998, 2000). Similarly, consistent with the idea that mania involves excessive sensitivity of a neurobiologically based approach motivation system (Depue & Iacono, 1989; Gray, 1994), events involving goal attainment also have been found to precede manic symptoms (Johnson et al., 2000; Nusslock, Abramson, Harmon-Jones, Alloy, & Hogan, 2007). Neither of these types of events has been found to predict the course of depression.

In sum, studies have shown that both goal attainment and negative life events are related to symptoms in bipolar disorder. No prospective studies have used life event interviews to assess the impact of these varying forms of life events on the course of depression and mania in a large sample. This was the goal of this study.

In examining life events, we were particularly interested in whether baseline symptoms—the symptoms present before a life event occurred—would influence reactivity. In research on unipolar depression, baseline symptoms have been found to increase vulnerability to depression after life events (Hammen, Mayol, DeMayo, & Marks, 1986).

There are some conceptual reasons that one might expect that baseline manic symptoms would decrease reactivity to negative life events. Theorists have described mania as being a defensive response to threatening events for decades (Bentall & Thompson, 1990). Although little research has directly examined actual reactions to life events, other findings are consistent with this model. For example, support for this model has been drawn from findings that people with bipolar disorder tend to describe themselves positively on self-report measures of self-esteem even when other measures of self-views appear more negative (Lyon, Startup, & Bentall, 1999; Winters & Neale, 1985). Consistent with the idea that mania is tied to decreased sensitivity to threat, laboratory studies using cognitive paradigms and functional neuroimaging suggest that responses to cues of threat seem blunted during manic episodes compared with euthymic periods (Johnson, Gruber, & Eisner, 2007). None of these studies, though, have directly examined whether manic symptoms change the way people respond to life events.

Despite conceptual reasons for studying baseline symptoms, we were able to identify only one study of baseline symptoms as a moderator of life event reactions. Aronson and Shukla (1987) noted 10 relapses in 2 weeks following a hurricane among patients treated at a lithium clinic. They found that baseline instability in mood predicted relapse. In sum, although clinical and small research reports suggest that it will be important to examine baseline symptoms and reactivity to life events, little empirical research has done so.

In this study, we examined the role of negative and goal-attainment life events in predicting both depression and mania. We had four hypotheses. First, negative life events were expected to predict increases in depression but not mania. Second, goal-attainment life events were expected to predict increases in depression but not mania. Third, baseline depressive symptoms were expected to predict greater increases in depressive symptoms after negative life events. Fourth, baseline hypomanic symptoms were expected to predict decreased depressive reactions to negative life events and increased manic reactions to goal-attainment life events.

Method

Participants

Participants were recruited in the South Florida and Rhode Island communities through support groups, clinics, hospitals, and advertising. Previous reports have described treatment effects in the Rhode Island sample (Miller, Solomon, Ryan, & Keitner, 2004) and cognitive and personality predictors within the South Florida sample (Johnson & Fingerhut, 2004; Meyer, Johnson, & Winters, 2001). We selected individuals to participate on the basis of a diagnosis of bipolar I disorder confirmed by the Structured Clinical Interview for DSM-IV (First, Spitzer, Gibbon, & Williams, 1995) and an age of 18 or older. Participants were excluded for the following reasons: neurological disorders, substance abuse or dependence in the past year, and language or cognitive barriers that would impede completion of self-report measures.

Demographic and Clinical Characteristics

The sample included 50% women and 25.6% minorities. Participants were most frequently married or cohabitating (32.8%), followed by divorced or separated (30.4%), single (28.8%), and widowed (1.6%). The average number of years of education was 14.15 (SD = 2.67), with a range from 7 to 21 years. Only 32.6% of the sample were employed full time, and 13.6% were employed part time at study intake, in parallel with other samples with bipolar disorder (Harrow, Goldberg, Grossman, & Meltzer, 1990).

Upon entry to the study, only 4 participants did not meet criteria for a current mood episode, whereas 56% met criteria for mania, 29.6% met criteria for depression, and 11.2% met criteria for mixed or cyclic episodes. The mean number of lifetime mood episodes was 10.21 for depression (SD = 14.03) and 10.57 for mania (SD = 14.26). No history of a depressive episode was reported by 17.6% of participants, consistent with other bipolar samples (cf. Karkowski & Kendler, 1997; Kessler, Rubinow, Holmes, Abelson, & Zhao, 1997).

Compared with participants from Rhode Island, participants from Florida reported more years of education, t(123) = −2.41, p < .05, earlier age of onset, t(120) = 2.39, p < .05, less adequate pharmacotherapy, t(123) = 2.09, p < .05, considerably more depressive, t(97) = −4.61, p < .001, and manic, t(97) = −3.94, p < .001, episodes but less severe episodes at study entry, t(120) = 6.66, p < .0001. Florida and Rhode Island participants were equivalent in hospitalization rates. The cross-site differences are not surprising given that Miami is one of the poorest urban areas in the United States, with well-documented limits in access to medical resources (U.S. Census Bureau, n.d.).

Procedure

The attending psychiatrist was asked for permission before study personnel contacted hospitalized potential participants about the study. Written informed consent was obtained from all partic-
ipants. After completing consent and diagnostic procedures, symp-
tom severity interviews were conducted monthly by telephone or
in person, depending on participant preference. Telephone inter-
views have been shown to be a reliable and valid manner of
gathering symptom severity data (Potts, Daniels, Burnam, &
Wells, 1990; Simon, Revicki, & Von Korff, 1993). Another exper-
imenter, who was unaware of participant symptom status, con-
ducted life event interviews in person at 2-, 6-, 12-, 18-, and
24-month follow-up assessments.

One hundred and forty-five participants completed informed
consent and diagnostic measures. After study entrance, some peo-
ple declined participation, were rediagnosed with schizoaffective
disorder, moved, or were unable to provide enough detailed infor-
mation for life events coding, yielding a final sample size of 125.
Persons who did and did not complete the study did not differ
significantly on age, number of years of education, gender, Holl-
ingshead occupational status, mean age of onset for depression,
number of hospitalizations for depression or mania, nor baseline
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scores. On the other hand, those who did not finish the study
obtained higher baseline mania scores ($M = 14.66, SD = 12.16$)
than those who did finish ($M = 7.62, SD = 8.80$), $t(34.08) = 2.89$,
$p = .04$. Those who did not finish the study also reported an earlier
age of manic onset ($M = 20.76, SD = 8.24$) than those who did
finish ($M = 27.29, SD = 12.30$), $t(28.01) = -2.83$, $p < .01$. The
125 participants included in analyses completed a total of 3,418
symptom severity interviews, with a mean follow-up length of
27.35 months.

**Measures**

**Training**

Prior to conducting any interview measure, all interviewers were
trained by Sheri L. Johnson and/or Ivan Miller. Reliability was
established before the first study interview was conducted, and
tapes of diagnostic, symptom severity, and Bedford College Life
Events and Difficulties Schedule (LEDS; Brown & Harris, 1978a,
interviews were routinely reviewed to ensure reliability. In ad-
dition, regular meetings were held to review diagnostic and symptom
severity interviews and coding. Difficult interviews were routinely
reviewed in supervision, and supervisors also listened to and rated
tapes on an ongoing basis throughout the study. LEDS rater
reliability was monitored at every ratings meeting.

**LEDS**

The LEDS is a semistructured interview designed to assess life
events while taking into account the personal context of the par-
ticipant. For example, a pregnancy would have quite different
implications for a 14-year-old compared with a 34-year-old. Each
event, along with relevant contextual details, is presented to team
of raters who are blind to the participants’ subjective feelings and
interpretations of events. The LEDS is a widely accepted instru-
ment that has been found to have significantly higher reliability
and validity compared with self-report measures of life stress
(Brown & Harris, 1978b, 1989; Gorman, 1995; McQuaid et
al., 1992). The LEDS provides extensive coverage, as more than
200 types of life stressors are enquired about.

Several LEDS procedures were used to improve recall and
dating of events. For example, participants were asked to bring
calendars to the interviews. Interviewers began by marking an-
chors, such as birthdays, holidays, or other significant dates on a
calendar (Loftus & Marburger, 1983), and then life events were
added to this calendar during the interview. At monthly follow-
ups, participants were asked to briefly list and date any major
events occurring over the course of the month. During follow-up
interviews, any event that appeared similar to a previously reported
event was checked to ensure that it was a new event (Neter &
Waksberg, 1964). Empirical research confirms that these proce-
dures greatly reduce problems with forgetting and bias in dating
events (McQuaid et al., 1992; Katschnig, 1986; Sobell, Toneatto,

A “dictionary” of events, which provides rating guidelines and
numerous event examples, was used to increase reliability of
ratings (Brown & Harris, 1978a). Reliability was monitored during
every meeting for the LEDS threat, goal attainment, and illness-
related scales, and formal statistical analyses were conducted to
examine reliability every 3 months. In each check, interrater reli-
ability, measured using intraclass correlations, remained at or
above .76 (range = .76 to .94). When discrepancies in ratings
occurred, consensus was used to achieve final ratings. To control
for the possibility that manic or depressive symptoms could create
life events, each event was rated as definitely, possibly, or unre-
lated to an episode of psychiatric illness. Events rated as definitely
or possibly related to psychopathology were excluded from anal-
yses.

**Threat scale.** Events were rated on the degree of unpleasant-
ness associated with the event using the Brown and Harris (1978a)
threat scale. Each event is rated on a 5-point scale, ranging from 1
(marked negativity) to 5 (little to no negativity). Participants with
no event were rated 5. Counterintuitively, then, ratings of 1 reflect
the most negative rating possible. Examples of a marked negativity
rating include death of confidant, whereas examples of moderate
negativity ratings include threat to immediate family relationships,
and some negativity includes severe arguments or relationship
changes. Events that were directed toward another person (i.e.,
focus was rated “other”) but involved direct repercussions for the
participant were rated but were considered half a point less severe
for threat.

**Goal-attainment scale.** All events were rated on a 4-point
goal-attainment scale, with ratings based on the amount of striving,
the importance of the goal, and success in achieving the goal. The
goal-attainment scale has been used previously in research on
unipolar depression and anxiety literature (Leenstra, Ormel, &
Giel, 1995). Goal-attainment event ratings ranged from 1 to 4, with
events rated 1 if they involved the highest amount of goal attain-
ment and 4 if they involved no or little goal attainment. Parallel to
the threat ratings, lower numbers correspond to a higher goal
attainment. Ratings of 1 include events such as acceptance into
graduate school, making partner in a law firm, or getting married.
Examples of a 2 include winning a local poetry award or being
hired at a new job. Events rated 3 include limited goal striving,
such as moving or starting a technical training program. For an
event to qualify for a 3 or lower, a goal must have been reached;
goal striving without attainment would be rated a 4.
Diagnosis

A diagnosis of bipolar I disorder was confirmed using the Structured Clinical Interview for the DSM-IV (First et al., 1995). Participants whose manic episodes were induced by antidepressant medication were excluded from the study, as well as participants with mania due to a general medical condition. Sheri L. Johnson and or Ivan Miller trained all assessors and supervised diagnoses. A psychiatrist was consulted when diagnoses involved possible organicity. Interrater reliability was high, with $k = .84$ reported for bipolar disorder (Williams et al., 1992). Within our group, interrater reliability estimates taken repeatedly were consistently high for reviews of audiotaped interviews, with intraclass correlations for specific symptoms $>.92$.

Symptom Severity

Severity of depressive symptoms was measured with the Modified Hamilton Rating Scale for Depression (MHRSD; Miller, Bishop, Norman, & Maddever, 1985). To facilitate use by novice interviewers, the modified version includes standardized probes and anchors. Despite these modifications, the MHRSD achieves an interclass correlation of .84 with the original Hamilton Rating Scale for Depression. The MHRSD is both a sensitive and reliable instrument. It is capable of detecting changes in depression severity (cf. Keitner, Ryan, Miller, & Norman, 1992; Miller, Norman, & Keitner, 1989) and has yielded high interrater reliability on our team (intraclass correlation $=.93$, calculated using methods described in Shrout & Fleiss, 1979). Internal consistency was high, with $\alpha = .92$, $N = 164$.

Severity of mania was measured with the Bech-Rafaelsen Mania Scale (BRMS; Bech, Bolwig, Kramp, & Rafaelsen, 1979). The BRMS contains 11 items that assess symptoms such as flight of thoughts, elevated mood, decreased need for sleep, and heightened sexual interest. Each item is rated on a 5-point scale. Reliability is reported to be high, as assessed by an average intercorrelation of four raters using the Kendall coefficient of concordance $W (N = 12) = .95$, $p = .0001$ (Bech, 2002). The BRMS is also highly sensitive to changes in mania, $\chi^2 = 41.95$, $p = .001$. This measure is sensitive to changes in manic symptoms after 1 week, as well as to group differences in medication versus placebo (Bech, 2002). To increase reliability, our team has used a standardized interview format and behavioral anchors for each scale point. With this method, reliability has been high, intraclass correlation for review of audiotaped interviews $=.92$, and internal consistency $\alpha = .94$, $N = 164$. Both symptom severity instruments were used to rate the most severe week of symptoms in the past month.

Somatotherapy Index

Pharmacological treatment adequacy was assessed using the Somatotherapy Index (Bauer, McBride, Shea, & Gavin, 1997). On the basis of the treatment adequacy scale used in the National Institute of Mental Health Program on the Psychobiology of Depression Clinical Studies Project (Mueller et al., 1999), the Somatotherapy Index is a 6-point scale designed to assess the adequacy of treatment of bipolar disorder, with a score of 5 for the most adequate dose. Participants provided information about dosage, compliance, and blood serum levels for mood-stabilizing, antidepressant, antipsychotic, anxiolytic, and other psychotropic medications.

Scoring is based on a fairly detailed set of tables, but as an example, Level 3 is defined as 200–299 mg of imipramine or an equivalent antidepressant for 4 consecutive weeks, 4–7 doses of electroconvulsive therapy, or 600–899 mg of lithium carbonate for 4 consecutive weeks. Our team obtained high interrater reliability, and complex regimens were rated by consensus. Our team has found this scale to be externally valid, with Somatotherapy Index ratings negatively associated with subsequent suicidality (Johnson, McMurrich, & Yates, 2006).

Hollingshead Occupational Status

The Occupational subscale of the Hollingshead Two-Factor Index of Social Position, one of the most widely used measures of socioeconomic status, was used to code occupational status on a 7-point scale (Hollingshead, 1957). High interrater reliability, as well as strong external validity of the Hollingshead with academic and cognitive measures, has been reported (Cirino et al., 2002).

Analysis Plan

All tests were conducted using a $p$ value of .05. Most analyses were completed using SPSS for Windows (Version 10.1), but multilevel analyses were carried out using HLM 6.04. Throughout analyses, we examined symptom severity as a continuum. This is somewhat of a departure from previous analyses of life events, which have often focused on episodes, rather than on continuous measures of symptom severity. However, manic episodes frequently include symptoms of depression, and similarly, depressive episodes often include symptoms of mania (see John- son & Kizer, 2002, for discussion). Moreover, recent evidence suggests that subsyndromal symptoms are more frequently present than episodes are for people with bipolar I disorder (Judd et al., 2002). Relatively few individuals experienced severe depression and mania throughout the 3 months after negative life events. No participants maintained a MHRSD score in the major depression range ($>17$) or a BRMS score in the manic range ($>16$) across the 3 months after the most severe negative event, nor during the 3 months after the most intense goal attainment event. Hence, this data set did not allow for an examination of clinically significant relapse. Separate models were examined for depression and mania, as these syndromes have been found to be uncorrelated within individuals (Johnson, Morriss, et al., 2007).

To examine hypotheses, we conducted two sets of analyses to examine how life events influence symptom severity. First, we used simultaneous multiple regression analyses. In these analyses, we selected the largest life event of each type for each individual and looked at changes in symptoms following the event. That is, we selected the largest goal-attainment life event and the most negative life event. To reduce confounds in the effects of life events, we only examined goal attainment events that were “pure” and did not meet criteria for a severe negative life event. Only 2 individuals reported life events that were rated as both highly negative and high in goal attainment within this sample. For any given individual, the most negative and most goal-attainment life events occurred on different dates; given this, we conducted one set of analyses to examine symptom changes after negative events,
and another set of analyses to examine symptom changes after goal attainment life events. Hence, two parallel analyses (negative and goal attainment events) were conducted for mania and two for depression; conducting separate analyses allowed us to tightly control for baseline symptom levels before the life event occurred. In each model, we examined baseline symptoms (before the life event occurred), life events, and the interaction of life events with baseline symptoms. Sample sizes varied slightly within these analyses, as some persons had an event that occurred too early or too late to yield adequate baseline and follow-up data.

In the second set of analyses, we did not restrict analyses to the most severely negative or most intense goal-attainment life event. Rather, we used multilevel modeling (Raudenbush, Bryk, & Congdon, 2007) to examine all life events that occurred to participants across the entire study. We conducted two separate multilevel analyses to examine changes in depression and changes in mania. Within these analyses, we examined a two-level model, such that life event and symptom variables were nested within each individual. Symptom scores (MHRSD or BRMS) for each month in the study were the outcome variables. Level 1 predictors included number of days in the study, symptom severity score in the month before the life event occurred, and negative and goal-attainment life events in the month before the symptom severity assessment. Multilevel analyses allow for differing number of observations per individual.

The multilevel models contrast with the multiple regression analyses in several ways. The multilevel analyses have the advantage of considering all data points per person. In doing so, they examine the relative ability of life events to explain a given person’s change in symptoms (a within-subjects analysis), whereas the multiple regression models compare the degree of change between persons after a single event. The multilevel models also assess the effects of milder life events as well as the most intense life event for each person and examine how symptoms change in the month after an event rather than 3 months following a life event. Power is also more limited for multilevel analyses.

Results

Univariate distributions were examined for each variable. Goal-attainment events were relatively rare: 14.7% of individuals reported a major goal-attainment event during the entire follow-up period, 23.8% reported a minor event, and 61.5% reported no life events involving goal attainment. Severe negative life events were less rare: 43.4% of individuals experienced at least one severe negative event, 47.8% reported only minor events, and 8.8% reported no negative life event during the time period.

As would be expected, skew and kurtosis estimates indicated significant deviations from normality for mania scores, in that very few individuals reported extremely high symptoms. This was the case both for mania scores used in multilevel models, as well as each aggregate index used in regression models. Given this, all mania indices were square root transformed before conducting analyses. Transformed variables did not differ significantly from normalcy. Power would be expected to be limited for current analyses by the relatively low rates of symptoms, as well as the low incidence of major life events.

Independence of Mania and Depression Scores

We conducted two analyses to consider whether BRMS and MHRSD scores were correlated. First, a principal-components factor analysis of the BRMS and MHRSD ratings from the first month in the study yielded two factors: a depression factor consisting of all MHRSD items and a mania factor consisting of all BRMS items. Second, we conducted multilevel modeling to examine the correlation of BRMS and MHRSD scores within persons over time. In these analyses, a two-level model was specified with scores nested within individuals. At Level 1, MHRSD scores for each month were the outcome variables. Level 1 predictors included MHRSD in the previous month, study location, days enrolled as control variables, and BRMS scores. BRMS was not significantly related to MHRSD, coefficient = .07, SE = .06, t(122) = 1.02, ns.

Multiple Regression Models

Confounds

Before conducting regression models, analyses were conducted to examine potential demographic or illness variables that could be confounds. That is, we conducted bivariate correlations to examine whether either negative or goal-attainment life events were tied to potential confounds of age of first manic episode, age of first depressive episode, number of lifetime episodes of mania; number of lifetime episodes of depression; number of hospitalizations for mania; number of hospitalizations for depression; presence of psychosis at study entry; age; gender; education; and the adequacy of lithium, antidepressant, antiseizure, and overall medication regimens. We also conducted chi-square analyses to examine whether either negative or goal-attainment life events were related to the polarity of the index episode (manic, depressed, mixed, or rapid cycling), marital status, Hollingshead occupational status, employment status, or ethnic background.

Negative life event severity was unrelated to most potential confounds, with two exceptions. First, severity of negative life events was related to the number of lifetime manic episodes, r(125) = −.27, p < .01. Because the number of manic episodes was not correlated with depressive or manic symptoms after negative life events, it was not controlled for in analyses. Severity of negative life events also was related significantly to location of residence, with people living in Florida reporting more severe negative life events than those in Rhode Island, F(1, 124) = 8.60, p < .01. Location was significantly related to depression scores in the month before the negative life event, r(122) = 3.09, p < .01, and in the 3 months after a negative life event, F(1, 118) = 4.75, p < .05. Location was also related to mania scores in the month before the negative life event, r(122) = 2.45, p < .05, and in the 3 months after a negative life event, F(1, 119) = 4.35, p < .01. In all cases, participants in Florida had higher symptoms than those in Rhode Island. Given this, we controlled for location in analyses of negative life events.

We examined the same set of potential confounds for goal-attainment life events as for severe negative life events. The magnitude of goal-attainment life events was related only to location of residence in Florida or Rhode Island, F(1, 120) = 4.07, p = .05, and number of lifetime manic episodes, r(120) = −.23, p < .01. As above, we examined whether these variables were related
to dependent variables. Location was related to follow-up depression scores, $F(1, 120) = 6.21, p = .01$, and to follow-up mania scores, $F(1, 119) = 5.20, p < .05$. Finally, number of lifetime manic episodes was correlated with follow-up mania scores, $r(120) = .29, p < .01$, but not follow-up depression scores, $r(121) = .13, ns$. Given this pattern, number of lifetime manic episodes was controlled for in analyses of goal-attainment life events and mania, while location was controlled for in analyses of depression and mania.

Next, we examined bivariate correlations of negative life events and goal-attainment life events with baseline (preevent) symptom severity scores. Severity of negative life events was not significantly related to baseline manic, $r(124) = .04, ns$, or to depressive symptoms, $r(124) = -.04, ns$. Similarly, intensity of goal-attainment life events was not significantly correlated with baseline manic, $r(122) = .10, ns$, or baseline depressive, $r(121) = -.10, ns$, symptoms. Thus, the severity of symptoms in the month before the life event was not an influence on the magnitude of stressors or goal attainment, which is congruent with our focus on independent life events in analyses. We included baseline symptom scores in analyses, though, to allow for an examination of change in symptom levels over time.

Regression Findings

Simultaneous multiple regression analyses were used to examine change in symptom severity after the most intense (either negative or goal-attainment) life events. In each model, the dependent variable was the level of symptoms averaged across the 3 months after the life event occurred. We controlled for baseline manic and depressive symptoms (the month before the life event) as well as relevant variables drawn from the confound analyses above. Central to testing hypotheses, we entered the magnitude of life events. We also entered two interaction terms to capture the interaction between baseline depressive symptoms and life events, and then the interaction between baseline manic symptoms and life events. We conducted $z$ transformations on all independent variables before regression analyses were conducted.

Negative Life Events

With regard to depression (MHRSD scores), neither the interaction of Baseline Depression Scores $\times$ Event Severity ($\beta = .06, t = 0.74, ns$) nor the interaction of Baseline Mania Scores $\times$ Event Severity ($\beta = -.08, t = -.98, ns$) was significant in the prediction of follow-up depression in the 3 months after the life event. The final model without these interaction terms was highly significant, $r^2 = .35, F(4, 114) = 15.224, r^2$ total = .35, $p < .0005$. As shown in Table 1, follow-up depression scores were predicted significantly by baseline depression scores, baseline mania scores, and event severity, but not by location. Persons with higher MHRSD and BRMS scores, as well as those with more severe negative events, were likely to experience greater increases in depression scores.

With regard to mania (BRMS scores), neither the interaction of Baseline Mania $\times$ Event Severity ($\beta = -.01, t = -0.06, ns$) nor of Baseline Mania $\times$ Event Severity ($\beta = -.05, t = -.59, ns$) was significant. The final model without these interaction terms was highly significant, $r^2 = .38, F(4, 114) = 17.72, p < .0005$. As shown in Table 1, mania scores in the 3 months after the life event were predicted by baseline mania, but not by baseline depression, location, or the severity of negative life events. Persons with higher baseline mania scores were likely to have higher follow-up mania scores.

### Table 1

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<tr>
<th>Predictor</th>
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<tbody>
<tr>
<td><strong>Dependent variable: MHRSD</strong></td>
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<tr>
<td>Baseline MHRSD</td>
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<td>.45***</td>
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<td>Baseline BRMS</td>
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<td>.26**</td>
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<td>Location</td>
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<td>Baseline BRMS</td>
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<td>−0.66</td>
<td>−.05</td>
</tr>
<tr>
<td>Event severity</td>
<td>−1.15</td>
<td>−.09</td>
</tr>
</tbody>
</table>

Note. Several participants were excluded from analyses because the timing of any event occurred too early or too late in the follow-up period to examine changes in symptom severity. MHRSD = Modified Hamilton Rating Scale for Depression; BRMS = Bech-Rafaelsen Mania Rating Scale.

$^p < .05. ^{**} p < .01. ^{***} p < .001.$

Goal-Attainment Life Events

With regard to depression scores, neither the interaction of Baseline Depression Scores $\times$ Goal-Attainment Magnitude ($\beta = .01, t = 0.02, ns$) nor the interaction of Baseline Mania Scores $\times$ Goal-Attainment Magnitude ($\beta = .04, t = 0.62, ns$) were significant. The overall model without these interaction terms was significant, $r^2$ total = .50, $F(4, 115) = 29.26, p < .0005$. As shown in Table 2, depression follow-up scores were predicted by baseline depression scores, but not by baseline mania scores, location, or the magnitude of goal-attainment life events. People with higher baseline depression scores were likely to have higher follow-up depression scores.

With regard to mania scores, the interaction of Baseline Depression $\times$ Goal-Attainment Magnitude was not significant ($\beta = -.13, t = -1.85, ns$) nor was the interaction of Baseline Mania $\times$ Goal-Attainment Magnitude ($\beta = .12, t = 1.74, ns$). The final model without these interaction terms was highly significant, $r^2$ total = .46, $F(5, 114) = 19.13, p < .0005$. As shown in Table 2, follow-up BRMS scores were predicted by baseline BRMS scores, number of manic episodes, and the magnitude of goal-attainment life events. Persons with higher baseline BRMS scores, more previous episodes of mania, and higher magnitude goal-attainment life events were likely to have higher mania scores over time.

1 Parallel multiple regression analyses were conducted with 1-month follow-up periods to be more comparable with the time windows used in multilevel models. Findings were entirely parallel with those obtained using the 3-month follow-up periods.
Table 2
Goal-Attainment Life Events as Predictors of Depressive and Manic Symptoms (N = 120)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>t</th>
<th>β</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dependent variable: MHRSD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline MHRSD</td>
<td>8.92</td>
<td>.64***</td>
</tr>
<tr>
<td>Baseline BRMS</td>
<td>1.55</td>
<td>.11</td>
</tr>
<tr>
<td>Location</td>
<td>1.28</td>
<td>.09</td>
</tr>
<tr>
<td>Event magnitude</td>
<td>1.05</td>
<td>.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dependent variable: BRMS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline MHRSD</td>
<td>-0.85</td>
<td>-.06</td>
</tr>
<tr>
<td>Baseline BRMS</td>
<td>8.29</td>
<td>.63***</td>
</tr>
<tr>
<td>Number of manic episodes</td>
<td>3.06</td>
<td>.23****</td>
</tr>
<tr>
<td>Location</td>
<td>-0.005</td>
<td>.000</td>
</tr>
<tr>
<td>Event magnitude</td>
<td>-2.45</td>
<td>-.18***</td>
</tr>
</tbody>
</table>

Note. MHRSD = Modified Hamilton Rating Scale for Depression; BRMS = Bech-Rafaelsen Mania Rating Scale. ***p < .001. ****p < .0005.

Multilevel Modeling

Two parallel multilevel analyses were conducted to examine depressive symptoms and then manic symptoms separately. In each case, we assessed the same confounds described earlier by entering them into the multilevel models to determine whether they moderated the relationship between life events and symptoms. Unless noted, the confounds were not significant predictors of outcomes. Number of days enrolled in the study was included because symptom severity did decrease over time in this study.

With respect to the multilevel models, a two-level model was specified for each type of symptom (MHRSD and BRMS) with observations nested within individuals. At Level 1, monthly symptom assessments (either MHRSD or BRMS) were the outcome. Level 1 predictors included number of days enrolled in the study, symptom level 1 month before, and the magnitude of negative and goal-attainment life events within the month before the symptom. Level 2 equations were unconditional in that they had no specific Level 2 predictors of the Level 1 coefficients.

The first analyses considered the role of negative and goal-attainment life events in predicting depressive symptoms. Negative life events were not a significant predictor of MHRSD symptoms, t(123) = 1.43, p = .15, though the nonsignificant pattern was in the expected direction (coefficient = .22, SE = .16) with more negative events associated with more subsequent depressive symptoms. Goal-attainment life events also were not associated with depressive symptoms, t(123) = 0.77, p = .44.

The second analyses considered the role of negative and goal-attainment life events in predicting manic symptoms (transformed BRMS scores). Negative life events were a significant predictor of decreases in manic symptoms, t(123) = -2.44, p = .02 (coefficient = -.09, SE = .04). Goal-attainment life events also predicted subsequent manic symptoms, t(123) = 2.36, p = .02. The greater the goal attainment, the greater the subsequent level of manic symptoms (coefficient = .22, SE = .09).

Given that location appeared to be an important confound, we examined the effects of location within the multilevel models. That is, we entered location into the Level 2 equations predicting the negative and goal-attainment Level 1 coefficients. Location was significantly related to depression scores at the time of enrollment, t(122) = 3.09, p < .01, and to mania scores at the time of study enrollment, t(122) = 2.70, p < .01. We conducted further analyses of whether location moderated the effects of life events on symptoms. In both models, location did not moderate the effects of life events (either negative or goal attainment) on symptoms (either BRMS or MHRSD). In other words, negative or goal-attainment life events did not have different effects on symptoms depending on whether a person was in Florida or Rhode Island.

Finally, to assess whether baseline symptom severity moderated the effects of life events, we repeated the above multilevel analyses for goal attainment and negative events. However, we now included interaction terms between baseline symptoms and life events to determine whether the effects of life events on subsequent symptoms varied depending on the person’s baseline symptoms. Specifically, neither the interaction between baseline manic symptoms and goal attainment, t(123) = 0.84, p = .40, nor the interaction between baseline manic symptoms and negative life events, t(123) = -0.59, p = .56, predicted subsequent manic symptoms. Likewise, neither the interaction between baseline depressive symptoms and negative life events, t(123) = -1.79, p = .08, nor the interaction between baseline depressive symptoms and goal-attainment life events, t(123) = -0.91, p = .36, predicted subsequent depressive symptoms.

Discussion

Although a growing number of studies have used careful life event and symptom interviews to examine the role of stressors in bipolar disorder, the current study is distinguished from most previous studies of life events in bipolar I disorder by the large sample, prospective analyses, 2-year follow-up period, and assessment of medication adequacy. This study was also novel in examining the role of baseline symptom severity levels as a potential moderator of the effects of life events. Before considering findings, however, it is important to acknowledge weaknesses of this study.

First, even though our attrition rates were comparable with those seen in other studies of bipolar disorder (Ellicott, 1988; Hunt, Bruce-Jones, & Silverstone, 1992), high mania scores and more lifetime episodes of mania predicted failure to complete the study. The current sample, then, may be biased toward people with less severe mania. This methodological issue limits our ability to comment on those individuals with the most severe cases of mania. Indeed, overall, this study is relevant for understanding only sub-syndromal shifts in symptoms, as no participants developed manic or depressive episodes in the months after a life event.

Second, it must be acknowledged that any given life event may stem from a confluence of a person’s lifelong symptoms, judgment, coping, and other psychosocial resources (Hammen, 1992). We attempted to provide control over these issues by analyzing only life events that were rated as independent of symptoms and by considering a broad range of potential confounds. Nonetheless,

2 Parallel multilevel models were examined to determine whether results differed when severe negative events were recoded into those that were rated as severe or not. Findings were entirely comparable with those when negative life events were examined as a continuum.
people with more severe histories of mania reported more negative life events, and it remains possible that indirect effects of the mania on relationships, occupational status, and other domains may have changed the nature of life events differentially. Third, although we used a number of procedures to try to enhance recall accuracy, it remains possible that participants were biased in dating life events in order to provide some explanation for changes in symptoms. Naturalistic studies of major life events must be complemented by laboratory research on minor stressors to control for memory biases and to evaluate the potential role of third variables.

Despite the limitations, the current findings provide some insight into the role of life events in bipolar disorder. Findings add to the burgeoning evidence for the need to disentangle psychosocial predictors of depression and mania (Johnson & Meyer, 2004). We consider the findings separately for goal-attainment life events and then for negative life events.

Both multiple regression and multilevel model analyses suggested that goal-attainment life events predicted increases in manic but not depressive symptoms. These findings parallel those of the previous studies of goal-attainment life events in bipolar I disorder (Johnson et al., 2000) and among students with hypomanic symptoms (Nusslock et al., 2007).

Findings for negative life events were not parallel across analytic methods, for either mania or depression. Secondary analyses suggest that the disparate effects were not due to differences in the length of the outcome period nor to the focus on severe versus minor negative life events. Changes in depressive symptoms were predicted by negative life events within multiple regression models but not within the multilevel model. The regression findings are consistent with previous research suggesting that negative life events increase risk of depressive symptoms (Monroe & Hadjyannakis, 2002). Nonetheless, effects were small and so multilevel models likely were underpowered for detecting effects of this size. With regard to mania, negative life events did not predict symptom changes within regression models, but the multilevel models suggested that negative life events did diminish risk of manic symptoms. The multilevel analyses differed from the regression analyses in three ways: (a) covarying both negative and goal attainment life events, (b) including all life events for a given person rather than just the most intense event, and (c) examining the rate of within-person change across the entire study, rather than focusing only on the between-persons change after the most severe event. Such differences in the statistical approaches may account for the different findings.

This was one of the first studies to examine baseline symptoms as a moderator of life event effects. Contrary to hypotheses, baseline symptoms did not increase reactivity to life events. Although some analyses supported a role for life events, the magnitude of effects for events was small. It seems possible that the highly biological nature of this disorder, with heritability estimates as high as 80% (McGuffin et al., 2003), limits the extent to which the psychosocial environment will be predictive. Other researchers have suggested that the role of life events may diminish with repeated episodes (Wals et al., 2005), and our sample had experienced multiple recurrences. Future studies would do well to consider more specific interactions of psychosocial variables and genetic vulnerability. Better studies of individual differences in psychological characteristics may help with this goal (cf. Swendsen, Hammen, Heller, & Gitlin, 1995).

As current results replicate previous findings for goal-attainment life events as a risk factor for manic symptoms, it is worth considering potential mechanisms that could help explain these effects. Among people who are vulnerable to mania, confidence seems to become unrealistic in response to standardized success cues (Johnson, Ruggero, & Carver, 2005; Stern & Berenberg, 1979). Speculatively, as people become more confident, they may become more active in pursuing goals. This increased activity, coming at a time when individuals are already destabilized, may intensify goal pursuit, sleep loss, and other processes thought to be risk factors for mania (Johnson, 2005).

In sum, the current results fit well with a set of findings suggesting that it is important to consider processes guiding the development of mania and depression separately. That is, goal-attainment life events appear relevant for the course of mania but not depression. Cognitive findings provide some glimpses into mechanisms that could help explain this, but there is a need for studies that more directly examine reactions to negative and goal-attainment life events among people with bipolar disorder.

References


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Correction to Johnson et al. (2008)

In the article, “Life Events as Predictors of Mania and Depression in Bipolar I Disorder,” by Sheri L. Johnson, Amy K. Cueller, Camilo Ruggero, Carol Winett-Perlman, Paul Goodnick, Richard White, and Ivan Miller (Journal of Abnormal Psychology, 2008, Vol. 117, No. 2, pp. 268–277), Amy K. Cuellar’s last name was misspelled.