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Affective Disruption from Social Rhythm and Behavioral Approach System (BAS) Sensitivities: A Test of the Integration of the Social Zeitgeber and BAS Theories of Bipolar Disorder

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Abstract

The Behavioral Approach System (BAS)/Reward Hypersensitivity Theory and the Social Zeitgeber Theory are two biopsychosocial theories of bipolar spectrum disorders (BSD) that may work together to explain affective dysregulation. The present study examined whether BAS sensitivity is associated with affective symptoms via a) increased social rhythm disruption in response to BAS-relevant life events, or b) greater exposure to BAS events leading to social rhythm disruption and subsequent symptoms. Results indicated that high BAS individuals were more likely to experience social rhythm disruption following BAS-relevant events. Social rhythm disruption mediated the association between BAS-relevant events and symptoms (hypothesis a). High BAS individuals experienced significantly more BAS-relevant events, which predicted greater social rhythm disruption, which predicted greater levels of affective symptoms (hypothesis b). Individuals at risk for BSD may be sensitive to BAS-relevant stimuli, experience more BAS-relevant events, and experience affective dysregulation due to the interplay of the BAS and circadian rhythms.

Keywords

bipolar spectrum disorder; behavioral approach system; social rhythms; life events

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Author Contributions

Elaine M. Boland developed the study concept and contributed to data collection and database organization. Lauren B. Alloy and Lyn Y. Abramson designed the parent study and assessments from which this current analysis stems and were involved in the generation of the integrated theoretical model. Jonathan P. Stange and Denise R. LaBelle performed statistical analysis and interpretation. Elaine M. Boland, Jonathan P. Stange, Denise R. LaBelle and Benjamin G. Shapero drafted the paper. Rachel B. Weiss contributed significantly to the construction of the study database. Lauren B. Alloy provided multiple critical revisions. All authors approved the final version of the paper for submission.

Introduction

Bipolar spectrum disorders (BSD) affect approximately 4.4% to 6.7% of the population in the United States (Merikangas et al., 2007; Judd & Akiskal, 2003; Kessler, Chiu, Demler, & Walters, 2005), but are relatively understudied compared to other mental health disorders. “Softer” bipolar diagnoses, such as cyclothymia and bipolar II, have been shown to sometimes progress to more severe forms (e.g., Akiskal et al., 1977; Alloy et al., 2012b; Birmaher et al., 2009; Kochman et al., 2005), thus warranting specific attention.

BSDs are known to be highly heritable. A recent examination of monozygotic twins demonstrated concordance rates of 43%, and family history of BSD is one of the more reliable predictors of mania (Axelson et al., 2011; Birmaher et al., 2009; Kieseppä et al., 2014). However, the underlying mechanisms of BSDs are not purely genetic. Research has long supported a stress-vulnerability conceptualization of BSD, although the specifics of the types of stressors as well as the underlying vulnerabilities have differed. In an effort to inform the development of early identification tools as well as prophylactic psychosocial interventions, examinations of BSD ought to seek out areas of convergence among existing theories. Toward that end, the present study builds upon a relatively new and innovative line of research integrating two leading biopsychosocial theories of BSD: the Behavioral Approach System (BAS)/Reward Theory and the Social Zeitgeber Theory. Importantly, the present study examines the interplay of these theories in a bio-behavioral high-risk sample previously shown to be at increased risk for first onset of BSD (Alloy et al., 2012a). As such, it has the potential to contribute to an understanding of the causes of affective dysregulation in individuals vulnerable to BSD before they become ill, and thus, to the development of potential preventive interventions.

BAS/Reward Theory of Bipolar Spectrum Disorders

The BAS/reward hypersensitivity theory of BSD (Alloy & Abramson, 2010; Alloy, Abramson, Urošević, Bender, & Wagner, 2009a; Alloy, Nusslock, & Boland, 2015; Depue & Iacono, 1989; Johnson, Edge, Holmes, & Carver, 2012; Urošević, Abramson, Harmon-Jones, & Alloy, 2008) is based on Gray's (1994) conceptualization of a unified biopsychosocial system regulating orientation toward reward. BAS-activating stimuli such as goals, challenges, rewards, achievements, and associated expectancies, are theorized to initiate a chain of behavioral, cognitive and affective responses (e.g. goal-related orientation and focus, motor actions, planning, excitement). Conversely, BAS-deactivating stimuli (e.g., failure, loss) evoke behavioral, cognitive, and affective responses with corresponding but inverse properties. Individuals with BSD are thought to have a hypersensitive BAS characterized by heightened responsivity to reward-relevant stimuli. A substantial literature supports this theory (see Alloy & Abramson, 2010; Alloy et al., 2009a; 2015; Johnson et al., 2012; Urošević et al., 2008 for reviews), with several studies demonstrating that BAS hypersensitivity predicts a worse course of BSD (e.g., Alloy et al., 2008; 2009b; 2012b; Meyer, Johnson, & Winters, 2001; Salavert et al., 2007). Although not all individuals at familial high risk for developing BSD have been shown to exhibit reward hypersensitivity (see Jones et al., 2006), controlling for family history of BSD, individuals with BAS hypersensitivity, but no prior history of bipolar disorder, have been found to have a greater

likelihood and shorter time to first onset of BSD than those with more moderate levels of BAS sensitivity (Alloy et al., 2012a).

According to the BAS theory, BAS-activating and deactivating events initiate a cascade of biobehavioral responses leading to manic/hypomanic and depressive mood states, respectively (Alloy & Abramson, 2010; Alloy et al., 2009a, 2015; Johnson, 2005; Johnson et al., 2012; Meyer, Beevers, & Johnson, 2004; Urošević et al., 2008). Consistent with the theory, BAS-relevant life events have been shown to predict mood episodes in individuals with BSD (Johnson et al., 2000; 2008; Nusslock et al., 2007). Moreover, increased rates of BAS-activating and BAS-deactivating events have been observed among individuals with BSD compared to demographically similar healthy controls (Urošević et al., 2010). These findings suggest that there may be increased risk for developing bipolar mood episodes due to increased exposure to BAS-relevant events in individuals with BSD, over and above their theorized hypersensitivity to the occurrence of such events.

Social Zeitgeber Theory of Bipolar Spectrum Disorders

The Social Zeitgeber Theory (Ehlers, Frank, & Kupfer, 1988) suggests that life events disturb social zeitgebers (“time givers”), which, in turn, disturb biological rhythms, resulting in affective symptomatology in vulnerable individuals. The occurrence of life events, or the stress associated with their occurrence, disrupts daily social rhythms (such as bedtimes, mealtimes, and the beginning and ending of work), which are theorized to entrain internal circadian rhythms. In turn, the disruption of the circadian rhythms is thought to lead to depressive or manic episodes.

Several studies have reported significant associations between BSD and disrupted social rhythms (see Alloy et al., 2015; Grandin, Alloy, & Abramson, 2006, for reviews). For example, compared to sex- and age-matched healthy controls, individuals with BSD exhibit less regularity of their daily social rhythms or routines (Ashman et al., 1999; Jones, Hare, & Evershed, 2005; Shen, Alloy, Abramson, & Sylvia, 2008). Similarly, greater irregularity among bipolar participants predicts a shorter time to onset of both major depressive and hypomanic or manic episodes over prospective follow-up (Shen et al., 2008). Research also has found that life events that disrupt social rhythms predict bipolar mood episodes. Social rhythm disrupting events are more likely to precede manic episodes relative to control periods without an episode in bipolar I patients (Malkoff-Schwartz et al., 1998, 2000), and an increase in social rhythm disrupting events predicted a shorter time to onset of major depressive episodes among participants with bipolar II or cyclothymia (Sylvia et al., 2009). Moreover, in response to the occurrence of equivalent magnitude positive and negative events, individuals with BSD experienced more social rhythm disruption and sleep loss compared to healthy controls (Boland et al., 2012).

Circadian and social rhythms also have been explored in high-risk samples. Jones et al. (2006) examined aspects of cognition, mood, and sleep in a sample of children of bipolar parents and healthy controls. No differences in social rhythms were detected between groups, but children of bipolar parents exhibited a trend toward greater subjective sleep disturbance compared to healthy controls. Objective assessment via actigraphy, however, failed to yield significant differences in most sleep variables except for reduced sleep onset

latency and a trend toward longer sleep duration among high risk children. Individuals with BSDs, however, may be affected by smaller overall disruptions in circadian rhythms (i.e., possess a greater *sensitivity* to disruption) compared to healthy individuals, thus creating a scenario whereby individuals with BSD can experience objectively healthy sleep (i.e., sleep measured by actigraphy appears “normal”) as being of poor overall quality (Jones et al., 2006).

Integration of BAS/Reward and Social Zeitgeber Theories

A growing line of research suggests that the circadian and reward systems may share a bidirectional relationship. Murray and colleagues (2009) demonstrated circadian influence on the reward system, revealing a 24-hour rhythm in positive affect that was synchronous with the circadian rhythm in core body temperature in the absence of environmental variations in reward potential both with and without sleep deprivation. Moreover, circadian clock genes are expressed in brain regions associated with the reward system (e.g., ventral tegmental area, nucleus accumbens, amygdala) and dopaminergic reward circuits have been found to interact with the suprachiasmatic nucleus (SCN), the brain's “circadian pacemaker” (Murray & Harvey, 2010; Murray et al., 2009; Sleipness, Sorg, & Jansen, 2007; Yujnovsky, Hirayama, Doi, Borrelli, & Sassone-Corsi, 2006; see also Clark, Watson, & Leeka, 1989; Hasler, Allen, Sbarra, Bootzin, & Bernert, 2010; Hasler, Mehl, Bootzin, & Vazire, 2008; Murray, Allen, & Trinder, 2002; Thayer, Takahashi, & Pauli, 1988 for similar findings). These findings are consistent with the hypothesis that the circadian system modulates human reward motivation and lend credence to the existence of an integrated circadian-reward neurobiological system (Murray et al., 2009). Notably, positive affect also has been shown to disrupt sleep in bipolar samples. In a laboratory examination of sleep onset latency and REM sleep, positive mood induction was associated with increased onset latency among euthymic bipolar individuals, but no significant association was noted for healthy controls (Talbot et al., 2009).

Building upon this important conceptual foundation, the current study examined another possible overlap between the BAS/reward and social zeitgeber theories, namely that BAS-relevant life events (e.g., goal-striving) are likely to disrupt social rhythms (see Alloy et al., 2015). The present study examined whether social rhythm disruption incurred by BAS-relevant events would be associated with affective symptoms via two distinct pathways. First, we tested whether individuals with a hypersensitive BAS would exhibit greater *sensitivity* by experiencing greater social rhythm disruption when experiencing BAS-relevant life events than would individuals with more moderate levels of BAS sensitivity – a differential reactivity model (see Figure 1). We hypothesized that the social rhythm disruption associated with greater reactivity to life events would subsequently predict (hypo)manic and depressive symptoms, and that the social rhythm disruption would at least partially mediate the relationship between BAS sensitivity and symptoms. Second, we examined whether individuals with a hypersensitive BAS would experience greater *exposure* to BAS relevant events, which, in turn, would produce greater social rhythm disruption, which would then be associated with hypomanic or depressive symptoms. We hypothesized that hypersensitive BAS participants would experience more BAS-relevant events than moderate BAS participants (and thus, greater levels of event-specific social rhythm

disruption), resulting in greater affective symptoms (a differential exposure model – see Figure 2).

Method

Participants and Procedure

Participants in the present study were selected for participation in the Teen Emotion and Motivation (TEAM) Project, a longitudinal investigation of predictors of prospective onset of BSDs, at Temple University in Philadelphia, PA (Alloy et al., 2012a). All procedures were approved by the Institutional Review Board of Temple University, and all participants 18 provided written informed consent, whereas written assent and written parental consent were obtained for participants aged < 18. Adolescents (ages 14 to 19) were selected for Project TEAM based on a two-phase screening procedure. In Phase I, students (grades 9 – 12, ages 14 – 18) from 13 Philadelphia public high schools were screened, as were college students (ages 17 to 19) from two universities through the dorms and universities' online research screening systems. Following procedures in Alloy et al. (2006a), students were screened on demographics and two self-report BAS sensitivity measures: the Behavioral Inhibition System/Behavioral Activation System (BIS/BAS) scales (Carver & White, 1994) and the Sensitivity to Punishment Sensitivity to Reward Questionnaire (SPSRQ; Torrubia, Avila, Molto, & Caseras, 2001). Students scoring in the highest 15th percentile on *both* the BAS-Total scale of the BIS/BAS (high BAS-T score cutpoint 43) and Sensitivity to Reward (SR) subscale of the SPSRQ (high SR cutpoint 16) were categorized as High BAS. Participants were classified as Moderate BAS if they scored between the 40th and 60th percentiles on *both* the BAS-T (cutpoints 37 and 39) and SR (cutpoints 10.4 and 12.6) subscales. Of 9991 Phase I students, 7.77% (n=776) qualified for High BAS and 4.04% (n=404) for Moderate BAS status. The age range of 14 – 19 was chosen because it is a major “age of risk” for first onset of BSD (see Alloy et al., 2012a for review).

A subset of participants who met the Phase I criteria for the High or Moderate BAS groups were invited to participate in Phase II screening; 244 High BAS (31.4%) and 146 Moderate BAS (36.1%) students completed Phase II. In Phase II, participants were assessed with the mood and psychosis disorder sections of an expanded Schedule for Affective Disorders and Schizophrenia – Lifetime (exp-SADS-L) interview, as well as with the Beck Depression Inventory (BDI; Beck, Steer, & Brown 1996) to assess depressive symptoms and the Altman Self-Rating Mania Scale (ASRM; Altman, Hedeker, Peterson, & Davis, 1997) to assess (hypo)manic symptoms. Exp-SADS-L interviewers were blind to participants' BAS risk group.

Exclusion criteria from the final sample were: 1) a *DSM-IV-TR* (American Psychiatric Association, 2000) or Research Diagnostic Criteria (RDC; Spitzer et al., 1978) diagnosis of any BSD (Bipolar I, Bipolar II, Cyclothymia, Bipolar NOS – defined as either a diagnosable hypomanic episode without diagnosable depressive episodes or cyclothymic mood pattern falling below duration (<2 day) or frequency (>1 year) thresholds) or a hypomanic episode with onset prior to the participant's Phase I screening date, and 2) any lifetime psychotic disorder (Schizophrenia, Schizoaffective Disorder, Major Depressive Disorder/Manic episode with psychosis). Participants who lacked fluency in English also were excluded.

They were not excluded if they met criteria for a non-psychotic *DSM-IV-TR* or RDC major depressive or RDC minor depressive episode with onset prior to Phase I screening, because prior depressive episodes without mania or hypomania may reflect unipolar depression rather than bipolar disorder. Further details of the sample screening and selection criteria and evidence that the final sample was representative of both the Phase I and Phase II screening samples may be found in Alloy et al. (2012a).

At the time of this report, complete data including diagnoses, symptom data, and life events data for the first follow-up period (average of 8.4 months) were available for 204 participants (71% female, 29% male; Mean age = 18.09 [SD = 1.53]), 119 in the High BAS group, and 85 in the Moderate BAS group. The sample was 55% Caucasian/White, 29% African American/Black, 13% Asian, 1% Native American, 1% Hispanic/Latino, and 2% Other race.

The present sample did not differ from the Phase II screening sample on age ($t(289) = -0.69, p = .49$), gender ($\chi^2(1) = 1.27, p = .26$), race ($\chi^2(7) = 9.98, p = .19$), or ethnicity ($\chi^2(1) = 0.02, p = .88$). The risk groups in the final sample did not differ significantly from each other on age ($t(202) = 1.70, p = .08$), gender ($\chi^2(1) = 1.38, p = .24$), race ($\chi^2(1) = 2.53, p = .28$), or ethnicity ($\chi^2(1) = 11.19, p = .13$).

At follow-up assessment, participants completed symptom questionnaires and a Life Events Scale (LES; Francis-Raniere, Alloy, & Abramson, 2006 - see measures), in which they indicated whether or not they experienced each of 193 specified life events, as well as the number of times each event occurred since baseline. A Life Events Interview (LEI; Francis-Raniere et al., 2006) also was administered at follow-up to obtain more detailed information about the life events, the events' dates of occurrence, and information on levels of social rhythm disruption associated with each event.

Measures

The Behavioral Inhibition System/Behavioral Activation System (BIS/BAS) Scale—The BIS/BAS Scale (Carver & White, 1994) is a widely used, 20-item, self-report measure that assesses individual differences in BIS and BAS sensitivities. The scale includes three BAS subscales and one BIS subscale and all items are rated on 4-point Likert scales. A BAS-Total score also may be calculated as the sum of all BAS items. This total score was used as part of the screening criteria for selecting the High and Moderate BAS groups. The BIS/BAS scales have demonstrated internal consistency and retest reliability (Carver & White, 1994), as well as construct validity, exhibiting expected associations with affect, personality traits, and performance on reaction-time and learning tasks involving incentives (Colder & O'Connor, 2004; Kambouroupolis & Staiger, 2004; Zinbarg & Mohlman, 1998). Internal consistencies of the BAS-Total score and BIS scale in the Phase I screening sample were α 's = .80 and .72, respectively.

Sensitivity to Punishment Sensitivity to Reward Questionnaire (SPSRQ)—The SPSRQ (Torrubia et al., 2001) is another measure of BIS and BAS sensitivities designed to include items that focus on sensitivity to specific types of rewards and punishments, whereas the BIS/BAS Scale items focus on generalized sensitivity to punishment and

reward. The SPSRQ has 24 sensitivity to reward and 24 sensitivity to punishment “yes” or “no” items that assess BAS and BIS sensitivity, respectively. Both subscales have acceptable internal consistency, with α 's = .75-.83 (Torrubia et al., 2001). In Phase I of this study, α 's for the SR and SP scales were .76 and .84, respectively. Three-month retest reliabilities are .87 for the SR and .89 for the SP scale (Torrubia et al., 2001). BAS-T and SR scores correlated $r = .40$ in our Phase I sample.

Schedule for Affective Disorders and Schizophrenia – Lifetime—The Schedule for Affective Disorders and Schizophrenia – Lifetime (SADS-L; Endicott & Spitzer, 1978) is a semi-structured diagnostic interview used in Phase II of screening to assess current and lifetime history of Axis I disorders. The mood disorders and psychosis sections of an expanded SADS-L (exp-SADS-L; see Alloy et al., 2008; Nusslock et al., 2007) were given during Phase II to determine eligibility for the final Project TEAM sample and the remainder of the interview was given to the final sample at the baseline (Time 1) assessment. The expanded SADS-L assesses the occurrence, duration, and severity of symptoms related to mood, anxiety, eating, substance use, and psychotic disorders over an individual's lifetime. Specific alterations were made to the SADS-L to obtain project-specific information and included: 1) additional probes to allow for *DSM-IV-TR* 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 medical history, family history, and organic rule-out conditions. Project interviewers were blinded to participants' BAS risk group and Phase I BIS/BAS and SPSRQ scores. The exp-SADS-L has demonstrated excellent inter-rater reliability, with $\kappa > .90$ for unipolar depression diagnoses based on 80 jointly rated interviews (Alloy et al., 2000) and $\kappa > .96$ for BSDs based on 105 jointly rated interviews (Alloy et al., 2008). Further details regarding the exp-SADS-L administration and diagnoses for Project TEAM may be found in Alloy et al. (2012a).

Life Events Scale and Life Events Interview—Life events were assessed at follow-up via a combination of self-report and interview. Expanded from an earlier 134-item version, the 193-item Life Events Scale (Francis-Raniere et al., 2006) assessed positive and negative life events that occurred since baseline. Items were carefully selected to reduce ambiguity and were removed if considered too directly reflective of affective symptomatology. The Life Events Scale demonstrates good reliability and validity (Francis-Raniere et al., 2006; Safford, Alloy, Abramson, & Crossfield, 2007), and also was utilized in the LIBS Project, a multi-site longitudinal study that involved the same setting and administrators as the current project (see Alloy et al. 2008). Each item on the Life Events Scale 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.

In the present study, we examined two distinct categories of BAS-relevant events: BAS Activating events (e.g., “Began a relationship with new boyfriend/girlfriend/spouse”) and BAS Deactivating events (e.g., “Laid off or fired from job”). Events were categorized *a priori* based on levels of BAS-activation (i.e., the degree to which the event involved goal-

striving, opportunity to obtain goals/rewards, or overcoming challenges to goals/rewards) and BAS–deactivation (i.e., the degree to which the event triggers cessation of approach, and/or represented a loss or failure to obtain rewards/goals) (see Uroševi et al., 2010). Three raters utilized a 4-point Likert scale ranging from 0 (not at all) to 3 (extremely) to categorize the events across these two dimensions. Reliability of BAS ratings was high (Cronbach's $\alpha = .79$ for BAS activation, and $.94$ for BAS deactivation (Uroševi et al., 2010).

Following the completion of the Life Events Scale, participants completed a Life Events Interview that elicited detailed information about the events endorsed on the Life Events Scale and dated their occurrence. Life events interviewers were blind to BAS risk group status, BIS/BAS, SPSRQ, and exp-SADS-L diagnostic status. The Life Events Interview 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 Life Events Interview assessed levels of social rhythm disruption associated with each life event. Social rhythm disruption 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 from sleep that was irrespective of the total amount of actual sleep the participant had following the event). Importantly, social rhythm disruption does not represent a different category of “schedule disrupting events,” but rather reflects the degree to which any event the participant experienced during the follow-up period disrupted daily routines. Ratings for social rhythm disruption ranged from 1 (*little to no effect*) to 4 (*marked effect*) and were designed to reflect the acute impact of life events on social rhythms. For the current analyses, social rhythm disruption scores were re-coded into dichotomous “yes/no” scores (ratings of 1 were recoded to 0, and ratings of 2 – 4 were recoded to 1). Event-specific social rhythm disruption was calculated by summing the interviewer-assessed social rhythm disruption scores for each event category. For example, if a participant reported 3 BAS Activating events with recoded social rhythm disruption ratings of 0, 1, and 1 respectively, that participant would have a social rhythm disruption score of 2 for that category.

The combination of the Life Events Scale and Life Events Interview results in greater accuracy of reporting of life events. Francis-Raniere et al. (2006) 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 and 80% of minor life events utilizing the combined Life Events Scale and Life Events Interview approach. Average inter-rater reliability for the dating of life events was $.89$, based on 40 LEIs reviewed in the same study (see Francis-Raniere et al., 2006).

Beck Depression Inventory—The BDI (Beck, Steer & Brown, 1996) has 21 items assessing the severity of affective, cognitive, motivational, and somatic symptoms of depression. It has good internal (α 's = $.81$ -. $.86$) and retest reliability (r 's = $.48$ -. $.86$) and validity in nonclinical samples (Beck, Steer, & Garbin, 1988). In our Phase II sample, $\alpha = .87$.

Altman Self Rating Mania Scale—The ASRM (Altman et al., 1997) has 5 items rated on 5-point Likert scales that assess five symptoms of (hypo)mania: inflated self-confidence, talkativeness, elation, reduced need for sleep, and excessive activity. ASRM items load on a single factor and ASRM scores are highly correlated with both clinical interview and other self-report mania measures (Altman, Hedeker, Peterson, & Davis, 2001). In our Phase II sample, $\alpha = .75$.

Internal States Scale—The Internal States Scale (ISS; Bauer et al., 1991) is a 15-item self-report measure that discriminates internal mood states and tracks depressive and manic symptoms. The ISS contains four subscales: Activation, Well-Being, Perceived Conflict, and Depression. The ISS shows good discriminant validity; the Depression Index correlates highly with the Hamilton Rating Scale for Depression (Hamilton, 1960), whereas the Activation Index score correlates highly with clinician ratings of mania (Bauer et al., 1991) and has been used in numerous studies of BSD to reflect manic and hypomanic symptomatology (Harmon-Jones et al., 2008; Nusslock et al., 2012; Jones et al., 2014). The ISS was included in follow-up assessments to address research suggesting increased activity is a central symptom of mania (Cheniaux et al., 2014). The version of the ISS used in this study used a 5-point Likert scale as opposed to a 1-10 visual analog scale for increased feasibility (Meyer, Johnson, & Carver, 1999). Both the Depression and Activation indices were used in the present analyses. The ISS was administered at the follow-up assessment.

Statistical Analyses

We first evaluated BAS risk group differences in study variables using t-tests. To evaluate whether High BAS participants, relative to Moderate BAS participants, were more reactive to BAS-activating and BAS-deactivating life events in the form of social rhythm disruption, we conducted hierarchical linear regressions and probed significant interactions using the procedures recommended by Aiken and West (1991). To evaluate whether these reactivity pathways predicted greater levels of prospective symptoms of hypomania and depression, we conducted moderated mediation analyses using the bootstrapping procedure described by Preacher and Hayes (2008). Bootstrapping was conducted using 1000 re-samples and a 95% confidence interval. Because the ISS was not administered until after the Phase II baseline visit, when predicting ISS symptoms of activation and depression, we controlled for levels of the respective symptom type at baseline using other measures (i.e., ASRM or BDI, respectively).

To test the hypothesis that High BAS individuals would experience greater prospective levels of mood symptoms as a result of greater exposure to BAS-activating and BAS-deactivating events and subsequent social rhythm disruption, we employed path analyses using Hayes's (2013) conditional processing model, using bootstrapping with 1000 re-samples and a 95% confidence interval, while controlling for the relevant type of mood symptoms at baseline.

Results

Preliminary Analyses

We first evaluated whether High BAS and Moderate BAS groups differed on the study variables. Relative to Moderate BAS participants, High BAS individuals had more BAS-activating events (High BAS $M = 102.77$ (122.02); Moderate BAS $M = 69.63$ (64.93)), $t(183.56) = 2.69$, $p < .01$, more BAS-deactivating events (High BAS $M = 52.04$ (98.42); Moderate BAS $M = 27.55$ (25.74)), $t(138.89) = 2.51$, $p = .01$, greater social rhythm disruption from BAS-activating events, $t(149.81) = 2.87$, $p < .01$, greater social rhythm disruption from BAS-deactivating events, $t(139.62) = 2.34$, $p = .02$, greater levels of baseline hypomanic symptoms on the ASRM, $t(188.44) = 3.57$, $p < .001$, greater levels of hypomanic symptoms on the ISS at follow-up, $t(201.62) = 4.14$, $p < .001$, and marginally greater levels of baseline depressive symptoms on the BDI, $t(188.16) = 1.91$, $p = .06$, but did not differ significantly on depressive symptoms on the ISS at follow-up, $t(189.51) = 1.12$, $p = .26$. ISS scores ranged from 5 to 24 for activation, and from 2 to 10 for depression. ISS activation was significantly correlated with baseline ASRM ($r = .29$, $p < .001$); and ISS depression was significantly correlated with baseline BDI scores ($r = .43$, $p < .001$). Mean ISS activation and depression scores were 9.8 and 2.7 respectively, representing hypomanic symptoms on the lower end of the clinical range and depressive symptoms in the subclinical range¹.

Given that this study examined event-specific social rhythm disruption, and that life events are the predominant source of social rhythm disruption in both the BAS/reward hypersensitivity and social zeitgeber theories, life events and social rhythm disruption were expected to be correlated by definition. Accordingly, BAS-Deactivating events shared 55% of variance with subsequent social rhythm disruption, and BAS-Activating events shared 42% of variance with subsequent social rhythm disruption, likely representing common method variance as well as the necessary relatedness of the two indices. Participants' reporting of social rhythm disruption remained relatively stable over time, with an average monthly decline of roughly 3% per month.

Stress Reactivity Analyses

To examine whether High BAS individuals were more likely than Moderate BAS individuals to experience social rhythm disruption following BAS-activating and BAS-deactivating events, we conducted hierarchical linear regressions. Consistent with our reactivity hypotheses, there was a significant interaction between BAS group and BAS-activating events predicting social rhythm disruption, $t = 3.04$, $p < .005$, $R^2 = .68$, such that BAS-activating events predicted greater social rhythm disruption among High BAS individuals, $t(200) = 12.45$, $p < .0001$, than among Moderate BAS individuals, $t(200) = 1.96$, $p = .05$ (Figure 3a). Although only trending toward significance, there was a similar interaction between BAS group and BAS-deactivating events predicting social rhythm disruption

¹The ISS version in this study utilized a 5 point Likert scale as opposed to a 1-100 bin scoring system in the original version. This was incorporated for increased feasibility in an adolescent sample and has precedent in the literature (Meyer, Johnson, & Carver, 1999). The benchmarks are identical to the Bauer version (Bauer et al., 2000), only scaled down to reduced absolute minimum/maximum scores. For example, the bin scoring system has a threshold of 155 for Activation out of a maximum possible score of 500. This translates to 31% of the possible score. Our version's maximum score for activation is 25, with 31% translating to a cutoff of 7.75 for activation.

following BAS-deactivating events, $t = 1.75$, $p = .08$, $R^2 = .75$, such that BAS-deactivating events predicted significantly greater social rhythm disruption among High BAS individuals, $t(200) = 15.43$, $p < .0001$, but not among Moderate BAS individuals, $t(200) = 1.54$, $p = .13$ (Figure 3b). These results generally support the reactivity hypothesis that relative to Moderate BAS individuals, High BAS individuals were more likely to experience social rhythm disruption following BAS-activating and BAS-deactivating events.

Simple slopes tests also indicated that relative to Moderate BAS individuals, High BAS participants experienced significantly greater social rhythm disruption when experiencing high levels of BAS-activating events ($t(200) = 3.22$, $p < .005$), but not when experiencing low levels of BAS-activating events ($t(200) = -1.52$, $p = .13$). Similarly, relative to Moderate BAS individuals, High BAS participants experienced a trend toward greater social rhythm disruption when experiencing high levels of BAS-deactivating events ($t(200) = 1.86$, $p = .06$), but not when experiencing low levels of BAS-deactivating events ($t(200) = -1.28$, $p = .20$). These results suggest that BAS sensitivity was most influential in leading to social rhythm disruption in the context of events that activated or deactivated the BAS.

Consistent with differential reactivity hypotheses and the integrated Reward/Circadian Rhythm theory, moderated mediation analyses (Figure 1a) indicated that event-specific social rhythm disruption mediated the association between BAS-activating events and prospective hypomanic symptoms, and this pathway was stronger among High BAS individuals than among Moderate BAS individuals.² Similarly, although the interaction between BAS group and BAS-deactivating events predicting social rhythm disruption was only trending toward significance, moderated mediation analyses indicated that event-specific social rhythm disruption mediated the association between BAS-deactivating events and prospective depressive symptoms, and this pathway was stronger among High BAS individuals (Figure 1b).

Stress Exposure Analyses

Consistent with the differential stress exposure hypotheses, path analyses indicated that relative to Moderate BAS individuals, High BAS individuals experienced significantly more BAS-activating events, which predicted greater BAS activating event-specific social rhythm disruption, which predicted greater prospective levels of hypomanic symptoms, and the indirect effect of BAS group on hypomanic symptoms through BAS-activating events and subsequent social rhythm disruption was significant (Figure 2a).³

High BAS individuals also experienced more BAS-deactivating events, which predicted BAS deactivating event-specific social rhythm disruption, which predicted greater

²In order to be certain that activation symptoms were not reflective of anxiety, we repeated the above analyses controlling for current or lifetime history of anxiety disorder, sensitivity to punishment on the SPSRQ (to represent trait anxiety), and behavioral inhibition on the BIS measure (also representative of trait anxiety). When doing so, the indirect effects in the reactivity model predicting ISS Activation remained significant (Low Risk: $B = .002$, $CI = .0001 - .006$; High Risk: $B = .004$, $CI = .0003 - .009$), indicating that increases in activation as measured by the ISS were not better explained by anxiety symptoms.

³In order to be certain that activation symptoms were not reflective of anxiety, we repeated the above analyses controlling for current or lifetime history of anxiety disorder, sensitivity to punishment on the SPSRQ (to represent trait anxiety), and behavioral inhibition on the BIS measure (also representative of trait anxiety). When doing so, the indirect effects in the exposure model predicting ISS Activation remained significant ($B = .108$, $CI = .003 - .355$), indicating that increases in activation as measured by the ISS were not better explained by anxiety symptoms.

prospective levels of depressive symptoms, and the indirect effect of BAS group on depressive symptoms via BAS-deactivating events and subsequent social rhythm disruption was significant (Figure 2b). However, there was not a significant direct effect of BAS risk group on prospective levels of depressive symptoms, providing mixed support for the BAS-deactivation test of the exposure model.

Although BAS risk group predicted a relatively small amount of variance in prospective symptoms, the effects of event-specific social rhythm disruption on symptom levels was moderate, suggesting that social rhythm disruption could play an important role in the development of mood dysregulation. Overall, these results provide evidence that High BAS individuals may be vulnerable to experiencing greater levels of bipolar mood symptoms in part due to both greater exposure and greater reactivity to BAS-activating and BAS-deactivating life events and corresponding social rhythm disruption.

Discussion

The aim of this study was to integrate aspects of the BAS/reward hypersensitivity and social zeitgeber theories of BSD to obtain a more comprehensive understanding of the development of affective symptoms in individuals at high behavioral risk of developing BSDs. Overall, our findings support the integration of these two theories as presented in the integrated Reward/Circadian Rhythm theory (Alloy et al., 2015). Taken together, we propose a more unified theory that suggests that individuals with high BAS sensitivity tend to experience: 1) increased exposure to BAS-relevant life events, and 2) increased social rhythm disruption when they experience BAS-relevant events compared to individuals with more moderate BAS sensitivity. Upon experiencing these events, the resultant social rhythm disruption leads to depressive or hypomanic symptoms. This integrated theory suggests a tendency to experience a large number of BAS-relevant stimuli coupled with a heightened sensitivity to the occurrence of these BAS-relevant stimuli in the form of social rhythm disruption.

Although on the surface these two components may appear similar, we believe they represent important distinctions that have particular relevance to the treatment and prevention of BSD onset and relapse. To illustrate the differential reactivity model, consider an individual who is experiencing financial strain and is pursuing a job (a BAS-activating event). Individuals with a hypersensitive BAS will be more reactive to such events and may engage in more aggressive goal-striving, including behaviors such as staying up all night working on a resume or looking for and responding to job advertisements. These behaviors may disrupt daily routines and affect regularity of bedtimes and mealtimes, etc., leaving high BAS individuals susceptible to mood dysregulation as a consequence of these marked changes in routine (see Alloy et al., 2015; Nusslock et al., 2009). Treatment strategies that provide specific emphasis on psychoeducation about the routine-disrupting effects of extreme goal-striving behavior could be efficacious in buffering against the development of depressive or hypomanic symptoms by helping individuals with BSDs maintain regular routines. Indeed, schedule regularity is a cornerstone of Interpersonal and Social Rhythm Therapy (IPSRT; Frank et al. 2005). Findings from this study suggest that emphasizing the potent schedule disrupting capacity of reward-relevant events could be particularly useful.

We also found that individuals with a hypersensitive BAS are prone to engaging in greater numbers of BAS-relevant events, which produces greater social rhythm disruption, which leads to affective symptoms (differential exposure model). In keeping with the previous example, pursuit of a job could involve repeated exposure to BAS-deactivating events (e.g., unsuccessful interviews, unreturned job inquiries) as well as increased rates of BAS-activating events (e.g., promising job leads, positive appraisals of work-related potential) which bring with them increased opportunities for social rhythm disruption. These findings are consistent with prior work extending the stress generation theory to bipolar samples (Bender et al., 2010; Urošević et al., 2010; Weiss et al., 2015), and extend stress generation further to individuals at risk for developing BSD based on BAS/reward hypersensitivity. Individuals with or at risk for BSD may not only be unduly reactive to the events that occur in their lives, but they also may actively contribute to their occurrence (Bender et al., 2010; Molz et al., 2014; Urošević et al., 2010). Given that individuals' BAS hypersensitivity is a risk factor for the development of BSD (Alloy et al., 2012a), this sensitivity may pull them toward increased exposure to BAS-relevant life events, which, in turn, generates increased social rhythm disruption leading to symptom onset. From a treatment perspective, psychoeducation about the ways in which individuals with BSDs may play a part in generating more opportunities for social rhythm disruption would be as important as knowledge about their tendency to be more sensitive to its effects. Indeed, knowledge about the ways in which individuals may work to control their exposure to social rhythm disruption may help to confer a sense of agency and control over their disorder, which may translate into better treatment adherence as well as improved functioning.

The present analysis examined symptoms, not episodes, of depression and hypomania, and overall, the symptoms exhibited were in the low clinical/subthreshold range. This is important because our present analyses demonstrate meaningful relationships between reward sensitivity, social rhythm disruption, and affective symptoms in a non-clinical sample specifically chosen to have no current or past BSD, but demonstrated to be at risk for future onset of BSD (Alloy et al., 2012a). The interrelationships between reward sensitivity, social rhythm disruption, and symptoms may be even stronger in individuals with bipolar disorder. Indeed, our effect sizes were modest and mediation was partial, suggesting that other factors should be explored within this integrated theory (e.g., genetic contributors) and among individuals with BSD. Nevertheless, these findings highlight the need for 1) earlier intervention for high-risk adolescents and 2) more comprehensive assessments of risk that go beyond family history to include elements of reward responsivity. Moreover, findings from this study can help inform modifications to treatments for high-risk individuals (e.g., Interpersonal and Social Rhythm Therapy for adolescents [IPSRT-A; Goldstein et al., 2014]) that are currently in development. A core focus of IPSRT-A, like its adult counterpart IPSRT, is on stabilization of social rhythms. Pilot data from a sample of adolescents at high genetic risk for bipolar disorder suggest the treatment is well-tolerated and potentially efficacious (Goldstein et al., 2014). In their report of findings, the authors noted that the effects of the academic year on adolescents' sleep/wake cycles should be explored as this was a limitation of their analysis. Indeed, reward hypersensitivity would be a particularly useful lens through which to explore the impact of the academic school year on sleep/wake cycles given the

preponderance of goal-striving, achievement, and loss associated with academics (e.g., Nusslock et al., 2009).

This study has several important strengths. First, these results are particularly important because they demonstrate social rhythm disruption in a bio-behavioral high-risk sample rather than a clinical sample with BSDs, and thus, suggest further mechanisms that may be involved in the onset of BSD. Moreover, the integrative approach to analysis highlighted areas of convergence of established biopsychosocial theories, thus opening the door to further examinations of bipolar psychopathology that encompass a broader, integrated understanding of dysregulation. Second, life events were assessed via both self-report and interview formats, utilizing context-based interviewer ratings of objective event impact and social rhythm disruption. Moreover, the events included in the Life Events Scale were selected to accurately represent the normative spectrum of life events, and thus, add to the generalizability of our findings. Life event interviewers were blind to participants' BAS risk group and symptom status, thus reducing potential rating biases. Finally, the use of a behavioral high risk sample allowed for prospective analysis of the effects of event-specific social rhythm disruption on mood symptoms in individuals with no previous history of BSD, but known to be at risk for developing BSD in the future.

There are limitations to this study that should be noted as well. As mentioned above, our sample consisted of high school and college students, which may limit generalizability of our findings to the adult population. However, our sample was drawn from the community and spanned the target age range for first onset of BSD, making our findings important and germane to the study of BSD onset. A second limitation is that participants were required to report life events over a several month period rather than provide reports of life events as they occurred. Thus, mood-congruent memory biases may have occurred, although disqualification of events that did not meet definitional criteria by the interviewers helped to address potential report biases, and recall accuracy for events was good. More finely tuned analyses of life events and mood episodes and symptoms, ideally conducted in real time, are warranted. In addition, the Life Events Interview, although strengthened by its multi-method approach and direct prompts about disruptions to sleep/wake cycles, did not encompass other aspects of daily life (e.g., house guests, construction noise) that do not fit neatly in the category of "life events," thus preventing a more comprehensive understanding of how life events impact social rhythms. Future studies should incorporate additional ecologically valid measures of schedule disruption and daily hassles. Another limitation was that the ISS was included only at follow-up assessment, and thus, different measures of hypomanic and depressive symptoms were used to control for baseline symptomatology. Given the difference in instruments, the results should be interpreted with some caution, as there is the possibility that more of the variance in the ISS outcome variables would have been accounted for if we had controlled for baseline ISS scores. Next, our measures of life events and event-specific social rhythm disruption were necessarily moderately correlated, raising the possibility that shared method variance in part accounted for the observed relationships. Finally, our study did not disentangle social rhythms from circadian rhythms. The association between circadian and social rhythm disruption has yet to be solidified empirically, and thus, we cannot make claims about biological disruption based upon our findings. Studies examining the disruption of circadian biology as a consequence of life

events and reward sensitivity would help elucidate the biological associations between the reward and circadian systems in individuals with or at risk for bipolar spectrum disorder.

In conclusion, our findings support a more unified theory of the pathogenesis of bipolar mood symptoms that takes into account both reward and social rhythm sensitivity (Alloy et al., 2015). Individuals vulnerable to BSDs may be prone to experiencing greater numbers of and reacting more strongly to BAS-relevant life events, from which the resultant social rhythm disruption may contribute to the generation of mood symptoms. Further research into the developmental trajectory of both BAS and social rhythm sensitivities may aid in the development of early interventions for these individuals.

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A

B

Figure 1.
Moderated mediation analyses with bootstrapping evaluating the differential reactivity hypothesis of social rhythm disruption (SRD) leading to prospective symptoms of (a) activation and (b) depression.

Figure 2.

Path analyses with bootstrapping evaluating the differential exposure hypothesis of behavioral approach system (BAS) risk group predicting (a) BAS-activating life events, leading to social rhythm disruption (SRD) and prospective symptoms of activation, and (b) BAS-deactivating life events, leading to social rhythm disruption (SRD) and prospective symptoms of depression.

Figure 3.

Interactions between Behavioral Approach System (BAS) Group and (a) BAS-activating events, and (b) BAS-deactivating events, predicting event-specific social rhythm disruption.

* $p < .05$.