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# Life Events and Social Rhythms in Bipolar Spectrum Disorders: An Examination of Social Rhythm Sensitivity

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# Abstract

**OBJECTIVES**—To examine the presence of an underlying social rhythm sensitivity in individuals with bipolar spectrum disorders.

**METHODS**—The present study examined the impact of life events on sleep loss and social rhythm disruption in 184 individuals with bipolar spectrum disorders (BSD) compared to 197 demographically similar normal controls (NC) drawn from the Longitudinal Investigation of Bipolar Spectrum Disorders (LIBS) project. Life events data were obtained at three time points, each spaced four months apart, and included information on the intensity of the event (high or low), valence (negative or positive), and levels of sleep loss and social rhythm disruption brought about the event. We hypothesized that BSD participants would exhibit higher levels of social rhythm disruption and sleep loss than normal controls as a consequence of the same life events.

**RESULTS**—BSD participants experienced significantly more social rhythm disruption and sleep loss following all classes of life events.

**LIMITATIONS**—The cross-sectional design of this study limits the strength of the conclusions that can be drawn, primarily cause and effect relationships between social rhythms and symptoms.

**CONCLUSIONS**—Findings support the presence of an underlying social rhythm sensitivity in individuals with bipolar spectrum disorders. An additive effect of sleep loss and social rhythm disruption may contribute to subsequent mood symptomatology. Results from this study may inform early psychosocial interventions for at-risk individuals.

#### Keywords

bipolar disorder; social rhythms; circadian rhythms; life events

CONFLICT OF INTEREST

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### INTRODUCTION

There is mounting evidence to support the conceptualization of bipolar disorder as existing along a spectrum of severity from "softer" clinical diagnoses of cyclothymia to the most severe manifestation of bipolar I disorder (Akiskal et al., 2000; Angst et al., 2003, Axelson et al., 2006). Despite the fact that approximately 6.7% of Americans suffer from bipolar spectrum disorders (i.e. bipolar II disorder and cyclothymia) (Judd & Akiskal, 2003), these disorders remain relatively understudied compared to other mental health disorders (Hyman et al., 2000). This lack of attention stands in particular contrast to the relative focus placed on bipolar I disorder (Hyman et al., 2000). Bipolar spectrum disorders (BSD) warrant additional investigation because individuals with these spectrum conditions, particularly youth and adolescents, are at increased risk to develop bipolar I disorder (Alloy et al., in press; Birmaher et al., 2006; Birmaher et al., 2009; Cassano, et al., 1999; Shen et al., 2008).

One of the prominent theories of the etiology of mood symptoms in BSD is the Social Zeitgeber Theory (Ehlers et al., 1988), which suggests that life events disturb social zeitgebers ("time givers") by impacting daily social rhythms, which in turn disrupt biological rhythms, resulting in affective symptoms. Social rhythms, such as bedtimes, mealtimes, and the beginning and ending of work, are theorized to entrain endogenous circadian rhythms, the disruption of which is thought to lead to depressive or manic episodes.

There is substantial research that supports the influence of endogenous circadian cycling disruption in depression and bipolar disorder (Gruber et al., 2011; Kennedy et al., 1996; Leibenluft et al., 1996; Mendlewicz, et al., 1982; Shi et al., 2008). Using a mix of actigraphy and cross-sectional mood assessment, Jones, Hare and Evershed (2005) found that circadian rhythm and sleep loss patterns of BPS individuals were less stable and more variable than those of control participants. These differences persisted while participants were euthymic. Additionally, studies of sleep disruption and deprivation have also shown associations between circadian disruptions and affective episodes (Colombo et al., 1999; Gruber et al., 2011; Proudfoot et al., 2010).

Considerable research has been conducted on the role of life events in the etiology and course of affective episodes in both unipolar depression and bipolar disorder (Alloy et al., 2005; Alloy et al., 2006; Johnson, 2005). Despite methodological concerns inherent in the study of life events and psychopathology (see Alloy et al., 2006 and Johnson, 2005 for a thorough review of these issues), the bulk of the research has revealed a consistent and robust influence of negative and severe life events on bipolar disorder (Ellicot et al., 1990; Hunt et al., 1992; Johnson et al., 2008; Johnson and Kizer, 2002). Investigations of the influence of positive, goal- and achievement-relevant life events in bipolar disorder are considerably less common. Evidence suggests that goal- and achievement-related events are likely to precede hypomanic or manic episodes in individuals with bipolar spectrum disorders (Alloy et al., 2009; Johnson, 2005; Johnson et al., 2000; Nusslock et al., 2007; Uroševi et al., 2008).

The impact of social rhythm disrupting (SRD) events also has been studied. Employing a prospective, longitudinal design examining the social zeitgeber theory, Sylvia and colleagues (2009) found no predictive relationship between life events and social rhythm regularity, although, consistent with the social zeitgeber theory, SRD life events did prospectively predict bipolar symptoms and episodes. Malkoff-Schwartz and colleagues (1998) observed an association between the onset of bipolar episodes, specifically manic episodes, and acute event-related social rhythm disruption in the eight weeks preceding episodes relative to a control period. A replication supported this previous finding and

revealed that, compared to participants with unipolar depression and participants cycling between episodes, participants in manic episodes had more SRD events in the 8 and 20-week periods prior to onset (Malkoff-Schwartz, et al., 2000).

There is a growing literature to suggest that baseline social rhythm regularity is disrupted in mood disorders (see Grandin et al. (2006) for an extensive review). In one study, depressed participants' scores on the Social Rhythm Metric, a self-report instrument used to assess daily social rhythm regularity, were significantly lower than those of controls, and negatively correlated with Hamilton Rating Scale for Depression scores, indicating that depressed participants exhibit significantly less social rhythm regularity and that social rhythm irregularity is associated with depressive symptoms (Szuba et al., 1992). Shen, Alloy, Abramson, and Sylvia provided further evidence of social rhythm irregularities in bipolar spectrum disorder (2008). In a sample of 414 undergraduates, those diagnosed with either cyclothymia or bipolar II disorder reported significantly fewer regular activities than normal controls. Additionally, approximately half of the bipolar spectrum sample experienced a worsening of symptoms over the course of the study. A survival analysis indicated that both diagnosis and less social rhythm regularity were predictive of shorter time to onset of major depressive and manic or hypomanic episodes.

Further evidence of social rhythm disruption in bipolar disorder lies in the efficacy of social rhythm stabilization on mood symptoms. Interpersonal and Social Rhythm Therapy (IPSRT), a psychotherapy that combines elements of Interpersonal Psychotherapy with a sleep and social rhythm stabilizing regimen, has been shown to increase time to relapse in individuals with bipolar I disorder (Frank et al., 2005). Additionally, following a randomized controlled trial of acute and maintenance IPSRT or intensive clinical management, those participants randomized to IPSRT had higher regularity of social rhythms, and this regularity was significantly associated with reduced likelihood of relapse during maintenance treatment (Frank et al., 2005). IPSRT is also showing promise as a treatment for individuals with bipolar II disorder. Following 12 weeks of acute and 8 weeks of follow-up treatment with IPSRT (and adjunctive lamotrogine as needed), 41% of a sample of 17 individuals with unmedicated bipolar II depression saw at least a 50% decrease in depression symptoms (Swartz et al., 2009). By week 20, 53% achieved at least a 50% decrease in depression symptoms, while 29% achieved full remission (Swartz et al., 2009).

Thus, prior research indicates that social and circadian rhythms are disrupted in individuals with BPS. There is also evidence pointing to life events as the initiators of these disruptions. However, little is known about whether life events impact all individuals in the same way regardless of diagnosis, or whether some pathogenic process in bipolar disorder renders the individual more susceptible to circadian and social rhythm disruptions in response to life events.

The present study aimed to take the first step in examining this potential difference by testing whether increased social rhythm sensitivity exists in individuals with bipolar spectrum disorders. We thus hypothesized that BSD participants would differ significantly from normal controls on their degree of sleep loss and social rhythm disruption as a consequence of the same type of life event. We theorized that whereas minor life events may not provide sufficient SRD or sleep loss to trigger an affective episode, individuals with BSD would still experience these events as more disruptive compared to normal controls. Additionally, we hypothesized that significant differences would be apparent for positive, as well as negative, life events.

### METHODS

#### Participants and Screening

Participants for this study were recruited for participation in the two-site Longitudinal Investigation of Bipolar Spectrum (LIBS) Project, a longitudinal investigation of predictors of the course of bipolar spectrum disorders, conducted at the University of Wisconsin (UW) in Madison, WI and at Temple University (TU) in Philadelphia, PA (Alloy et al., 2008). All procedures were approved by the Temple University and University of Wisconsin Institutional Review Boards and all participants provided informed consent. Males and females ranging in age from 18 to 24 years were invited to participate in a two-phase screening procedure.

In the first phase, approximately 20,500 students at TU and UW completed the revised General Behavior Inventory (GBI; Depue et al., 1989). Those students who met or exceeded initial GBI screening criteria of 11 on the Depression scale and 13 on the Hypomanic/ Biphasic scale were invited to participate in the second screening phase as potential BSD participants, whereas those who scored below those cutoffs were considered potential normal controls. The second phase consisted of a diagnostic interview utilizing an expanded version of the Schedule for Affective Disorders and Schizophrenia – Lifetime (SADS-L; Endicott and Spitzer, 1978) interview. Those participants who met the GBI cutoffs and met either DSM-IV (APA, 1994) or Research Diagnostic Criteria (RDC; Spitzer, Endicott and Robins, 1978) for cyclothymia or bipolar II disorder formed the BPS group and were invited to participate in the full longitudinal study. Participants who scored below the GBI cutoffs and who did not meet diagnostic criteria for any lifetime disorder (with the exception that they could have a specific phobia) formed the normal control group. Participants in the normal control group were matched to the BSD group on age, sex, and ethnicity. Further details about participant selection and representativeness in the LIBS Project may be found in Alloy et al. (2008).

Complete life event data for the first year of follow-up were available for 408 participants. Of those, 27 individuals did not have complete data for the Social Rhythm Metric-Trait measure (SRM-T; Monk et al., 1990). Independent samples t-tests revealed no significant differences in sex, diagnostic status, ethnicity, or site between those participants with and without SRM-trait data and thus, the participants missing these data were excluded from analysis. The final sample for the present study consisted of 381 participants (225 female, 156 male), 184 in the BSD group, and 197 in the normal control group. Participants ranged in age from 18 to 24 (M=20.15, +/- 1.74 years). The bipolar group was predominantly comprised of participants with bipolar II disorder (134 bipolar II, 50 cyclothymia). Demographic characteristics of this sample are in Table 1.

#### Procedure

Participants were assessed at baseline (Time 1) and at four-month intervals (regular prospective assessments [RPA]) for a total of up to seven years of follow-up. The present study includes data from the first year of follow-up (RPAs 1 through 3). At each RPA, participants were administered a SADS-Change diagnostic interview (SADS-C; Spitzer and Endicott, 1978) to obtain information on affective symptoms and episodes for the previous four months. Participants completed a Life Events Scale (LES; see measures), in which they indicated whether or not they experienced each of 194 specified life events, as well as the number of times each event occurred over the previous 4-month period. A Life Events Interview (LEI; see measures) was also administered at each RPA to obtain more detailed information on whether the life events each participant reported on the LES met the event

definition criteria, the events' dates of occurrence, as well as information on levels of sleep loss and social rhythm disruption associated with each event.

#### Measures

**General Behavior Inventory (Phase I)**—The General Behavior Inventory (Depue et al., 1989) is a self-report questionnaire utilized in Phase I to screen for potential participants on the bipolar spectrum and normal controls. Revised in 1989, the GBI has been validated in a number of populations including undergraduates, outpatients, and relatives of individuals with bipolar I disorder (Depue et al., 1989). The GBI is a psychometrically sound measure, with internal consistency a's of 0.90 to 0.96, test - retest reliability r's of 0.71 - 0.74, satisfactory sensitivity (0.78) and superior specificity (0.99) for bipolar spectrum disorders (Depue et al., 1981). Discriminant validity is also strong. More specifically, research has shown that the GBI distinguishes individuals with affective disorders from those with no diagnosis (Mallon et al., 1986).

The revised GBI consists of 73 items measuring depressive (D scale) and hypomanic/ biphasic (HB scale) symptoms. Responses to items are made on a 4-point Likert scale ranging from 1 (*not at all*) to 4 (*very often or almost constantly*). Following Depue et al.'s (1989) guidelines, an item was scored as positive if the respondent answered with either a 3 (*often*) or 4 (*very often or almost constantly*). Two subscores were obtained by summing separately the scores of depressive and hypomanic/biphasic items. Utilizing the case-scoring method outlined in Depue et al. (1989), cutoff scores of D 11 and HB 13 were used to identify potential BPS participants and D < 11 and HB <13 to indicate normal control participants.

**Schedule for Affective Disorders and Schizophrenia – Lifetime (Phase II)**—The Schedule for Affective Disorders and Schizophrenia – Lifetime (SADS-L; Endicott and Spitzer, 1978) is a diagnostic interview used in Phase II of the screening process to confirm diagnoses of bipolar II or cyclothymia. This expanded version of the SADS assesses the occurrence, duration, and severity of symptoms related to mood, anxiety, eating, substance use, and psychotic disorders over the course of an individual's lifetime. Specific alterations were made to the SADS to obtain project-specific information and included 1) additional probes to allow for DSM as well as RDC diagnoses; 2) additional probes regarding mood episodes to better capture individual symptom differences, duration, and frequency of episodes; and 3) additional sections on eating disorders, ADHD, acute stress disorder, medical history, family history, and organic rule-out conditions.

Interviewers for this project were extensively trained in the administration of the SADS-L and were blind to GBI status. Interviews were audiotaped for inter-rater reliability and to obtain consensus diagnoses. Inter-rater reliability within the project was high, with kappas for major depressive disorder diagnoses (based on 80 jointly rated interviews) exceeding .95 and kappas for bipolar spectrum diagnoses (based on 105 jointly rated interviews) exceeding .96 (Alloy et al., 2008).

#### Schedule for Affective Disorders – Change (Regular Prospective

**Assessments)**—The Schedule for Affective Disorders – Change (SADS-C; Spitzer and Endicott, 1978) was administered at each Regular Prospective Assessment (RPA) to assess for occurrence, duration, and frequency of affective symptoms throughout the preceding 4-month study period. Like the expanded version of the SADS-L, the SADS-C used in this study was expanded to allow for assignment of DSM-IV as well as RDC diagnoses (see Alloy et al., 2008; Francis-Raniere, Alloy and Abramson, 2006) and allowed for detailed

reporting of days spent in affective episodes. Interviewers at each RPA were also blind to GBI scores, as well as Phase II SADS-L diagnoses, and life events data.

The SADS-C exhibited strong psychometrics. Inter-rater reliability, based on 60 jointlyrated LIBS Project interviews, was high (kappas > .80; Francis-Raniere, Alloy and Abramson, 2006) and a validity study indicated that symptom dating on the SADS-C was at least 70% accurate (Francis-Raniere, Alloy and Abramson, 2006). Items were included in the symptom count if the interviewer rated the participant's endorsement of them with a minimum severity of 3, indicating clinical significance. Days spent in affective episodes were calculated using the detailed symptom and date information obtained from the SADS-C.

**Social Rhythm Metric – Trait Version (Time 1)**—The Social Rhythm Metric is a selfreport instrument used to capture the frequency with which activities are performed, as well as levels of regularity and social contact associated with these activities (Monk et al., 1990). The version utilized in this study asks the participant to indicate the timing of 15 specific events as well as two write-in events. The daily tracking version of the SRM demonstrated moderate consistency (r = .44) and validity in a sample of 50 healthy control participants (Monk et al., 1990, Monk et al., 1991, Monk et al., 1994).

The present study utilized a modified version of the SRM (SRM-T) to assess the frequency with which participants performed activities at approximately the same time (i.e., within +/- 45 minutes) over the previous 30 days before baseline assessment. An activity was defined as regular if it occurred within 45 minutes of the same time at least three days per week for the past 30 days. Higher scores on the SRM-T indicate higher regularity of daily activities. Frequency of activities was also assessed and given a frequency score that was equal to the number of times per week (ranging from 3 to 7) that each regular activity occurred. The modified SRM-T was consistent over 8 months in a subsample of 101 bipolar spectrum and 100 normal control participants in the LIBS Project (r = .62) (Shen et al., 2008). In addition, the Time 1 SRM-T exhibited construct validity by predicting state SRM scores four months later (r = .58) (Shen et al., 2008).

#### Life Events Scale and Life Events Interview (Regular Prospective

**Assessments)**—Life events were assessed via a combination of self-report and interview measures. The Life Events Scale (LES; (Alloy and Clements, 1992; Francis-Raniere, Alloy and Abramson, 2006) is a self-report measure administered at each RPA. Expanded from an earlier 134-item version, the 193-item scale assesses positive and negative life events that may have occurred during the previous 4-month assessment period. Items were carefully selected to reduce ambiguity and were removed if considered too directly reflective of affective symptomatology. The LES demonstrates good reliability and validity (Francis-Raniere, Alloy and Abramson, 2006, Safford et al., 2008). Each item on the LES received a consensus-based, *a priori* objective impact rating and valence categorization as determined by the principal investigators and senior research staff of the LIBS project. Events were rated on a 5-point scale ranging from 0 (*no/slight impact*) to 4 (*extreme impact*), and categorized as negative or positive. Additionally, if events were considered to have a substantial disrupting effect on social rhythms, they were categorized as social rhythm disrupting (SRD) events.

Following the completion of the LES, participants completed a Life Events Interview that elicited detailed information about the events endorsed on the LES and dated their occurrence. LEI interviewers were blind to GBI and SADS-L diagnostic status, as well as diagnostic information obtained during the SADS-C. The LEI utilized manualized, event-specific criteria probes to maintain consistency across interviews. Any event not meeting

pre-determined definitional criteria was disqualified. In addition to objective impact ratings, the LEI assessed levels of sleep loss and social rhythm disruption (SRD) associated with each life event. Sleep loss ratings reflect the total number of hours of sleep lost due to the event. Ratings for sleep loss ranged from 1 (*little to no sleep loss/losing < 1 hour of sleep*) to 5 (ex*treme sleep loss/losing 7 hours of sleep*). SRD ratings reflect the degree of disruption in the sleep/wake cycle (i.e., a change in the time at which the participant went to bed or woke up that was irrespective of the total amount of actual sleep the participant had following the event). Ratings for SRD ranged from 1 (*little to no effect*) to 4 (*marked effect*). Ratings for sleep loss and SRD were designed to reflect the acute impact of life events on each construct.

The combination of the LES and LEI interview results in greater accuracy of reporting of life events. Alloy and Abramson (1999) reported that, when compared to a list of life events prospectively generated by each participant throughout a month-long period, participants correctly recalled 100% of major life events utilizing the combined LES and LEI approach. Average inter-rater reliability for the dating of life events was .89, based on 40 LEIs reviewed in the same study (Alloy and Abramson, 1999).

In the present study, we examined four distinct categories of events: major impact negative events, minor impact negative events, major impact positive events, and minor impact positive events. Events were categorized a priori based on normative data obtained from a sample of TU and UW undergraduates who were demographically comparable to the study sample. The characteristics of the life events included in the LES were designed to reflect the normative characteristics of life events.

#### Statistical Analyses

Study hypotheses were tested using ranked Analyses of Covariance (ANCOVA). Considering the sleep loss and hypersomnia often associated with depressive and hypomanic/manic episodes, days spent in either of these episodes were included as covariates. Additionally, as we were interested in the acute impact of life events on SRD, we controlled for baseline Social Rhythm Metric trait scores to better isolate life-event specific SRD from trait social rhythm disruption. Initial descriptive analyses revealed significant positive skewness on all dependent variables, as well as all covariates. Extreme univariate outliers were also present in all covariates. To address these violations of univariate normality, a rank-based, nonparametric ANCOVA was chosen to analyze the data. Nonparametric analyses of covariance have been shown to be robust to violations of normality and homoscedasticity; however, they are a somewhat liberal test of study hypotheses when sample sizes are small (Conover and Iman, 1982; Knoke, 1991; Olejnik and Algina, 1984). A power analysis was conducted and a minimum sample size of 210 participants was deemed necessary for adequate power. Considering the large sample size of the present study (n = 381), nonparametric methods were considered appropriate in this case. Participants were ranked using ties for identical SRD and SL scores.

# RESULTS

#### **Preliminary Analyses**

Basic demographic characteristics of the sample are in Table 1. BSD participants did not differ significantly from normal controls on age, t(403.33) = -.715, gender,  $\chi 2 (1) = .55$ , p = .46, or ethnicity,  $\chi 2 (1) = 2.81$ , p = .73. Compared with normal controls, BSD participants had a significantly greater number of days spent in a depressive episode over the first year of follow up, t(214.39) = 5.14, p < .001, days spent in a hypomanic/manic episode over the first year of follow up, t(201.15) = 7.18, p < .001, and lower social rhythm regularity, t(374.13) =

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-3.14, p = .002. Bipolar spectrum participants also endorsed more total qualifying life events than normal controls, t(384.23) = 4.474, p < .001. When broken down into individual classes of events, all significant differences remained (p < .009 for all analyses), indicating that BSD participants experienced more of each type of event than the control group. There were significantly more females than males within the BSD group, t(201) = 11.36, p < .001. This is consistent with other research that included similarly higher percentages of females to males within their bipolar II samples (see Cassano et al. 1992 and Depue et al. 1989 for examples). Days spent in affective episodes, trait social rhythm regularity, and total number of qualifying life events were ranked and entered as covariates in the main analyses.

#### Social Rhythm Disruption

To test for group differences in social rhythm disruption, we utilized ANCOVA on ranked variables of SRD associated with major positive, minor positive, major negative, and minor negative life events. After controlling for both days in depressive and hypomanic/manic episodes, SRM-trait scores, and total number of qualifying events, BPS participants were rated as experiencing significantly more SRD than normal controls as a consequence of both major positive life events, F(1) = 19.76, p = .043, and major negative life events, F(1) = 20.31, p < .001. BSD participants were also significantly more disrupted following both minor negative life events, F(1) = 37.73, p < .001, and minor positive life events, F(1) = 9.58, p = .002.

#### **Sleep Loss**

To test for group differences in sleep loss, we utilized ANCOVA on ranked variables of sleep loss associated with major positive, minor positive, major negative, and minor negative life events. After controlling for both days in depressive and hypomanic/manic episodes, SRM-trait scores, and total number of qualifying events, BSD participants were rated as experiencing significantly more sleep loss than normal controls as a consequence of both major negative life events, F(1) = 32.39, p < .001, and minor negative life events, F(1) = 37.46, p < .001. BSD participants also experienced significantly more sleep loss as a consequence of major positive life events, F(1) = 6.05, p = .014 and minor positive life events, F(1) = 16.92, p = < .001.

Post-hoc analyses were conducted to examine whether SRM-T regularity scores moderated the association between group and SRD and sleep loss ratings for different types of life events. No significant group by SRM-T score interactions were present for any category of life event (p > .37 for all analyses). Full ANCOVA results can be found in Tables 2 and 3. Table 4 displays the means and standard deviations of SRD and sleep loss ratings for bipolar and normal control participants.

#### DISCUSSION

The aim of this study was to determine whether individuals with bipolar spectrum disorders were more sensitive to sleep and social rhythm disrupting effects of life events than normal controls as a means of identifying the presence of a social rhythm sensitivity. Consistent with our hypotheses, we found that, when experiencing life events of the same magnitude and valence, BSD participants were rated as having significantly greater levels of social rhythm disruption and sleep loss compared to normal controls as a consequence of major positive, major negative, minor positive and minor negative life events. The fact that BSD participants experienced more social rhythm disruption and sleep loss following all life events than controls, despite controlling for group differences in trait levels of social rhythm regularity, suggests that bipolar individuals' sensitivity to disruption by events is not attributable to their lower social rhythm regularity in general.

Although the literature on the role of positive life events in bipolar disorder is sparse, what exists on this topic points toward positive life events preceding hypomanic or manic episodes. Our findings suggest that individuals with bipolar spectrum disorders experience significantly more sleep loss and social rhythm disruption following both minor and major positive events. It is possible that sleep loss and social rhythm disruption combined with the elevated mood and affect associated with a positive event may interact to incite a manic or hypomanic episode. Although a causal relationship between positive event-related sleep loss and social rhythm disruption and affective episodes was not demonstrated in this study, it is a theoretical path worth pursuing in future studies.

Research on the impact of minor life events on mood episodes and symptoms is also sparse. A key component of the social zeitgeber theory lies in the capacity of a life event to disrupt social rhythms. As a result, most studies in the literature have focused on "stressful" life events, or major life events thought to extol a large enough disruption of social rhythms to observe resultant affective symptomatology. The results of this study suggest that even minor, low-impact life events are significantly more social rhythm disrupting and sleep-loss inducing in individuals with bipolar spectrum disorders compared to normal controls. To our knowledge, this is the first study to examine the effects of these more minor, yet higher prevalence, events on social rhythms and sleep loss. However, the distinction between statistical significance and clinical significance of this finding ought to be examined in future studies. We are seeing that minor events disrupt social rhythms in BSD participants to a greater extent than controls, but we have not examined whether this increase in SRD is associated with clinically observable changes in symptoms. A longitudinal examination of a potential additive effect of SRD from minor events is warranted as positive findings could inform treatment strategies for individuals with "softer" bipolar diagnoses.

Our analyses included events that were categorized by valence and magnitude, but did not include a separate category for events deemed "social rhythm disrupting" events. Malkoff-Schwartz et al. hypothesized that social rhythm disruption may be specific to onset of manic episodes in light of their finding of comparatively more social rhythm disrupting events preceding mania onset in the 8 and 20 week pre-onset periods compared to cycling and unipolar depression participants (Malkoff-Schwartz et al., 1998). Our results, however, suggest that individuals with BSD may have a general social rhythm sensitivity that renders them more susceptible to disruption following nearly all types of life events. Although analyses of the association between life events and episode onset were not conducted in this study, our findings suggest that it may not be the specific type of event that is important, but perhaps the overall level of disruption incurred. No analyses of the number of all events reported prior to episodes were reported in the Malkoff-Schwartz et al. report, although we found in our analysis that significantly more life events were reported by bipolar spectrum participants than controls. If nearly all types of events are experienced as significantly more social rhythm disrupting in individuals with bipolar disorder, there may be an additive effect of social rhythm disruption that occurs, and it is possible that the number of events rather than a particular class of event may produce enough disruption to trigger an affective episode. This has important implications for how individuals with BSDs are treated, especially those with cyclothymia or bipolar NOS. These findings, while preliminary, would suggest that individuals with more mild bipolar presentations would still benefit from social rhythm stabilization as well as psychoeducation about their responses to seemingly benign life events or disruptions.

It is important to note that this study examined the first step of a causal chain of events leading toward affective symptomatology, and that the focus has been placed on examining an individual's susceptibility to life-event specific sleep loss and social rhythm disruption rather than an individual's susceptibility to having his or her moods disrupted by the

aforementioned disruption. It is possible that individuals with bipolar spectrum disorders may have individual differences in either or both of these characteristics. Indeed, those individuals who may be susceptible to both characteristics may be significantly more likely to experience a poorer illness course. Future studies should examine whether individuals with bipolar disorder are more likely than controls to develop mood episodes when confronted with equal levels of sleep loss or social rhythm disruption. Studies of this nature may shed light on whether there is a specific "social rhythm disruption threshold" below which affective symptoms are not generated.

It should also be noted that the connection between social rhythms and circadian biology is purely theoretical at this point and has not been tested empirically. Our results provide preliminary support for a social rhythm sensitivity in individuals with bipolar spectrum disorders, but this should not be confused with findings of a circadian rhythm sensitivity. Thus, our findings do not deviate from the theoretical path of the social zeitgeber model, but we have not confirmed circadian rhythm disruption in this sample. As recent research has produced valid methods of measuring circadian biology in ambulatory samples (namely, core body temperature) future research should test the long theorized connection between social rhythms and circadian biology.

Future studies should also examine whether and to what extent social rhythm disruption and sleep loss contribute unique variance to affective symptomatology. Social rhythm disruption and sleep loss are not mutually exclusive, and thus are highly correlated. If a relationship between life event-specific sleep loss and social rhythm disruption and mood episodes is demonstrated, it would be important to examine whether this relationship is more likely due to the SRD features of the event, the sleep loss features of the event, or an interaction of the two.

This study has several important strengths. First, life events were assessed via both selfreport and interview formats, utilizing context-based interviewer ratings of objective event impact and social rhythm disruption and sleep loss, resulting in highly reliable and valid data. The events included in the Life Events Scale were selected to accurately represent the normative spectrum of life events and thus, are highly generalizable. Furthermore, life event interviewers were blind to participants' diagnostic status, thus reducing potential rating biases. Second, this study parsed out life event-induced social rhythm disruption from trait measures of social rhythm regularity. By controlling for differences in regularity of daily routines, we were able to statistically isolate disruption specific to the occurrence of life events. Finally, the specific focus on bipolar spectrum disorders, which are more prevalent in the population than bipolar I, suggests the applicability of the social zeitgeber theory to the more mild clinical presentations seen in cyclothymia and bipolar NOS, diagnoses which comprised a good portion of our sample. As this was a younger sample with a proportion of individuals who may go on to develop more severe manifestations of bipolar disorder, our findings suggest that SRD is present in the early stages of this differentiation. While the full theorized path of the social zeitgeber theory was not examined in this study, our observations of the initial steps in these milder cases of bipolar disorder provides further support for a dimensional conceptualization of the bipolar spectrum.

There are important limitations to this study that deserve discussion. First, we conducted cross-sectional analyses, and thus, we did not examine the predictive effects of life events on social rhythm disruption or sleep loss, nor did we examine any change in these disruptions over the course of repeated assessment. As the aim of this study was to examine differences in social rhythm disruption specific to life events, a cross-sectional design was appropriate in this case. However, a longitudinal examination that allows for the analysis of the temporal relationship between these differences in social rhythm disruption and sleep loss and

affective episodes should be conducted. Moreover, due to the cross sectional design, we cannot say whether this social rhythm sensitivity contributes to the onset of bipolar spectrum disorders or whether this sensitivity is a result of the affective instability inherent in the disorder. A similar study conducted with individuals who are at-risk for the development of bipolar disorder would help resolve these temporal issues. A second limitation is the retrospective reporting of life events. Participants were required to report life events over a 4-month period rather than provide ratings of life events as they occurred. Thus, it is possible that mood-congruent memory biases may have occurred. Although the current analyses controlled for days spent in depressed or hypomanic/manic episodes in order to control for any effects of affective symptomatology on reporting, more finely tuned, temporal analyses of life events and mood episodes are again warranted. Finally, the majority of the participants in this sample were college students, thus potentially limiting the generalizability of the findings.

Bipolar spectrum disorders are complex illnesses, rife with biological and social influences that often prove difficult to disentangle. The present study attempted to introduce some clarity by examining whether individuals with BSDs are more vulnerable to social rhythm disruptions and sleep loss as a consequence of all types of life events compared to healthy individuals. Our most novel finding that even minor events, which are lower in severity but higher in frequency, still lead to higher levels of sleep loss and social rhythm disruption in BSD individuals opens the door to examinations of whether an additive effect of sleep and social rhythm disruption may contribute to subsequent mood symptomatology. Whether the underlying social rhythm sensitivity suggested in this study is present prior to illness onset should be addressed in future research.

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#### References

- Akiskal H, Bourgeois ML, Angst J, Post R, Möller HJ, Hirschfeld R. Reevaluating the prevelence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. Journal of Affective Disorders, Suppl. 2000; 1:S5–S30.
- Alloy LB, Abramson LY. The Temple-Wisconsin Cognitive Vulnerability to Depression Project: Conceptual background, design, and methods. J Cogn Psychother. 1999; 13(3):227–262.
- Alloy LB, Abramson LY, Urosevic S, Walshaw PD, Nusslock R, Neeren M. The psychosocial context of bipolar disorder: Environmental, cognitive, and developmental risk factors. Clinical Psychol Rev. 2005; 25:1043–1075. [PubMed: 16140445]
- Alloy LB, Abramson LY, Walshaw PD, Cogswell A, Grandin LD, Hughes ME, Iacoviello BM, Whitehouse WG, Urosevic S, Nusslock R, Hogan ME. Behavioral approach system (BAS) and behavioral inhibition system (BIS) sensitivities and bipolar spectrum disorders: Prospective prediction of bipolar mood episodes. Bipolar Disord. 2008; 10:310–322. [PubMed: 18271911]
- Alloy LB, Abramson LY, Walshaw PD, Cogswell A, Smith JM, Neeren AM, Hughes ME, Iacoviello BM, Gerstein RK, Keyser J, Uroševi S, Nusslock R. Behavioral approach system (BAS) sensitivity in bipolar spectrum disorders: Retrospective and concurrent behavioral high-risk design. Motiv Emot. 2006; 30:143–155.
- Alloy LB, Bender RE, Wagner CA, Abramson LY, Uroševi S. Longitudinal predictors of bipolar spectrum disorders: A behavioral approach system perspective. Clin Psychol. 2009; 16(2):206–226.
- Alloy LB, Bender RE, Whitehouse WG, Wagner CA, Liu RT, Grant DA, Jager-Hyman S, Molz A, Choi JY, Harmon-Jones E, Abramson Lyn Y. High behavioral approach system (BAS) sensitivity,

reward responsiveness, and goal-striving predict first onset of bipolar spectrum disorders: A prospective behavioral high risk design. J Abnorm Psychol. 2011 In press.

- Alloy LB, Clements CM. Illusion of control: invulnerability to negative affect and depressive symptoms after laboratory and natural stressors. J Abnorm Psychol. 1992; 101(2):234–245. [PubMed: 1583214]
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4. Washington, DC: Author; 1994. rev
- Angst J, Gamma A, Benazzi F, Ajdacic V, Eich D, Rössler W. Toward a re-definition of subthreshold bipolarity: epidemiology and proposed criteria for bipolar-II, minor bipolar disorders and hypomania. Journal of affective disorders. 2003; 73(1–2):133–46. [PubMed: 12507746]
- Axelson D, Birmaher B, Strober M, Gill MK, Valeri S, Chiappetta L, et al. Phenomenology of children and adolescents with bipolar spectrum disorders. Archives of General Psychiatry. 2006; 63:1139– 1148. [PubMed: 17015816]
- Birmaher B, Axelson D, Monk K, Kalas C, Goldstein B, Hickey MB. Lifetime psychiatric disorders in school-aged offspring of parents with bipolar disorder. The Pittsburgh bipolar offspring study. Arch Gen Psychiatry. 2009; 66:287–296. [PubMed: 19255378]
- Birmaher B, Axelson D, Strober M, Gill MK, Valeri S, Chiappetta L, Ryan N, Leonard H, Hunt J, Iyengar S, Keller M. Clinical course of children and adolescents with bipolar spectrum disorders. Arch Gen Psychiatry. 2006; 63:175–183. [PubMed: 16461861]
- Cassano GB, Akiskal HS, Savino M, Musetti L, Perugi G. Proposed subtypes of bipolar II and related disorders: With hypomanic episodes (or cyclothymia) and with hyperthymic temperament. J Affect Disord. 1992; 26:127–140. [PubMed: 1447430]
- Cassano GB, Dell'sso L, Frank E, Miniati M, Fagiolini A, Shear K, Maser J. The bipolar spectrum: A clinical reality in search of diagnostic criteria and an assessment methodology. J Affect Disord. 1999; 54:319–328. [PubMed: 10467978]
- Colombo C, Benedetti D, Barbini F, Campori E, Smeraldi E. Rate of switch from depression to mania after therapeutic sleep deprivation in bipolar depression. Psychiatry Res. 1999; 86:267–270. [PubMed: 10482346]
- Conover MJ, Iman RL. Analysis of covariance using the rank transformation. Biometrics. 1982; 38:715–724. [PubMed: 7171697]
- Depue RA, Krauss S, Spoont MR, Arbisi P. General Behavior Inventory: Identification of unipolar and bipolar affective conditions in a nonclinical university population. J Abnorm Psychol. 1989; 98:117–126. [PubMed: 2708652]
- Depue RA, Slater J, Wolfstetter-Kausch H, Klein D, Goplerud E, Farr D. A behavioral paradigm for identifying persons at risk for bipolar depressive disorder: A conceptual framework and five validation studies. J Abnorm Psychol. 1981; 90:381–437. [PubMed: 7298991]
- Ehlers CL, Frank E, Kupfer DJ. Social zeitgebers and biological rhythms. Arch Gen Psychiatry. 1988; 45:948–952. [PubMed: 3048226]
- Ellicott A, Hammen C, Gitlin M, Brown G, Jamison K. Life events and the course of bipolar disorder. Am J Psychiatry. 1990; 147:1194–1198. [PubMed: 1974746]
- Endicott J, Spitzer RA. A diagnostic interview: The Schedule for Affective Disorders and Schizophrenia. Arch Gen Psychiatry. 1978; 35:837–844. [PubMed: 678037]
- Francis-Raniere EL, Alloy LB, Abramson LY. Depressive personality styles and bipolar spectrum disorders: Prospective tests of the event congruency hypothesis. Bipolar Disord. 2006; 8(4):382– 399. [PubMed: 16879139]
- Frank E, Kupfer DJ, Thase ME, Malinger AG, Swartz HA, Fagiolini A, Grochocinski V, Houck P, Scott J, Thompson W, Monk T. Two-year outcomes for individuals with bipolar I disorder. Arch Gen Psychiatry. 2005; 62:996–1004. [PubMed: 16143731]
- Grandin LD, Alloy LB, Abramson LY. The social zeitgeber theory, circadian rhythms, and mood disorders: Review and evaluation. Clin Psychol Rev. 2006; 26:679–694. [PubMed: 16904251]
- Gruber J, Miklowitz DJ, Harvey AG, Frank E, Kupfer D, Thase ME, Sachs GS, et al. Sleep matters: sleep functioning and course of illness in bipolar disorder. Journal of affective disorders. 2011; 134(1–3):416–20. [PubMed: 21683450]

- Hunt N, Bruce-Jones W, Silverstone T. Life events and relapse in bipolar affective disorder. J Affect Disord. 1992; 25:13–20. [PubMed: 1624643]
- Hyman SE. Goals for research on bipolar disorder: The view from NIMH. Biol Psychiatry. 2000; 48:436–441. [PubMed: 11018216]
- Johnson SL. Life events in bipolar disorder: Towards more specific models. Clin Psychol Rev. 2005; 25:1008–1027. [PubMed: 16129530]
- Jones SH, Hare DJ, Evershed K. Actigraphic assessment of circadian activity and sleep patterns in bipolar disorder. Bipolar Disord. 2005; 7:176–186. [PubMed: 15762859]
- Johnson SL, Cueller AK, Ruggero C, Winett-Perlman C, Goodnick P, White R, Miller I. Life events as predictors of mania and depression in bipolar I disorder. J Abnorm Psychol. 2008; 117:268–277. [PubMed: 18489203]
- Johnson, SL.; Kizer, A. Bipolar and unipolar depression: A comparison of clinical phenomenology, biological vulnerability, and psychosocial predictors. In: Gotlib, IH.; Hammen, CL., editors. Handbook of Depression. New York: Guilford Press; 2002. p. 142-164.
- Johnson SL, Sandrow D, Meyer B, Winters R, Miller I, Solomon D, Keitner G. Increases in manic symptoms after life events involving goal attainment. J Abnorm Psychol. 2000; 109(4):721–727. [PubMed: 11195996]
- Judd LL, Akiskal HS. The prevalence and disability of bipolar spectrum disorders in the US population: re-analysis of the ECA database taking into account subthreshold cases. Journal of Affective Disorders. 2003; 73:123–131. [PubMed: 12507745]
- Kennedy SH, Kutcher SP, Ralevski E, Brown GM. Nocturnal melatonin and 24-hour 6sulphatoxymelatonin levels in various phases of bipolar affective disorder. Pyschiatry Res. 1996; 63:219–222.
- Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the national comorbidity survey replication (NCS-R). Arch Gen Psychiatry. 2005; 62:617–27. [PubMed: 15939839]
- Knoke J. Nonparametric analyses of covariance for comparing change in randomized studies with baseline values subject to error. Biometrics. 1991; 47:523–533. [PubMed: 1912259]
- Leibenluft E, Albert PS, Rosenthal NE, Wehr TA. Relationship between sleep and mood in patients with rapid-cycling bipolar disorder. Psychiatry Res. 1996; 63:161–168. [PubMed: 8878312]
- Malkoff-Schwartz S, Frank E, Anderson BP, Hlastala SA, Luther JF, Sherrill JT, Kupner DJ. Social rhythm disruption and stressful life event sin the onset of bipolar and unipolar episodes. Psychol Med. 2000; 30:1005–1016. [PubMed: 12027038]
- Malkoff-Schwartz S, Frank E, Anderson BP, Sherrill JF, Siegel L, Patterson D, Kupfer DJ. Stressful life events and social rhythm disruption in the onset of manic and depressive bipolar episodes. Arch Gen Psychiatry. 1998; 55:702–707. [PubMed: 9707380]
- Mallon JC, Klein DN, Bornstein RF, Slater JF. Discriminant validity of the general behavior inventory: An outpatient study. J Pers Assess. 1986; 50:568–577. [PubMed: 3820050]
- Mendlewicz J. Circadian variation of serum TSH in unipolar and bipolar depression. Psychiatry Res. 1982; 7:388–389. [PubMed: 6962443]
- Monk TH, Flaherty JF, Frank E, Hoskinson K, Kupfer DJ. The Social rhythm metric: An instrument to quantify the daily rythyms of life. J Ner Ment Dis. 1990; 178:120–126.
- Monk TH, Kupfer DJ, Frank E, Ritenour AM. The Social Rhythm Metric (M-SRM): Measuring daily social rhythms over 12 weeks. Psychiatry Rev. 1991; 36:195–207.
- Monk TH, Petrie SR, Hayes AJ, Kupfer DJ. Regularity of daily life in relation to personality, age, gender, sleep quality, and circadian rhythms. J Sleep Res. 1994; 3:196–205. [PubMed: 10607126]
- Nusslock R, Abramson LY, Harmon-Jones E, Alloy LB, Hogan ME. A goal-striving life event and the onset of hypomanic and depressive episodes and symptoms: Perspective from the behavioral approach system (BAS) dysregulation theory. J Abnorm Psychol. 2007; 116:105–115. [PubMed: 17324021]
- Olejnik SF, Algina J. Parametric ANCOVA and the rank transform ANCOVA when the data are conditionally non-normal and heteroscedastic. J Educ Behav Stat. 1984; 9:129–149.

- Proudfoot J, Doran J, Manicavasagar V, Parker G. The precipitants of manic/hypomanic episodes in the context of bipolar disorder: A review. Journal of affective disorders. 2010; 133(3):381–387. [PubMed: 21106249]
- Safford S, Alloy LB, Abramson LY, Crossfield AG. Negative cognitive style as predictor of negative life events in depression-prone individuals: A test of the stress generation hypothesis. J Affect Disord. 2008; 99:147–154. [PubMed: 17030064]
- Shen GC, Alloy LB, Abramson LY, Sylvia LG. Social rhythm regularity and the onset of affective episodes in bipolar spectrum individuals. Bipolar Disord. 2008; 10:520–529. [PubMed: 18452448]
- Shi J, Wittke-Thompson JK, Badner JA, Hattori E, Potash JB, Willour VL, McMahon FJ, Gershon ES, Liu C. Clock genes may influence bipolar disorder susceptibility and dysfunctional circadian rhythm. Am J Med Genet B: Neuropsychiatr Genet. 2008; 147 B:1047–1055. [PubMed: 18228528]
- Spitzer, RL.; Endicott, J. Schedule for Affective Disorders and Schizophrenia Change Version. Biometrics Research, New York State Psychiatric Institute; 1978.
- Spitzer RL, Endicott J, Robins E. Research diagnostic criteria: Rationale and reliability. Arch Gen Psychiatry. 1978; 35:221–230.
- Swartz HA, Frank E, Frankel DR, Novick D, Houck P. Psychotherapy as monotherapy for bipolar II depression: A proof of concept study. Bipolar Disord. 2009; 11:89–94. [PubMed: 19133971]
- Sylvia LG, Alloy LB, Hafne JA, Gauger MC, Verdon K, Abramson LY. Life events and social rhythms in bipolar spectrum disorders: A prospective study. Behav Ther. 2009; 40:131–141. [PubMed: 19433144]
- Szuba MP, Yager A, Guze BH, Allen EM, Baxter LR. Disruption of social circadian rhythms in major depression: A preliminary report. Psychiatry Res. 1992; 42:221–230. [PubMed: 1496054]
- Uroševi S, Abramson LY, Harmon-Jones E, Alloy LB. Dysregulation of the Behavioral Approach System (BAS) in bipolar spectrum disorders: Review of theory and evidence. Clin Psychol Rev. 2008; 28(7):1188–1205. [PubMed: 18565633]

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#### Table 1

Demographic Characteristics of Study Sample (N=381)

	BSD (n=184)		Control (n=197	
	n	%	n	%
Male	71	39.1	85	43.1
Female	113	60.9	112	56.9
Caucasian	129	70.1	139	70.6
African American	25	13.6	25	12.7
Hispanic	5	2.7	5	2.5
Asian	4	2.2	9	4.6
Native American	14	7.6	16	8.1
Other	7	3.8	3	1.5

#### Table 2

Differences in Ratings of Social Rhythm Disruption in BSD vs. Normal Controls

Variable	df	F	р	Partial $\eta^2$
Major Positive Life Event	1	19.76	.043	.011
Minor Positive Life Event	1	9.58	.002	.025
Major Negative Life Event	1	20.31	<.001	.051
Minor Negative Life Event	1	37.73	<.001	.090

#### Table 3

Differences in Ratings of Sleep Loss in BSD Participants vs. Normal Controls

Variable	df	F	р	Partial $\eta^2$
Major Positive Life Event	1	6.05	.014	.016
Minor Positive Life Event	1	16.92	<.001	.043
Major Negative Life Event	1	32.39	<.001	.079
Minor Negative Life Event	1	37.46	<.001	.090

#### Table 4

Mean (SD) Number of Life Events in BSD and Control Groups.

	Control		Bipolar Spectrum		
	SRD	SL	SRD	SL	
Major Positive Life Event	1.53 (2.42)	1.14 (2.09)	2.41 (3.46)	1.99 (2.89)	
Minor Positive Life Event	4.24 (6.06)	2.56 (4.00)	6.38 (7.47)	4.87 (6.50)	
Major Negative Life Event	1.61 (4.27)	1.46 (2.88)	4.56 (7.49)	5.35 (8.42)	
Minor Negative Life Event	7.99 (12.93)	7.45 (12.52)	20.81 (25.44)	20.14 (26.46)	