THE LONG-TERM COURSE OF BIPOLAR SPECTRUM DISORDER: APPLICATIONS OF THE BEHAVIORAL APPROACH SYSTEM (BAS) MODEL

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ABSTRACT

The Long-Term Course of Bipolar Spectrum Disorder: Applications of the Behavioral Approach System (BAS) Model

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In this study, I tested predictions of the Behavioral Approach System (BAS) model as applied to the course of bipolar spectrum disorders. In this model, when a vulnerable individual experiences a BAS activation-relevant event, the weak regulatory strength of the BAS interacts with pre-event BAS state and is likely to lead to hypomania/mania. In contrast, when a vulnerable individual experiences a BAS deactivation-relevant event, the weak regulatory strength of the BAS interacts with pre-event BAS state and is likely to lead to depression. A secondary goal of this study involved comparing the BAS model to the cognitive-vulnerability stress model of bipolar disorder. Toward this end, data from a sample of 217 individuals (112 individuals with a diagnosis in the bipolar spectrum and 105 demographically similar, normal controls) participating in the Longitudinal Investigation of Bipolar Spectrum Disorders (LIBS) Project, a two-site prospective examination of the role of BAS, cognitive styles, and life events in the course of bipolar disorders among college students, were analyzed.

The results of this study suggest that there is some support for both the BAS model and the cognitive-vulnerability stress model. Specifically, BAS-relevant cognitive styles, in interaction with congruent positive life events, predicted hypomanic episodes.

There was less support for either model in the prediction of depression. There was some support for BAS sensitivity and BAS-relevant events each predicting the course of bipolar disorder. However, there was no support for the interaction of BAS sensitivity and BAS-relevant events predicting the type and number of mood episodes. As such, this study found more support for a BAS-related cognitive vulnerability-stress model, as compared to the "pure" BAS model, as applied to bipolar spectrum disorders.

Following a review of the results, strengths and limitations, as well as clinical implications and potential future research directions are discussed.

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CHAPTER 1

INTRODUCTION

Bipolar disorder, occurring in 4.4% of the population (Merikangas et al., 2007), has steep economic and social costs. It often has a severe course that involves significant impairment in many areas of functioning. Indeed, bipolar disorder is the sixth leading cause of disability among physical and psychiatric disorders worldwide (Murray & Lopez, 1996). Within the bipolar category, a group of disorders appears to form a spectrum of severity from the milder cyclothymia, to bipolar II disorder, to full-blown bipolar I disorder (Akiskal, Djenderedjian, Rosenthal, & Khani, 1977; Birmaher et al., 2009; Cassano et al., 1999; Depue et al., 1981; Goodwin & Jamison, 1990; Shen, Alloy, Abramson, & Sylvia, 2008). This dissertation studied the full range of bipolar spectrum disorders to gain a fuller picture of the course of the disorder.

The course of bipolar disorder tends to be predominantly depressive, have an early onset, and include numerous episode recurrences (Goodwin & Jamison, 1990). In general, manic episodes tend to begin more abruptly than depressive episodes. Bipolar I mood episodes tend to last between 1 and 13 months, with studies finding longer mood episodes occurring before psychiatric medications were available (Goodwin & Jamison, 1990; Miller, Uebelacker, Keitner, Ryan, & Solomon, 2004). Episode duration may also vary by type of episode, with depressive episodes often lasting much longer than manic or hypomanic episodes (Kawa et al., 2005).

Evidence suggests that stressful life events, such as getting divorced or losing one's job, play a large role in predicting the course of bipolar disorder. Specifically, studies have found that individuals with a diagnosis in the bipolar spectrum tend to

experience stressful life events prior to the onset of episodes of the disorder (Alloy, Abramson, Neeren, et al., 2006; Alloy, Abramson, et al., 2005; Alloy, Reilly-Harrington, Fresco, & Flannery-Schroeder, 2005; Johnson, 2005a; Johnson & Kizer, 2002). In addition, it appears that negative life events play a role in predicting recovery and relapse, especially from depressive episodes. Although independent severe negative life events are not common before manic/hypomanic episodes, goal-attainment and goal-striving life events (such as getting an "A" on an exam), specifically, have been found to predict increases in manic/hypomanic symptoms and episodes (Johnson, Sandrow, et al., 2000; Johnson et al., 2008; Nusslock, Abramson, Harmon-Jones, Alloy, & Hogan, 2007).

Another factor that has been shown to influence the course of bipolar disorder is the Behavioral Approach System (BAS), a motivational system in the brain that may be dysregulated in individuals with bipolar disorder (Depue & Iacono, 1989)[1]. There is evidence that extreme fluctuations in activation and deactivation of the BAS may lead to episodes of mania, hypomania, and depression, characteristic of bipolar disorder (Alloy, Abramson, Walshaw, Cogswell, et al., 2006; Alloy, Abramson, Urosevic, Bender, & Wagner, 2009). Another motivational system in the brain, the Behavioral Inhibition System (BIS), is believed to regulate withdrawal and/or inhibition of behavior in response to threat, punishment, and non-reward (Fowles, 1988; Gray, 1991). There is some evidence that BIS sensitivity may be associated with depression; Alloy et al. (2008) found that BIS sensitivity marginally predicted a shorter time to onset of major depressive episodes when controlling for initial symptom levels. However, this paper

[1] BAS dysregulation may not be specific to bipolar disorder, but the focus of this dissertation will be on bipolar disorder only.

will focus on the BAS because theory and research have stressed its importance in the bipolar spectrum disorders.

Researchers have also investigated the neurological underpinnings of the BAS. Depue and Collins (1999) hypothesized that the BAS involves dopaminergic (DA) projections from the A10 nucleus in the ventral tegmental area (VTA) to the frontal cortex, amygdala, nucleus acumbens, ventral palladium, septum, and hippocampus, with the DA activity in the nucleus acumbens playing the central role. Additionally, considerable evidence suggests that left frontal cortical activity is a neurophysiological index of BAS activity (Davidson, Jackson, & Kalin, 2000; Harmon-Jones & Allen, 1998; Sobotka, Davidson, & Senulis, 1992; Sutton & Davidson, 1997). Specifically, Harmon-Jones et al. (2008) found that individuals with a diagnosis in the bipolar spectrum exhibited greater relative left frontal cortical activation to a challenging goal-striving (BAS-activating) task, compared to control participants. The authors also found that current manic symptoms predicted increased left frontal activation to the tasks.

Furthermore, these results fit well with conceptualizing depression as involving a hypoactive BAS, because previous research has indicated that depression and cognitive vulnerability to depression are associated with decreased left frontal cortical activity (Debener et al., 2000; Gotlib, Ranganath, & Rosenfield, 1998; Henriques & Davidson, 1990, 1991; Nusslock, Shackman et al., 2007). Also consistent with these ideas is research showing that increased left frontal cortical activity is associated with anger, which is a BAS-relevant emotion (Harmon-Jones & Allen, 1998; Harmon-Jones & Sigelman, 2001).

The expanded BAS dysregulation theory (Urosevic, Abramson, Harmon-Jones, & Alloy, 2008) integrates recent findings in motivation, affect, and bipolar disorder to further clarify and build on the important ideas of the original BAS model. More specifically, the expanded theory predicts that environmental stressors, such as life events, perturb the already dysregulated BAS, leading to episodes of depression and/or mania/hypomania.

Although the expanded BAS dysregulation theory makes direct predictions about the influence of the BAS on the course of bipolar disorder, few prospective studies have tested this theory yet. A better understanding of the influence of the BAS, in combination with stressful life events, on the course of bipolar disorder could aid in the generation of more informed and effective treatment strategies as well as targeting individuals at-risk for especially severe courses of bipolar disorder. However, no psychosocial interventions have been developed yet to modify or decrease the likelihood of activation in an overly sensitive BAS. Recent work suggests that BAS-relevant life events, such as goal-attainment or goal-striving events, perturb the weakly regulated BAS and lead to increases in hypomanic symptoms (Johnson, Sandrow, et al., 2000; Johnson et al., 2008; Nusslock et al., 2007). Further work is needed to determine if other types of stressful events, in combination with a dysregulated BAS, lead to increases in depressive or hypomanic symptoms as well as influence other aspects of the course of bipolar disorder.

Another model that has been applied to individuals with bipolar disorder is the cognitive vulnerability-stress model. Research on cognitive style in bipolar disorder has concluded that the cognitive styles of individuals with bipolar disorder have a distinctive,

BAS-relevant aspect to them (Alloy, Abramson, Walshaw et al., 2009; Alloy, Reilly-Harrington, et al., 2005). Specifically, these individuals have cognitive styles marked by BAS-relevant characteristics such as goal striving, autonomy, and perfectionism; in comparison, there is much less support for these individuals to have cognitive styles marked by sociotropic or dependent concerns (Alloy, Abramson, Walshaw, et al., 2009; Francis-Raniere, Alloy, & Abramson, 2006; Hammen, Ellicott, Gitlin, & Jamison, 1989).

Background

It is important to determine how the BAS and cognitive vulnerability-stress models explain the course of bipolar spectrum disorders. Important variables that contribute to the course of bipolar disorder include age of onset, as well as the number, cycling, duration, and type of bipolar mood episodes. Age of onset of bipolar disorder is a particularly important variable in offering clues about the likely course of the disorder. Median age of onset has been reported to be in the mid-20s (Goodwin & Jamison, 1990), although there is some variance in age of onset across studies. Goodwin and Jamison pooled data from 6 studies giving age of onset in 5-year intervals and found a peak age of onset in the 15 to 19 year range, followed closely by the 20 to 24 range. More recent research found that mean age of onset ranged from 18.2 years for bipolar I disorder to 20.3 years for bipolar II disorder (Merikangas et al., 2007). The four year peak of initial onset from 15 to 19 years is what Weissman et al. (1996) call the “hazard period” for bipolar disorder.

The course of bipolar disorder for most individuals tends to be recurrent and predominated by depression. Evidence suggests that within five years after an index episode, 70%-80% of individuals with bipolar disorder will experience at least one

recurrence (Miller et al., 2004). Further evidence also suggests that subsyndromal levels of symptoms frequently exist between mood episodes and cause impairment. Suppes et al. (2001) found that 37% of individuals with bipolar disorder reported having mild symptoms between episodes, and 33% reported having significant symptoms between episodes. Individuals with bipolar disorder also tend to spend significantly more time with depressive symptoms than with manic symptoms (Miller et al., 2004).

Onset and duration of episodes are also important course variables and often depend on the type of episode and length of illness. On average, manic episodes begin more abruptly than depressive episodes, with the former developing over a few days or even hours (Goodwin & Jamison, 1990). In contrast, bipolar depression episodes tend to develop over a few weeks. Episode duration in bipolar I disorder ranges from 4 to 13 months, with a longer duration found in studies of untreated populations (Goodwin & Jamison, 1990). However, a more recent study found that median episode length was 1 month, and the median number of episodes per year was 1.2 (Miller et al., 2004). Episode length also may vary by type of episode; indeed, another recent study found that the median length of a severe manic episode was 1 month, median length of a severe depressive episode was 3 months (Kawa et al., 2005), and median length of a hypomanic episode was 2-3 days (Bauer et al., 2006; Benazzi, 2001). Episode duration tends to be stable through the course of bipolar disorder. However, cycle length, defined as the time from the onset of one episode to the onset of the next, tends to get shorter with each episode recurrence (Cusin, Serretti, Lattuada, Mandelli, & Smeraldi, 2000; Goodwin & Jamison, 1990; Kessing, Hansen, & Andersen, 2004).

The Role of Stressful Life Events

A growing body of research suggests that the current environment has an important role in the onset, course, and expression of bipolar spectrum disorders (Alloy, Abramson, et al., 2005; Grandin, Alloy, & Abramson, 2007; Johnson & Kizer, 2002; Johnson & Roberts, 1995). Specifically, the literature has been consistent in suggesting that individuals with a diagnosis in the bipolar spectrum tend to experience increased stressful life events prior to the onset of episodes of the disorder (Alloy, Abramson, et al., 2005; Alloy, Reilly-Harrington, et al., 2005; Grandin, Alloy, & Abramson, 2007; Johnson & Kizer, 2002; Johnson & Roberts, 1995). However, much of the life events literature is characterized by important methodological limitations, such as use of retrospective designs, poorly defined events, self-report measures, and failure to distinguish between types of episodes (Alloy, Abramson, et al., 2005). As greater weight should be given to the more methodologically sound studies, I only review those studies here.

The more methodologically sound studies provide strong, but not completely consistent, evidence for the role of stressful life events in the onset of bipolar mood episodes. Several prospective studies (Ellicott, Hammen, Gitlin, Brown, & et al., 1990; Hammen & Gitlin, 1997; Hunt, Bruce-Jones, & Silverstone, 1992) found that individuals with bipolar disorder had a significantly higher relapse rate after a period of many negative life events than following periods of low stress. However, other studies either did not replicate these findings (McPherson, Herbison, & Romans, 1993) or found this effect only for particular types of events (Hall, Dunner, Zeller, & Fieve, 1977; Pardoen, Bauwens, Tracy, Martin, & Mendlewica, 1993) or only in women (Christensen et al., 2003).

Overall, there is somewhat inconsistent evidence that negative life events predict increases in depressive symptoms. Johnson et al. (2004) found evidence that negative life events predicted increases in depressive symptoms over several months, even after controlling for baseline levels of depression. Two studies (Alloy, Reilly-Harrington, Fresco, Whitehouse, & Zechmeister, 1999; Reilly-Harrington, Alloy, Fresco, & Whitehouse, 1999) suggest that the effects of life events are more pronounced in individuals with negative cognitive styles. Both studies found that in undergraduates with a history of hypomanic or depressive symptoms, negative life events predicted increases in depressive symptoms only among students with a negative cognitive style. However, both of these studies examined mainly subsyndromal forms of bipolar disorder in college students; thus, it is unclear if these results would generalize to other populations.

There is also inconsistent evidence as to whether negative life events predict manic/hypomanic symptoms in bipolar disorder. Five such studies (Alloy et al., 1999; Johnson & Fingerhut, 2004; Johnson, Sandrow, et al., 2000; McPherson et al., 1993; Reilly-Harrington et al., 1999) found no direct effect of negative life events as a predictor of increases in manic/hypomanic symptoms. However, there was evidence that some subgroups, such as cognitively vulnerable individuals, may be vulnerable to increases in manic/hypomanic symptoms after experiencing negative life events (Alloy et al., 1999; Reilly-Harrington et al., 1999). Additionally, Johnson and Fingerhut (2004) found that symptoms in the month before a severe negative life event predicted increases in mania.

Goal-attainment and goal-striving life events, in particular, have been hypothesized to trigger episodes of hypomania/mania. Three prospective studies

(Johnson, Cueller, et al., 2008; Johnson, Sandrow, et al., 2000; Nusslock, et al., 2007) indeed found evidence that life events involving goal-attainment or goal-striving were particularly likely to trigger manic/hypomanic episodes among individuals with a diagnosis in the bipolar spectrum. These findings are particularly relevant to the expanded BAS dysregulation model.

The Behavioral Approach System (BAS) Model

Recent research on the BAS has shown that this motivational system also has important implications for the course of bipolar disorder. The BAS dysregulation theory of bipolar disorder was first proposed by Depue and colleagues (Depue & Fuhrman, 1987; Depue & Iacono, 1989) and has recently been expanded and reviewed by Urosevic et al. (2008). The theory suggests that individuals vulnerable to bipolar disorder may exhibit an overly sensitive BAS that is hyper-reactive to relevant cues. This vulnerability leads such individuals to experience great variability in their state levels of BAS activation over time and across situations. A hyper-responsive BAS leads to excessive BAS activity in response to BAS activation-relevant life events involving goal striving and attainment, reward incentive, and anger-evocation (Alloy et al., 2008; Alloy, Abramson, Urosevic et al., 2009). In vulnerable individuals, the excessive activation of the BAS is thought to lead to manic/hypomanic symptoms (Depue & Iacono, 1989; Urosevic, Abramson, Harmon-Jones, & Alloy, 2008). In contrast, excessive deactivation of the BAS in response to BAS deactivation-relevant events such as definite failure and non-attainment of goals is reflected in depressive symptoms (Depue & Fuhrman, 1987; Fowles, 1988, 1993; Urosevic et al., 2008). Thus, an important prediction of the BAS dysregulation model is that individuals who have a highly sensitive BAS should be

vulnerable to both manic/hypomanic and depressive states, or in other words, to bipolar spectrum disorders.

Consistent with the BAS model are results showing that individuals with a diagnosis of bipolar I disorder (Meyer, Johnson, & Winters, 2001) and individuals prone to hypomanic symptoms (Meyer, Johnson, & Carver, 1999) exhibited elevated self-reported BAS sensitivity and psychophysiological indices of BAS sensitivity (Harmon-Jones, et al., 2002; 2008). Individuals with a diagnosis of bipolar II disorder, bipolar NOS, and cyclothymia also exhibited higher self-reported BAS sensitivity than normal control individuals (Alloy et al., 2008). Additionally, high self-reported BAS sensitivity predicted levels of positive affect and hypomanic symptoms over 17 days in a daily diary study of students (Meyer, 2005), predicted an increase in manic symptoms over 6 months in a sample of recovered individuals with a diagnosis of bipolar I disorder (Meyer et al., 2001), and predicted shorter time to onset of hypomanic/manic episodes in a sample of individuals with bipolar spectrum disorders (Alloy et al., 2008). Furthermore, using a retrospective behavioral high-risk design, Alloy et al. (2006) found that individuals selected on the basis of high self-reported BAS sensitivity were 6 times more likely to have a lifetime diagnosis of a bipolar spectrum disorder than individuals with moderate BAS sensitivity.

The BAS dysregulation theory proposes that BAS activation-relevant events (e.g., reward incentives, goal striving) should be associated with an increase in hypomanic and manic, but not depressive, symptoms and episodes in individuals with bipolar disorder. In support of this hypothesis, Johnson et al. (2000, 2008) found that life events involving goal-attainment (BAS-relevant events) were significantly related to higher levels of

follow-up manic, but not depressive, symptoms. Nusslock et al. (2007) found that goal-striving events (e.g., taking final exams) predicted onset of hypomanic, but not depressive, episodes among individuals with a diagnosis in the bipolar spectrum. In addition, Urosevic et al. (2009) found that individuals with a diagnosis in the bipolar spectrum experienced more BAS activation- and deactivation- relevant life events than normal controls. Furthermore, Alloy, Abramson, Whitehouse, et al. (2009) found that BAS activation-relevant life events prospectively predicted increases in hypomanic symptoms, whereas BAS deactivation-relevant life events predicted increases in depressive symptoms in individuals with bipolar disorder.

A recent expanded BAS Dysregulation theory (Urosevic, Abramson, et al., 2008) expands on the original BAS model by specifying a causal chain of events leading to extreme states of BAS activity and inactivity. In the expanded theory, the weak regulatory system of the BAS interacts with pre-event BAS state to affect the creation or selection of BAS-relevant events, their appraisal, and the magnitude of the BAS responses to these events. The theory predicts that when an event is appraised as BAS activation-relevant and the weak regulation of the BAS interacts with an individual's pre-event BAS state, mania/hypomania is likely to occur. In contrast, the theory predicts that when an event is appraised as BAS deactivation-relevant and the weak regulation of the BAS interacts with an individual's pre-event BAS state, depression is likely to occur. Furthermore, the theory suggests that the absence of major BAS activation- or BAS deactivation-relevant events is likely to lead to euthymia. Finally, the expanded theory also proposes that the frequency of BAS activation- vs. BAS deactivation-relevant events will predict the predominance of mania/hypomania vs. depression, respectively.

The expanded BAS Dysregulation model might explain several aspects of the course of bipolar disorder. For example, the predominantly depressive course of bipolar disorder may be explained in terms of the experience and creation of BAS-deactivation relevant events among individuals with a diagnosis in the bipolar spectrum. As previously mentioned, bipolar disorder is extremely impairing, and often its effects can increase over time. Alternatively, excessive BAS-activation in a vulnerable individual may lead to excessive goal striving. If this results in a failure, this might be a BAS-deactivation event that may lead a vulnerable individual to experience depression.

Furthermore, it may be harder for individuals to return to euthymia following BAS-deactivation and depression as compared to following BAS-activation and mania. Depressed individuals often experience depressed mood, low motivation, and anhedonia, all of which make it unlikely that a depressed individual will create or select a goal-striving or goal-attainment event to try and pull themselves out of the depression. However, manic individuals may unknowingly create or select BAS-deactivation events as they fail to accomplish the high goals set for themselves in the episode. This makes it more likely that manic/hypomanic individuals might quickly switch to euthymia or depression, whereas depressed individuals are likely to have longer episode duration because of the difficulty involved in switching to euthymia.

The quick onset of mania might also be explained by the expanded BAS dysregulation model; in an early stage of mania, individuals may not be aware that increased sociability, increased self-confidence, and decreased need for sleep may be prodromes of mania (Lam & Wong, 2006). Some individuals may react to these prodromes with more approach behaviors, such as seeking social stimulation and taking

on challenges at work or home. This would further activate the BAS and might quickly send an individual spiraling into a manic episode. Additionally, individuals experiencing manic prodromes may ruminate on positive emotions (Johnson, McKenzie, & McMurrich, 2008), which may lead to efficacy and relevance appraisals that would make individuals vulnerable to increased BAS activation and thus, mania.

Finally, the expanded BAS dysregulation model may explain decreasing cycle length with each episode recurrence in bipolar disorder. Although it has not yet been tested, it may be the case that the BAS becomes more dysregulated with each episode over time, so that the BAS needs to be perturbed less and less each time for an individual to experience relapse. This would result in the individual experiencing more and more frequent episodes, but might not affect the duration of the episodes.

The Cognitive Vulnerability-Stress Model

Given the success of cognitive vulnerability-transactional stress models in understanding unipolar depression, the logic of these theories has been extended to bipolar disorder (Alloy, Abramson, Neeren, et al., 2006; Alloy, Abramson, et al., 2005; Alloy, Abramson, Walshaw, Keyser, & Gerstein, 2006). The transactional part of the cognitive vulnerability-stress model suggests that cognitive vulnerability itself leads to stress generation and greater exposure to life events, which can lead to bipolar mood episodes. Thus, the transactional part of the model applied to bipolar disorder suggests a two-hit model in which individuals with maladaptive cognitive styles not only react more strongly to relevant life events, but also are exposed to such events more frequently, which, in turn, precipitates bipolar mood episodes.

As in unipolar depression, maladaptive cognitive styles increase the likelihood of negative appraisals and processing of negative life events, thus leading to hopelessness and ultimately depressive symptoms (Alloy, Abramson, Neeren, et al., 2006). The same cognitive processes that contribute vulnerability to episodes of unipolar depression may also contribute vulnerability to episodes of bipolar depression.

There is some evidence that cognitive styles prospectively predict the expression and course of bipolar disorder, particularly in combination with stressful life events. Three studies tested Beck's (Beck, 1987) event congruence, vulnerability-stress hypothesis for sociotropic and autonomous cognitive styles in which the experience of stressful life events congruent with one's style (interpersonal events for sociotropic individuals and achievement events for autonomous individuals) should lead to an onset or worsening of symptoms. Two studies (Hammen, et al., 1989; Hammen, Ellicott, & Gitlin, 1992) reported that the interaction of sociotropy and negative interpersonal events predicted symptom severity, but not symptom onset. The Autonomy x Negative Achievement Events interaction did not predict symptom severity. Francis-Raniere, Alloy, and Abramson (2006) found that self-critical/perfectionistic cognitive styles interacted with congruent (self-criticism-relevant) negative life events to predict increases in depressive symptoms and with congruent positive life events to predict increases in hypomanic symptoms over a 4-month follow-up period.

Two studies tested the cognitive vulnerability-stress hypothesis of hopelessness theory (Abramson, Metalsky, & Alloy, 1989) and Beck's theory (Beck, 1967) for attributional style and dysfunctional attitudes. In support of the hopelessness theory, Alloy, Reilly-Harrington, et al. (1999) reported that, among individuals with a mild

diagnosis in the bipolar spectrum, a negative attributional style for negative events at Time 1 interacted with subsequent negative events to predict increases in depressive symptoms, and a positive attributional style for positive events combined with subsequent positive events to predict increases in hypomanic symptoms. Dysfunctional attitudes in combination with life events did not predict subsequent depressive or hypomanic symptoms. In support of both hopelessness and Beck's theories, Reilly-Harrington et al. (1999) found that, in a large sample of individuals with unipolar depression and bipolar disorder, controlling for initial symptom levels, Time 1 negative attributional styles, dysfunctional attitudes, and negative self-referent information processing each interacted significantly with subsequent negative life events to predict increases in depressive symptoms and, within the group of individuals with bipolar disorder, manic symptoms.

One factor that may contribute to some of the mixed findings on cognitive style in bipolar disorder is the type of cognitive styles examined. Recent research has focused on BAS-relevant cognitive styles, which include themes of high drive/incentive motivation associated with high BAS sensitivity. There is some agreement among researchers as to which measures of cognitive style are BAS-relevant (performance evaluation, autonomy, and self-criticism) and which are BAS-irrelevant (approval by others, sociotropy, and dependency) (Alloy, Abramson, Walshaw, et al., 2009).

Several studies on BAS-relevant cognitive styles have obtained results indicating that individuals with bipolar spectrum disorders do indeed exhibit a unique cognitive style profile with BAS-relevant characteristics. Results show that individuals with bipolar spectrum disorders, as compared to normal controls, exhibit higher self-criticism (Rosenfarb, Becker, Khan, & Mintz, 1998) and higher perfectionism (Goldberg, Gerstein,

Wenze, Welker, & Beck, 2008; Scott, Stanton, Garland, & Ferrier, 2000). As compared to unipolar depressed individuals, individuals with bipolar disorder scored higher on Goal Attainment dysfunctional attitudes, but not dependent or achievement dysfunctional attitudes (Lam, Wright, & Smith, 2004).

Most recently, Alloy, Abramson, Walshaw, et al. (2009) found that individuals with a diagnosis in the bipolar spectrum differed significantly from normal controls on BAS-relevant cognitive styles, but not on BAS-irrelevant dimensions of cognitive style. In addition, the authors found that some BAS-relevant cognitive styles significantly predicted the likelihood of onset of major depression and hypomania/mania. Specifically, results showed that higher levels of self-criticism and autonomy predicted a greater likelihood of hypomania/mania onset and higher autonomy was related to a smaller likelihood of major depression onset.

These studies suggest that individuals with bipolar spectrum disorders evidence cognitive styles marked by BAS-relevant traits of perfectionism, autonomy, self-criticism, and goal-striving; there is less consistent evidence that bipolar individuals' cognitive styles are marked by sociotropic, dependent, or approval-seeking themes as one typically sees in individuals with unipolar depression (see Zuroff, Mongrain, & Santor, 2004, for a review). Furthermore, researchers suggest that it may be the case that high BAS sensitivity contributes to the development of an autonomous cognitive style, which in turn, may contribute risk for the development of bipolar disorder (Alloy et al., 2009).

The Present Study

The purpose of the present study was to test some of the predictions of the expanded BAS Dysregulation model regarding the course of bipolar spectrum disorders

among individuals with a diagnosis of bipolar II, cyclothymia, and bipolar NOS. A secondary aim of this study was to compare the expanded BAS Dysregulation model to the Cognitive-Vulnerability Stress Model applied to the course of bipolar spectrum disorders. To this end, several hypotheses were tested.

Hypotheses

All hypotheses tested involve the entire sample, unless otherwise noted.

Hypothesis 1. According to the BAS model, individuals with a more sensitive BAS should be at higher risk for the onset of bipolar disorder. Consequently, one may expect the onset of bipolar disorder to occur earlier in individuals with a more sensitive BAS. Thus, BAS sensitivity would be associated with age of onset of bipolar spectrum disorders, such that individuals with a more sensitive BAS would have an earlier age of onset, and onsets of first episode mania/hypomania, in particular, than those with a less sensitive BAS.

Hypothesis 2. According to the BAS model, individuals with a more sensitive BAS are at higher risk for developing episodes of bipolar disorder. Thus, BAS sensitivity would predict time spent in a euthymic mood state, such that individuals with a more sensitive BAS would spend less time in euthymia, and more time in a mood episode, than individuals with a less sensitive BAS.

Hypothesis 3. BAS sensitivity would predict the predominance of depression vs. hypomania/mania in the course of bipolar spectrum disorders. Specifically, individuals with a more sensitive BAS would have a predominantly hypomanic/manic course of illness, whereas individuals with a less sensitive BAS would have a predominantly depressive course of illness. In addition, scores on BAS-relevant cognitive style

measures would predict the predominance of depression vs. hypomania/mania in the course of bipolar spectrum disorders.

Hypothesis 4. A higher number of stressful life events, and BAS-relevant events in particular, are associated with increased risk for developing episodes of bipolar disorder. Thus, a lower number of major BAS activation- and deactivation-relevant events would predict greater time in euthymia. Second, differences in the amount of time spent in euthymia between normal control individuals and individuals with bipolar disorder would be mediated by the number of BAS-activation and –deactivation relevant events each group experienced.

Hypothesis 5. It is possible that an increased number of BAS deactivation-relevant events makes an individual more vulnerable to depressive episodes, while an increased number of BAS activation-relevant events makes an individual more vulnerable to hypomanic episodes. Thus, those individuals with a predominantly depressive course of bipolar disorder would experience a greater number of BAS deactivation-relevant events than those with a predominantly manic/hypomanic course. Conversely, those individuals with a predominantly hypomanic/manic course of bipolar disorder would experience a greater number of BAS activation-relevant events than those with a predominantly depressive course. Similarly, the number of BAS-activation and –deactivation relevant events would predict the proportion of the number of hypomania/mania vs. depressive episodes and the proportion of days with hypomania/mania vs. depressive symptoms.

Hypothesis 6. If a sensitive BAS and an increased number of BAS activation-relevant events leaves individuals more vulnerable to hypomanic episodes, then individuals in a

depressive episode would be less likely than individuals in a manic/hypomanic episode to generate or select goal-striving or goal-attainment events.

Hypothesis 7. In the entire sample, the interaction of an individual's BAS sensitivity with the number of BAS activation-relevant events would predict the number of hypomania/mania episodes over time. Relatedly, the interaction of BAS sensitivity with the number of BAS deactivation-relevant events would predict the number of episodes of depression over time. These effects would be stronger for individuals with a diagnosis in the bipolar spectrum, as compared to normal controls. In addition, the interaction of an individual's BAS-relevant cognitive styles with the number of congruent positive events would predict the number of hypomania/mania episodes over time. Relatedly, the interaction of BAS-relevant cognitive styles with the number of congruent negative events will predict the number of depressive episodes over time.

Hypothesis 8. In the entire sample, the interaction of an individual's BAS sensitivity with the number of BAS-relevant events would predict the time period between episodes; a higher number of BAS-relevant events would predict less time between episodes for individuals with a more sensitive BAS. These effects would be stronger for individuals with a diagnosis in the bipolar spectrum.

CHAPTER 2

METHOD

Participants and Procedures

The participants for this study are a subset of individuals selected from the Longitudinal Investigation of Bipolar Spectrum Disorders (LIBS) Project (see Alloy et al., 2008 for a complete reference; Alloy, Abramson, Walshaw, et al., 2009). The LIBS study recruited participants at two sites, Temple University and the University of Wisconsin. Over the course of 4 years, a total of 20,543 individuals at the universities, ages 18-24, were screened using a Personal Data Sheet (PDS) and Depue et al.'s (1989) revised General Behavior Inventory (GBI). The PDS contained demographic information, such as the individual's age, sex, and ethnicity. The GBI is a first-stage screening instrument for identifying individuals with bipolar spectrum disorders. This self-report questionnaire consists of two scales: the depression scale and the hypomanic/biphasic scale. Cutoff scores based on Depue et al. (1989) were used to determine the two inclusion groups of the study: high GBI (as defined by depression scale scores $\geq$ 11 and hypomanic/biphasic scores $\geq$ 13) and low GBI (as defined by depression scale scores < 11 and hypomanic/biphasic scores < 13). The high GBI group was comprised of potential bipolar spectrum participants and the low GBI group was comprised of individuals who were potential normal controls. Identified high GBI participants were considered for the bipolar spectrum group, while low GBI individuals were considered for the normal control group. Normal control and bipolar groups were selected to be similar on the basis of age, sex, and ethnicity, resulting in a sample that

was representative of the overall gender and ethnicity distribution from Phase I. This set of high and low GBI participants was then invited into Phase II of the study.

Participants invited into Phase II of the study were given an expanded Schedule for Affective Disorders and Schizophrenia -Lifetime diagnostic interview (Endicott & Spitzer, 1978), which included both current and past *DSM-IV* and Research Diagnostic Criteria diagnoses. These interviews were administered by trained research assistants who were blind to participants' Phase I GBI status. During Phase II, participants also completed several self-report questionnaires to obtain information on baseline levels of functioning and symptomatology. Participants who met the relevant diagnostic criteria were then invited into the study in order to compose a bipolar spectrum group and a normal control group that were selected to be demographically similar. A total of 1,730 individuals were interviewed at Phase II.

Inclusion criteria for the bipolar group in Phase II consisted of 1) A current *DSM-IV* and/or RDC diagnosis of bipolar II disorder, cyclothymia, or bipolar NOS. If cyclothymic, the participant must have shown the pattern for at least 2 years; 2) If cyclothymic or bipolar NOS, a minimum of 2 days duration for the depressed or hypomanic mood states; 3) At least 2 of the 12 biphasic behavioral patterns as defined by Akiskal et. al. (1979), which include such biphasic patterns as psychomotor agitation versus retardation, and high versus low energy; and 4) criterion B from the RDC cyclothymic category was not used: "changes in mood often unrelated to external events or circumstances" (Spitzer, Endicott, & Robins, 1978).

Exclusion criteria for the bipolar group consisted of 1) diagnosis of bipolar I (i.e. current or past manic episodes as defined by either *DSM-IV* or RDC); 2) bipolar

symptomatology possibly caused by medications, illnesses, and/or substance use. Individuals who met criteria for bipolar I were excluded because a goal of the overall LIBS project was to predict first onset of manic episodes (i.e., conversion to bipolar I status). However, a number of individuals did go on to develop first onset of manic episodes during the study, and therefore manic episodes are included in this analysis. (Overall, 18 individuals experienced at least 1 episode of mania during the course of the study.) Exclusion criteria for the normal control group consisted of 1) current or past diagnosis of major depression, mania, hypomania, cyclothymia, or bipolar NOS; 2) any other current or past psychopathology as defined by *DSM-IV* or RDC; 3) possible organic causes of mood disturbances (medications, illnesses, and/or substance use).

Of the eligible participants from Phase II, 227 of the 285 eligible bipolar spectrum participants (110 at TU and 117 at UW) and 227 of the 308 (110 at TU, 117 at UW) eligible normal control participants completed Time 1 assessments. Of these, 224 bipolar spectrum participants (110 at TU, and 114 at UW) and 224 normal control participants (110 TU, 114 UW) participated in the longitudinal study. Due to a delay in being able to obtain the data from the UW site, only participants from the TU site were included in this study. This may bias the sample somewhat in terms of higher levels of psychopathology and lower socioeconomic status. The sample was representative of the large Phase I screening sample on gender (65% female, 35% male), age, and ethnicity. Participants in the final sample were assigned two interviewers, one to conduct the diagnostic interviews and one to conduct the life event interviews, in order to keep diagnostic and life events data independent. Participants were followed prospectively at approximately 4-month intervals for an average of 1138 days (3.12 years) for mood episode data and 1208 days

(3.3 years) for life event data. This discrepancy is due to missing data for several individuals and inclusion of life events from RPAs 1-12 only.

Measures

Phase I: Self-report Screening Measure. The revised GBI (Depue et al., 1989) is a time-efficient, economical screening measure to assess risk for affective disorders in large populations. In the present study, it was used to identify potential bipolar and normal control individuals to invite for the Phase II diagnostic screening interview. The revised GBI contains 73 items that assess core bipolar experiences and their frequency, duration, and intensity on two subscales: Depression (D) and Hypomania and Biphasic (HB) items combined. We used Depue et al.'s (1989) case-scoring method to identify potential bipolar and normal control participants. Only items rated a 3 (*often*) or 4 (*very often or almost constantly*) on the GBI 4-point frequency scale contributed a point toward the total score on each subscale. Based on the cutoffs recommended by Depue et al. (1989), those participants who scored ≥ 11 on the D scale and ≥ 13 on the HB scale were identified as potential bipolar spectrum participants, whereas those who had a D score < 11 and an HB score < 13 formed a potential Normal control group. The GBI has good internal consistency (αs = .90-.96), test-retest reliability (*rs* = .71-.74), high specificity (.99) and adequate sensitivity (.78) for bipolar spectrum conditions (Depue et al., 1989). Additionally, the GBI has been validated extensively in psychiatric outpatient, college, and offspring of bipolar I patient samples (Klein, 1994).

Phase II: Diagnostic Interview. The expanded-SADS-L (Endicott & Spitzer, 1978) is a semi-structured diagnostic interview that assesses current and lifetime history of Axis I disorders. The exp-SADS-L interview has yielded κs $\geq .96$ for bipolar spectrum

diagnoses (Francis-Raniere et al., 2006). Extensively trained research assistants and clinical psychology Ph.D.s blinded to participants' Phase I GBI status and scores conducted the interviews. Consensus *DSM-IV* and RDC diagnoses were determined by a 3-tiered standardized diagnostic review procedure involving senior diagnosticians and an expert psychiatric diagnostic consultant, Dr. Alan Gruenberg. The exp-SADS-L also contained a family history section and used the Family History-RDC (Andreasen, Endicott, Spitzer, & Winokur, 1977) to obtain information on family history of mood and other disorders.

Prospective diagnostic measure. An expanded SADS-Change interview (exp-SAS-C; Spitzer & Endicott, 1978) was administered every 4 months during the prospective follow-up period. The exp-SADS-C was used to assess onsets, remissions, relapses, and recurrences of diagnosable episodes of Axis I psychopathology. Interviewers were blinded to participants' BIS/BAS and cognitive style scores, as well as their Phase I GBI scores and Phase II diagnostic status. Features of the Longitudinal Interval Follow-up Evaluation (LIFE-II; Shapiro & Keller, 1979) were added to the exp-SADS-C in order to systematically track the course of symptoms and episodes during follow-up. Although the LIFE-II tracks symptoms on a weekly basis, the exp-SADS-C inquired about the presence of each symptom on a daily basis during each 4-month interval. Interrater reliability for the exp-SADS-C in joint ratings of 60 interviews for the LIBS Project was good ($\kappa > .80$) (Francis-Raniere et al., 2006). In a validity study, participants dated their symptoms on the exp-SADS-C with at least 70% accuracy compared with daily symptom ratings made over a 4-month period. In this study, clinician-rated depression and mania/hypomania symptom scores from the exp-SADS-C

were used in addition to DSM-IV and RDC mood episodes. The symptom scores were computed as a count of the number of depressive and hypomanic/manic symptoms rated as significant by the interviewer at each follow-up assessment.

Criteria for bipolar spectrum disorders. *DSM-IV* and RDC criteria were used for both the diagnosis of bipolar spectrum disorders and bipolar spectrum episodes. Bipolar II disorder was operationalized by the occurrence of one or more *DSM-IV* or RDC major depression (MD) episodes accompanied by at least one *DSM-IV* or RDC hypomania episode (see below for episode definitions). The presence of a manic or mixed episode precluded a bipolar II diagnosis. The symptoms of bipolar II disorder must have caused clinically significant distress or impairment in functioning. However, consistent with *DSM-IV*, hypomanic episodes themselves did not need to cause impairment, but must have been associated with an unequivocal change in mood and functioning that is observable to others.

Cyclothymic Disorder was operationalized as recurrent periods of depression (not meeting criteria for MD episode) and of hypomania (not meeting criteria for manic episode) that occurred over at least a 2-year period. During this 2-year period, any symptom-free interval lasted no longer than 2 months. Given that *DSM-IV* and RDC Criterion A for Cyclothymic Disorder does not specify the minimum duration of depressive or hypomanic periods required for the diagnosis, we required a 2-day minimum duration for both kinds of periods based on the RDC criteria for hypomania. We also required at least 2 hypomanic and 2 depressive periods within a year for a cyclothymic diagnosis. Based on consultation with Dr. Jean Endicott, author of the SADS-L, Criterion A symptoms for both depression (sadness or loss of interest) and

hypomania (elevated, expansive, irritable) needed to be present at least 50% of the day, and participants needed at least 2 additional symptoms, for both kinds of periods. Significant distress or impairment in important areas of functioning must have been reported as a result of Cyclothymic Disorder for *DSM-IV* diagnosis, but not for RDC diagnosis. Cyclothymic Disorder was diagnosed only if the initial 2-year period of cyclothymic symptoms was free of MD episodes. After the initial 2-year period, MD episodes could have been superimposed on the cyclothymic disorder, in which case both cylothymic and bipolar II disorder were diagnosed.

Criteria for bipolar spectrum episodes. For both exp-SADS-L and exp-SADS-C, full-blown hypomanic episodes were defined according to *DSM-IV* or RDC criteria. Hypomanic episodes required an abnormally and persistently elevated, expansive, or irritable mood that lasts at least 4 days for *DSM-IV* and 2 days for RDC diagnosis. Persistence of hypomanic mood must be ≥ 50% of waking hours in each hypomanic day accompanied by either 2 (RDC) or 3 (*DSM-IV*) additional hypomanic symptoms. If the mood is irritable rather than elevated or expansive, 1 more additional symptom must be present for both *DSM-IV* and RDC. Consistent with *DSM-IV*, the episode must be associated with an unequivocal change in mood and functioning that is observable to others; however, a hypomanic episode is not severe enough to cause marked impairment in social or occupational functioning, or necessitate hospitalization, and there are no psychotic features present (as this is the criteria for mania). Indeed, research suggests that hypomanic symptoms among individuals with a diagnosis in the bipolar spectrum may even enhance functioning (Judd, Akiskal, Schettler, & Endicott, 2005). MD episodes also were defined according to *DSM-IV* or RDC criteria requiring persistence of

depressed mood or pervasive loss of interest to be ≥ 90% of waking hours in each depressed day and accompanied by 4 (*DSM-IV*) or 5 (RDC) additional depressive symptoms. This depression has to be present for at least 2 weeks, cause clinically significant distress or impairment, and not be the result of a substance or medical condition.

Life events. A questionnaire and semi-structured interview were used to assess life events over each 4-month follow-up period. The original Life Events Scale (LES; Alloy & Abramson, 1999; Alloy & Clements, 1992; Needles & Abramson, 1990) includes 134 major and minor negative life events in a wide variety of content domains relevant to students. An expanded 177-item LES was used in this study that reduced the number of negative events, but added positive events. LES items were written to decrease ambiguous and redundant events and to eliminate "hierarchical" items where one event is a subset of another (e.g., failed an examination is a subset of doing poorly in school). In addition, items that reflect obvious symptoms of depression or hypomania/mania were eliminated from the LES. At each 4-month follow-up, participants were asked to report on whether each event had occurred and how many times it had occurred over the past 4-months.

Following completion of the LES, participants were interviewed with the Life Events Interview (LEI; Alloy & Abramson, 1999). The LEI served as a reliability and validity check on the LES by providing explicit definitional criteria for what experiences counted as each event (e.g., an aunt with the flu would not meet the definitional criteria for the event, "close family member had a serious medical illness") and *a priori* probes to determine whether the event definition criteria were met. On the LEI, the interviewer

reviewed every event endorsed by the participant on the LES to determine if the experience met the definitional criteria. If it did not, the event was designated as a DNQ ('Does Not Qualify') and was not counted in final event totals. The interviewer also dated the occurrence of each event that did qualify.

Both negative and positive event scores on the LES have shown excellent reliability and validity (Alloy & Abramson, 1999; Alloy & Clements, 1992; Needles & Abramson, 1990). The combined LES/LEI procedure has also yielded excellent reliability and validity. A rigorous interrater reliability study of 40 LEI interviews, in which different interviewers independently interviewed the same participant (within 2 days) with the LEI for the same 6-week interval, yielded an average $r = 0.89$ between interviewers for rating and dating of events (Francis-Raniere et al., 2006).

For this study, life events were classified into several different categories: BAS activation-relevant (e.g., starting a new job), BAS deactivation-relevant (e.g., not being accepted into a graduate program of choice), BAS-irrelevant (e.g., unwanted parental absence), goal attainment-relevant (e.g., won a significant award for your achievement), positive goal attainment-relevant (e.g., accepted into major of choice), positive achievement-relevant (e.g., getting onto a school sports team), negative goal attainment-relevant (e.g., flunked a class), and negative achievement-relevant (e.g., did poorly on a final exam). Each LES event was a priori categorized by a consensus team across each series of dimensions.

BIS/BAS Scales. The BIS/BAS Scales were developed by Carver and White (1994) to quantify individual differences in sensitivity of the BIS and BAS. The BIS/BAS scales are the most frequently used self-report measures for this purpose. The

scales include 20 items, on 4-point Likert scales, ranging from *strongly disagree* to *strongly agree*, and consist of one BIS subscale and three BAS subscales: Reward Responsiveness (RR), Drive (D), and Fun-Seeking (FS). All subscales have demonstrated adequate internal consistencies (αs range from .59 to .74) (Alloy et al., 2008; Carver & White, 1994) and good test-retest reliabilities and stabilities in both bipolar spectrum and normal control samples (Urosevic, Nusslock, et al., 2009). Confirmatory factor analyses of the BIS/BAS Scales have confirmed the latent structure of one BIS scale and three correlated BAS subscales (Campbell-Sills, Liverant, & Brown, 2004; Carver & White, 1994). Numerous studies support the construct validity of the BIS/BAS Scales, including their relation to prefrontal cortical activity, affect, personality traits, and performance on reaction-time and learning tasks involving incentives (Alloy et al., 2008; Campbell-Sills et al., 2004; Harmon-Jones & Allen, 1998; Sutton & Davidson, 1997). The BIS/BAS scales were administered to participants in the final sample at Time 1 of the study.

Cognitive Style Measures. The Dysfunctional Attitudes Scale (DAS), Form A (A. Weissman & Beck, 1978) is a 40-item questionnaire that assesses dysfunctional beliefs regarding concerns about others' approval and performance expectations on 7-point scales ranging from *totally agree* to *totally disagree*. Two factors have been extracted from the DAS: Approval by Others (ABO – 10 items: "My value as a person depends greatly on what others think of me"; "If others dislike you, you cannot be happy") and Performance Evaluation/Perfectionism (PE – 15 items; "If I do not do as well as other people, it means I am an inferior human being"; "If I fail partly, it is as bad as being a complete failure") (Cane, Olinger, Gotlib, & Kuiper, 1986; Segal, Shaw, & Vella, 1989).

PE has been found to be a BAS-relevant dimension of dysfunctional attitudes, but ABO is not relevant to BAS sensitivity (Alloy, Abramson, Walshaw et al., 2009). Cane et al. (1986) reported that PE accounted for 47% of the variance in DAS scores and had an α = 0.84, whereas ABO accounted for 14% of the variance in DAS scores and had an α = 0.76. Both factors have shown good construct validity (Francis-Raniere et al., 2006; Segal et al., 1989). The overall DAS has also shown strong internal consistency and test-retest reliability in undergraduate samples (Alloy et al., 2000; Oliver & Baumgart, 1985).

The Sociotropy-Autonomy Scale (SAS; Beck, Epstein, Harrison, & Emery, 1983) is a 60-item questionnaire designed to assess Beck's (1987) depressive personality modes, with 30 items each on the Sociotropy ("I find it difficult to be separated from people I love"; "I am afraid of hurting other people's feelings") and Autonomy ("It is very important that I feel free to get up and go wherever I want"; "I value work accomplishments more than I value making friends") subscales. Autonomy assesses valuing of achievement, mobility, and freedom from control and was determined to be BAS-relevant, whereas Sociotropy measures valuing of attachment and fears of abandonment and rejection by others and was determined to be BAS-irrelevant (Alloy, Abramson, Walshaw, et al., 2009). Each item is rated on % agreement on 5-point scales (0%, 25%, 50%, 75%, 100%). The Sociotropy and Autonomy scales have good internal consistency (α = 0.90 and 0.93, respectively) and high retest reliability (Beck et al., 1983; Zuroff et al., 2004). The Sociotropy scale also has high concurrent validity with other measures of dependency and affiliation (Clark, Beck, & Brown, 1992), whereas the Autonomy scale is moderately correlated with an autonomy subscale of another questionnaire (Clark et al., 1992).

The Depressive Experiences Questionnaire (DEQ; Blatt, D'Afflitti, & Quinlan, 1976) is 66 items, rated on 7-point scales (from *strongly disagree* to *strongly agree*), and has 3 factors

measuring the depressive personality styles hypothesized by Blatt et al. (1976): Dependency, Self-Criticism, and Efficacy. Self-Criticism ("There is a considerable difference between how I am now and how I would like to be"; "I have a difficult time accepting weaknesses in myself") and Efficacy ("I have many inner resources [abilities, strengths]"; "I set my personal goals and standards as high as possible") were determined to be BAS-relevant, whereas Dependency ("Without support from others who are close to me, I would be helpless"; "I have difficulty breaking off a relationship that is making me unhappy") was determined to be BAS-irrelevant (Alloy, Abramson, Walshaw et al., 2009). The DEQ has high internal and retest reliability (Blatt et al., 1976; Zuroff, Moskowitz, Wielgus, Powers, & Franko, 1983). The factors have shown good construct validity (Zuroff et al., 2004).

Statistical Analysis Plan

Preliminary Analyses.

Several course variables were examined to determine the course of bipolar disorder within our sample. Means and standard deviations were calculated for each course variable, life event variable, BAS sensitivity variable, and cognitive vulnerability score. Two-tailed t tests were conducted to determine differences between the bipolar and normal control groups on all of the above variables. To determine if there were significant differences among the average time between episodes as a function of the number of mood episodes, an ANOVA was conducted. ANOVAs and planned contrasts were also used to determine the effect of group on suicidal ideation and suicide attempts. (Due to missing data, the sample size for each analysis varies depending on which variables were included.) Pearson correlations were conducted to determine the

relationship between ethnicity, age, gender, comorbidity, treatment status, and mood episode and life event variables.

Hypothesis 1.

It was hypothesized that BAS sensitivity would be associated with age of onset of bipolar spectrum disorders, such that individuals with a more sensitive BAS would have an earlier age of onset, and onsets of first episode mania/hypomania, in particular, than those with a less sensitive BAS. To test this hypothesis, BAS sensitivity scores were correlated with age of onset of bipolar disorder, including first episode of hypomania and depression among individuals with a diagnosis in the bipolar spectrum. The sample size for this analysis was 32.

Hypothesis 2.

It was hypothesized that BAS sensitivity would predict time spent in a euthymic mood state, such that individuals with a more sensitive BAS would spend less time in euthymia than individuals with a less sensitive BAS. To test Hypothesis 2, BAS sensitivity scores were correlated with time spent in euthymia. The sample size for this analysis was 92, including 55 normal controls and 37 individuals with bipolar disorder.

Hypothesis 3.

It was hypothesized that BAS sensitivity would predict the predominance of depression vs. hypomania/mania in the course of bipolar spectrum disorders. In the first part of this hypothesis, BAS sensitivity scores were correlated with several measures of hypomanic and depressive course of bipolar disorder. In addition, a regression was conducted with covariates in step 1 and BAS sensitivity in step 2 to predict several measures of hypomanic and depressive course of bipolar disorder. The sample size for

these analyses was 92, including 55 normal controls and 37 individuals with bipolar disorder.

In the second part of this hypothesis, pearson correlations were conducted between cognitive vulnerability scores and several measures of depressive and hypomanic course of bipolar disorder. This hypothesis was also tested in another, more conservative way to determine the effect of BAS-relevant cognitive styles in predicting the course of bipolar disorder. A regression was conducted with covariates in step 1, BAS-irrelevant cognitive styles in step 2, and BAS-relevant cognitive styles in step 3. The sample size for both of these analyses was 200, including 105 normal controls and 95 individuals with bipolar spectrum disorder.

Hypothesis 4.

It was hypothesized that a lower number of major BAS activation-relevant events would predict greater time in euthymia. Normal control individuals would spend more time in euthymia than individuals in the bipolar spectrum and this group difference would be mediated by the number of BAS activation-relevant events each group experienced. To test this, pearson correlations were conducted between BAS activation events and time spent in euthymia, and a t-test was conducted to determine group differences on the number of BAS activation events. Although mediation hypotheses are often tested by using the causal steps approach popularized by Baron and Kenny (1986), a bootstrapping approach (Shrout & Bolger, 2002) was used here, as it is a more stringent test for mediation. This approach increases power and maintains reasonable control over the Type I error rate. Bootstrapping is a nonparametric resampling technique that empirically generates an approximation of the sampling distribution. The procedure

yields point estimates and percentile confidence intervals for direct and indirect total effects. The sample size for this hypothesis was 199, including 104 normal controls and 95 individuals with bipolar spectrum disorder.

Hypothesis 5.

It was hypothesized that individuals with a predominantly depressive course of bipolar disorder would experience a greater number of BAS deactivation-relevant events than those with a predominantly manic/hypomanic course. Conversely, those individuals with a predominantly hypomanic/manic course of bipolar disorder would experience a greater number of BAS activation-relevant events than those with a predominantly depressive course. Similarly, the number of BAS-activation and –deactivation relevant events would predict the proportion of the number of hypomanic/manic vs. depressive episodes and the proportion of days with hypomanic/manic vs. depressive symptoms.

Individuals who experienced more days in hypomanic episodes than depressive episodes were considered to have a predominantly hypomanic course of illness, whereas individuals who experienced relatively more days in a depressive episode were considered to have a predominantly depressive course of illness. Similarly, individuals who experienced more hypomanic episodes than depressive episodes were considered to have a predominantly hypomanic course of illness, whereas individuals who experienced more depressive episodes than hypomanic episodes were considered to have a predominantly depressive course of illness. T-tests were conducted to determine group differences in the number of BAS deactivation-relevant events and BAS activation-relevant events experienced by individuals with a predominantly hypomanic versus depressive course of illness. Thus, each analysis was conducted twice – once for the days

in episode course of illness and once for the number of episodes course of illness. The sample size for this hypothesis was 108.

To investigate this hypothesis a second way, linear regressions were conducted using the number of BAS activation-relevant and deactivation-relevant life events to predict the course of illness. The regressions were conducted with covariates in step 1 and BAS Activation (or Deactivation) relevant events in step 2. BAS Activation and BAS Deactivation events were tested separately.

Hypothesis 6.

It was hypothesized that individuals in a depressive episode would be less likely than individuals in a manic/hypomanic episode to create or select goal-striving or goal-attainment events. Logistic regression was used to determine if individuals in a hypomanic episode vs. in a depressive episode subsequently were more likely to experience a BAS activation-relevant or goal attainment event in the month following the onset of the episode. Regressions were conducted with covariates in step 1, and days in hypomania or depression (or hypomanic or depressive episodes) in step 2 predicting the occurrence of a BAS activation-relevant or goal attainment event in the month following the onset of the episode. BAS activation-relevant events were rated on relevance by a panel of experts; only those events rated >2, on average, were included. Participants were coded as "having a BAS activation or goal-attainment-relevant event" if they had at least one of these types of events in the 30-day period following the onset of a mood episode[2]. The sample size for this hypothesis was 98.

[2] This 30-day period was selected in order to capture a short period of time following the onset of a mood episode that tends to include stress generation

To investigate this hypothesis a second way, t-tests were conducted to determine if there were significant differences between the number of BAS activation relevant and goal attainment-relevant events after an episode of hypomania as compared to after an episode of major depression or minor depression.

Hypothesis 7.

The reformulated BAS dysregulation model hypothesizes that the interaction of an individual's BAS sensitivity with the number of BAS activation-relevant events would predict the number of hypomania/mania episodes over time. Relatedly, the interaction of BAS sensitivity with the number of BAS deactivation-relevant events would predict the number of episodes of depression over time. These effects would be stronger for individuals with a diagnosis in the bipolar spectrum, as compared to normal controls. In addition, the interaction of an individual's BAS-relevant cognitive styles with the number of congruent positive events would predict the number of hypomania/mania episodes over time. Relatedly, the interaction of BAS-relevant cognitive styles with the number of congruent negative events would predict the number of depressive episodes over time.

A power analysis was conducted to determine if we had a sufficiently large sample of bipolar individuals, who also completed the BAS sensitivity measure, to detect a medium effect size. Using 6 predictors (time in study, treatment status, comorbidity, BAS sensitivity, BAS relevant events, and BAS sensitivity x BAS relevant events) and a sample size of 88, our power is .37. Power of at least .8 is needed to detect a medium effect and thus, we did not have sufficient power to detect a medium size effect in the data. However, because this was a central hypothesis of the study, I did run the analyses

to at least examine the effect sizes in the data. The sample for this hypothesis included 35 individuals in the bipolar group and 53 in the normal control group.

Hierarchical regression was used to determine whether the interaction of BAS sensitivity and BAS-relevant life events predicted the number of hypomanic or depressive mood episodes over time. In all analyses, the length of time in the study was included in step 1. Step 2 included the other covariates, treatment status and comorbidity, step 3 included BAS sensitivity (or BAS subscale), step 4 included the appropriate life events term, and step 5 included the interaction of BAS sensitivity and the life events score. Initial regressions showed multicollinearity, indicating that there was a strong correlation between two or more predictors in a model. As suggested by Field (2009), all variables were centered around the grand mean. All regressions for this hypothesis used centered variables and interaction terms, unless otherwise noted. When BAS sensitivity significantly contributed to the regression model, subscales of the BAS were also examined.

In order to determine group differences, a regression was also conducted to determine the effect of the 3-way interaction between group, BAS sensitivity, and BAS activation-relevant (and deactivation relevant) events in the prediction of hypomanic (and depressive) episodes. The 3-way interaction was added to the previous regression analyses in step 6. Post hoc probing was conducted and considered the interactions between BAS sensitivity and BAS activation-relevant (and deactivation relevant) events for individuals with bipolar disorder as compared to the normal controls. Following procedures described by Aiken and West (1991) and Holmbeck (2002) for probing and graphing significant interactions, we computed two new conditional moderator variables

(± 1 *SD* from the mean of BAS sensitivity) and new interactions that incorporated the conditional variables. We then ran two post-hoc regressions, each of which involved simultaneous entry of BAS activation-relevant or deactivation-relevant events, BAS sensitivity and the BAS x BAS activation-relevant or deactivation-relevant events interaction term (Holmbeck, 2002). From these analyses, we derived unstandardized betas (slopes) and a regression equation for normal controls and bipolar spectrum participants with high (1 *SD* above the mean) and low (1 *SD* below the mean) BAS sensitivity.

In the cognitive vulnerability-stress analyses, the sample size was 200, including 105 normal controls and 95 individuals with bipolar disorder. Thus, there was sufficient power to detect at least a medium effect. Hierarchical regression was used to determine if the interaction of BAS-relevant or BAS-irrelevant cognitive styles and congruent life events predicted the number of hypomanic or depressive mood episodes over time. In all analyses, the length of time in the study was included in step 1. Step 2 included the other covariates, treatment status and comorbidity, step 3 included the specific cognitive vulnerability score, step 4 included the appropriate life events term, and step 5 included the interaction of the cognitive vulnerability score and the life events score. Initial regressions showed multicollinearity, indicating that there was a strong correlation between two or more predictors in a model. As suggested by Field (2009), all variables and interaction terms were centered around the grand mean. All regressions for this hypothesis used centered variables, unless otherwise noted.

When significant interaction effects emerged from the analyses, planned contrasts were conducted to determine the relationship between the number of life events and the

number of mood episodes for individuals with high vs. low cognitive vulnerability. Planned contrasts were conducted with a median split of the cognitive vulnerability scores to separate the high vs. low groups.

Hypothesis 8.

It was hypothesized that the interaction of an individual's BAS sensitivity with the number of BAS-relevant events would predict the time period between episodes; increasing numbers of BAS-relevant events would predict less time between episodes for individuals with a more sensitive BAS. These effects would be stronger for individuals with a diagnosis in the bipolar spectrum.

Hierarchical linear regression was conducted with BAS sensitivity, BAS-relevant events, and the interaction of BAS sensitivity and BAS-relevant events as predictors of the length of time between mood episodes. Initial regressions showed multicollinearity, indicating that there was a strong correlation between two or more predictors in the models. As suggested by Field (2009), all variables were centered around the grand mean. All regressions for this hypothesis used centered variables, unless otherwise noted. All regressions controlled for treatment status and comorbidity in Step 1. In order to determine group differences, a regression was conducted to examine the effect of the 3-way interaction between group, BAS sensitivity, and BAS activation-relevant events (or BAS deactivation-relevant events) in predicting time between episodes. The 3-way interaction was added on Step 4 of the previous regression analyses. The sample size for this hypothesis was 88, including 35 individuals in the bipolar group and 53 in the normal control group.

CHAPTER 3

RESULTS

Preliminary analyses

Demographics Information

SPSS version 16.0 was used for all major analyses. The bipolar group included 112 individuals and the normal control group included 105 individuals. The mean age at study entry was 19.77 years (*SD* = 1.87 years). The sample was 64.5% female and 55.6% Caucasian. The two groups did not differ significantly on gender ($F(1, 215) = .021$, $p > .05$, $B = .02$), ethnicity ($F(1, 215) = 3.850$, $p > .05$, $B = .27$), or age ($F(1, 215) = .313$, $p > .05$, $B = .13$). See Table 1 for complete demographic information.

Descriptive Statistics

Means and standard deviations were calculated for each variable (see Table 2). The longer individuals were in the study, the more likely they were to experience life events and mood episodes. Thus, length of time in study was controlled for in all analyses involving episodes or life events.

An ANOVA was conducted to determine if there were significant differences among the average times between episodes as a function of the number of mood episodes. The results show that there was a significant effect of the number of mood episodes on the time between mood episodes, $F(3, 63) = 4.063$, $p < .05$. This suggests that the more mood episodes participants experienced, the shorter the amount of time there was between the episodes.

Table 1. Demographic Characteristics of the Sample

	Normal Controls (N=105)	Bipolar Group (N=112)
Age in years, mean (S.D.)	19.9 (1.922)	19.66 (1.835)
Female	68 (64.8)	72 (64.3)
Male	37 (35.2)	40 (35.7)
Ethnicity		
Caucasian	60 (56.6)	62 (53.9)
African-American	22 (20.8)	33 (28.7)
Asian	3 (2.8)	5 (4.3)
Hispanic/Latino	7 (6.6)	4 (3.5)
Mixed/Other	14 (13.2)	11 (9.6)

Note. Values enclosed in parentheses represent the percentage of the group in each cell, except when noted.

Table 2. Descriptive Statistics and Group Differences Among Study Variables.

Variable	Normal Controls Mean (S.D.)	Bipolar Group Mean (S.D.)	Whole Sample Mean (S.D.)	T-Value	Effect Size (*r*)
LE Follow Up	1200.82 (726.82) n=99	1203.68 (740.58) n=102	1207.89 (732.69) n=201	.165	.00
EP Follow Up	982.96 (541.70) n=105	1289.35 (3377.46) n=114	1137.81 (2455.09) n=219	-.918	.14
Total ME	.55 (1.42)*** n=107	4.57 (9.08)*** n=116	2.63 (6.88) n=223	-4.532	-.30
DEP days	17.92 (60.38)*** n=107	106.04 (1195.38)*** n=116	63.34 (.13) n=223	-4.470	-.05
Hypo days	.73 (3.90)*** n=107	33.43 (77.52)*** n=116	17.59 (57.98) n=223	-4.358	-.28
DEP EPs	.46 (1.33)*** n=107	2.34 (5.59)*** n=116	1.43 (4.21) n=223	-3.394	-.22
Hypo EPs	.09 (.52)*** n=107	2.23 (5.75)*** n=116	1.20 (4.27) n=223	-3.839	-.25
BAS-A events	69.38 (63.32) n=98	87.89 (82.18) n=102	78.52 (73.81) n=200	-1.776	-.13
BAS-D events	49.76 (47.18)* n=98	74.92 (72.52)* n=102	62.35 (62.39) n=200	-2.892	-.20
		BAS Sensitivity			
BAS Total	36.73 (5.91)*** n=55	40.92 (5.65)*** n=37	38.41 (6.13) n=92	-3.397	-.34
Fun Seeking	10.28 (2.29)** n=58	11.87 (2.61)** n=39	10.92 (2.54) n=97	-3.180	-.31
Reward	16.05 (1.88)** n=57	17.29 (1.92)** n=38	16.55 (1.98) n=95	-3.113	-.31
Drive	10.38 (2.81)* n=56	11.76 (2.25)* n=38	10.94 (2.67) n=94	-2.544	-.26

	BAS-Relevant Cognitive Styles				
DAS-PE	2.22 (.73)*** n=102	3.20 (1.18)*** n=102	2.71 (1.09) n=204	-7.168	-.45
SAS-A	94.50 (12.67)*** n=104	104.20 (11.93)*** n=102	99.30 (13.21) n=206	-5.656	-.37
DEQ-SC	-.93 (.87)*** n=103	.46 (1.02)*** n=97	-.26 (1.17) n=200	-10.429	-.59
	BAS-Irrelevant Cognitive Styles				
DAS-ABO	3.47 (.86)* n=102	3.82 (1.12)* n=102	3.65 (1.01) n=204	-2.494	-.17
SAS-S	82.00 (16.39)* n=104	90.04 (19.83)* n=102	18.58 (85.98) n=206	-3.174	-.22
DEQ-DEP	-1.05 (.82)* n=103	-.72 (1.02)* n=102	-.89 (.93) n=205	-2.550	-.18

Note. * p<.05, ** p<.01, ***p<.001; all significance tests were 2-tailed; LE Follow Up= Average follow up period for life events, EP Follow Up = average follow up period for mood episodes, Total ME = total mood episodes, DEP days = days in a depressive episode, Hypo days = days in a hypomanic or severe hypomanic episode, DEP EPs = total depression episodes, Hypo EPs = total hypomanic or severe hypomanic episodes, BAS-A events = total BAS activation-relevant events, BAS-D events = total BAS deactivation-relevant events, DAS-PE = Dysfunctional Attitudes Scale-Performance Evaluation Subscale, SAS-A = Sociotropy-Autonomy Scale- Autonomy Subscale, DEQ-SC = Depressive Experiences Questionnaire – Self-Criticism Subscale, DAS-ABO = Dysfunctional Attitudes Scale- Approval By Others Subscale, SAS-S= Sociotropy-Autonomy Scale-Sociotropy Subscale, DEQ-DEP= Depressive Experiences Questionnaire – Dependency Subscale.

There was a significant effect of group on lifetime suicidal ideation, $F(2, 217) = 29.111$, $p<.05$, $r = .25$, and prospective suicidal ideation $F(2, 214) = 10.805$, $p<.05$, $r = .11$. Planned contrasts revealed a significant difference on lifetime suicidal ideation and prospective suicidal ideation between normal controls and bipolar individuals, $t(217) = 7.387$, $p<.05$, $r = .45$, and $t(214) = 4.228$, $p<.05$, $r = .28$, respectively. The bipolar spectrum group exhibited greater lifetime and prospective suicidal ideation than the normal control group. There was also a significant effect of group on lifetime suicide attempts, $F(2, 217) = 3.968$, $p<.05$, $r = .04$, but not prospective suicide attempts $F(2, 214) = 1.522$, $p>.05$, $r = .01$. Planned contrasts revealed a significant difference on lifetime suicide attempts between normal controls and bipolar individuals, $t(217) = 2.561$, $p < .05$, $r = .17$, such that bipolar individuals exhibited more lifetime suicide attempts.

Differences between Bipolar group and Normal control group

There were no significant differences between the bipolar group and the normal control group on demographic variables. The bipolar group scored significantly higher than the normal control group on total mood episodes, days in depression, days in hypomania, depression episodes, hypomania episodes, BAS deactivation-relevant events, BAS sensitivity, BAS subscales of Fun-Seeking, Reward, and Drive, DAS-PE, SAS-A, DEQ-SC, DAS-ABO, SAS-S, and DEQ-DEP (see Table 2 for means and standard deviations).

Relationship between Demographics and Study Variables

The relationship between ethnicity, age, gender, comorbidity, treatment status, and mood episode and life event variables were examined. Comorbidity, as determined by the presence of an Axis I disorder other than bipolar disorder and/or a phobia, and

treatment status, as defined by ever having sought therapy or psychiatric medication, were significantly positively correlated with total life events, BAS-relevant life events, total mood episodes, hypomanic episodes, and treatment status (see Table 3 for further information). Thus, comorbidity and treatment status were controlled for in analyses when BAS-relevant life events and mood episodes were the dependent variables.

Tests of Hypotheses

Hypothesis 1

It was hypothesized that BAS sensitivity would be associated with age of onset of bipolar spectrum disorders, such that individuals with a more sensitive BAS would have an earlier age of onset, and onsets of first episode mania/hypomania, in particular, than those with a less sensitive BAS. There were no significant correlations between BAS sensitivity and earliest age of onset of any type of mood episode, r=-.06, p (1-tailed) >.05, earliest age of onset of hypomania/mania, r=-.08, p (1-tailed) >.05, or earliest age of onset of depression, r=.07, p (1-tailed) >.05. Partial correlations were conducted controlling for family history of bipolar disorder; there were no significant correlations between BAS sensitivity and earliest age of onset of any type of mood episode r=-.09, p (1-tailed) >.05, earliest age of onset of hypomania/mania, r=-.12, p (1-tailed) >.05, or earliest age of onset of depression, r=.06, p (1-tailed) >.05.

Hypothesis 2

It was hypothesized that BAS sensitivity would predict time spent in a euthymic mood state, such that individuals with a more sensitive BAS would spend less time in euthymia than individuals with a less sensitive BAS. There were significant negative

Table 3. Correlations Among Study Variables.

Variable	1	2	3	4	5	6	7	8	9	10
1. Age	-									
2. Sex	.07	-								
3. Eth	.08	.09	-							
4. BAS	-.05	.03	.07	-						
5. LE Total	-.09	.06	-.06	.14	-					
6. BAS events	.00	-.05	-.06	.16	.10	-				
7. Eps Total	-.01	-.08	-.07	.21*	.03	.33***	-			
8. Dep Eps	-.04	-.03	-.01	.25*	.01	.25***	.81***	-		
9. Hypo Eps	.03	-.10	-.10	.09	.04	.29***	.81***	.31***	-	
10. CO	-.08	.05	-.09	.09	.18*	.30***	.17*	.13	.15*	-
11. TS	-.01	.13	-.08	-.13	.20**	.29***	.22**	.09	.27***	.38***

Note. * p<.05, ** p<.01, ***p<.001; Eth = Ethnicity, BAS = Behavioral Activation System Sensitivity, LE Total = total Life Events, BAS Events = total BAS-relevant life events, Eps Total = total mood episodes, Dep Eps = total episodes of depression, Hypo Eps = total episodes of hypomania or severe hypomania, CO = comorbidity, TS = treatment status.

correlations between BAS sensitivity and time spent in euthymia for the whole sample, r=-.23, p<.05, but not for the bipolar group alone, r=-.12, p >.05. Higher BAS sensitivity was associated with less time spent in euthymia. Controlling for family history of bipolar disorder, there were significant correlations for the whole sample, r=-.28, p <.01, but not for the bipolar group alone, r=-.26, p >.05. Given that the magnitude of the correlation for the bipolar group alone was the same as that for the whole sample with family history controlled, it suggests that the correlation for the bipolar group was nonsignificant because of insufficient statistical power (n = 37 for the bipolar group alone).

Hypothesis 3

It was hypothesized that BAS sensitivity would predict the predominance of depression vs. hypomania/mania in the course of bipolar spectrum disorders. Specifically, individuals with a more sensitive BAS would have a predominantly hypomanic/manic course of illness, whereas individuals with a less sensitive BAS would have a predominantly depressive course of illness. In addition, BAS-relevant cognitive style measures would predict the predominance of depression vs. hypomania/mania in the course of bipolar spectrum disorders.

Hypothesis 3a: BAS sensitivity would predict the predominance of depression vs. hypomania/mania in the course of bipolar spectrum disorders.

BAS sensitivity was significantly correlated with the number of hypomanic/severe hypomanic episodes, r=.18, p (1-tailed) <.05, and the percentage of days spent in a hypomanic/severe hypomanic episode, r=.24, p (1-tailed) <.05 (see Table 4 for detailed

Table 4. Hypothesis #3. Summary of Correlations between BAS Sensitivity, Cognitive Vulnerability Measures, and Course Variables.

	1	2	3	4	5	6	7	8	9	10
1. BAS	-									
2. DAS-PE	.18	-								
3. SAS-A	.41***	.09	-							
4. DEQ-SC	.33**	..66***	.27***	-						
5. DAS-ABO	-.03	.64***	-.20**	.39***	-					
6. SAS-S	.19	.50***	.04	.41***	.67***	-				
7. DEQ-DEP	.01	.38***	-.17*	.18**	.58***	.72***	-			
8. Hypo Eps	.18*	.22**	.22**	.33***	.08	.04	.02	-		
9. Dep Eps	.02	.22***	.06	.19**	.10	.10	.07	-.15*	-	
10. Hypo Days	.24*	.09	.19**	.27***	-.07	.02	.09	.46***	-.02	-
11. Dep Days	.27*	.28***	.09	.29***	.12	.09	.02	.15*	.34***	.45***

Note. All tests are one-tailed. * p<.05, ** p<.01, ***p<.001; BAS = Behavioral Activation System Sensitivity, DAS-PE = Dysfunctional Attitudes Scale-Performance Evaluation Subscale, SAS-A = Sociotropy-Autonomy Scale- Autonomy Subscale, DEQ-SC = Depressive Experiences Questionnaire – Self-Criticism Subscale, DAS-ABO = Dysfunctional Attitudes Scale- Approval By Others Subscale, SAS-S= Sociotropy-Autonomy Scale-Sociotropy Subscale, DEQ-DEP= Depressive Experiences Questionnaire – Dependency Subscale, Hypo Eps = total hypomanic or severe hypomanic episodes, Dep Eps = total depression episodes, Hypo Days = days spent in a hypomanic or severe hypomanic episode/total days in study, Dep Days = days spent in a depressive episode/total days in study.

information). BAS sensitivity was significantly correlated with the percentage of days spent in a depressive episode, r=.27, p (1-tailed) <.05, but not with the number of depressive episodes, r=.02, p (1-tailed) >.05. In addition, when using a regression model and entering covariates in the first step of the equation, BAS sensitivity did predict the percentage of days spent in a hypomanic episode, B=.187, $F(1, 83) = 9.317$, p<.05, and the number of depressive episodes, B=.226, $F(1, 83) = 3.476$, p<.05. However, BAS sensitivity did not significantly predict the number of hypomanic episodes or the percentage of days spent in a depressive episode.

Hypothesis 3b: BAS-relevant cognitive vulnerability scores would predict the predominance of depression vs. hypomania/mania in the course of bipolar spectrum disorders.

As determined by previous research (Alloy, Abramson, Walshaw, et al., 2009), measures of BAS-relevant cognitive styles included the Dysfunctional Attitudes Scale performance evaluation subscale (DAS-PE), Sociotropy-Autonomy Scale –Autonomy subscale (SAS-A), and Depressive Experiences Questionnaire - self-criticism subscale (DEQ-SC). Measures of BAS-irrelevant cognitive styles included the DAS approval by others subscale (DAS-ABO), SAS sociotropy subscale (SAS-S), and DEQ dependency subscale (DEQ-DEP). Results showed that the DAS-PE, SAS-A, and DEQ-SC were significantly positively correlated with the number of hypomanic episodes, SAS-A and DEQ-SC were significantly positively correlated with the percentage of days spent in hypomanic epsisodes, and DAS-PE and DEQ-SC were significantly positively correlated with the percentage of days spent in depression and the number of depressive episodes (see Table 4). BAS-irrelevant cognitive styles, such as the DAS-ABO, SAS-S, and DEQ-

DEP, were not significantly correlated with the number of hypomanic or depressive episodes or percentage of days spent in hypomania or depression.

Utilizing regression, results indicated that the BAS-relevant cognitive style of DEQ-SC significantly predicted the percentage of days spent in hypomania, B =.34, $F(1, 166) = 4.877$, $p<.01$. No BAS-relevant or BAS-irrelevant cognitive style significantly predicted the number of hypomanic episodes, depressive episodes, or the percentage of days spent in depression.

Hypothesis 4

It was hypothesized that a lower number of major BAS activation-relevant events would predict greater time in euthymia. Normal control individuals would spend more time in euthymia than individuals in the bipolar spectrum and this group difference would be mediated by the number of BAS activation-relevant events each group experienced.

Time spent in euthymia was significantly negatively correlated with BAS activation-relevant events, $r=-.20$, $p<.05$, and BAS deactivation-relevant events, $r=-.20$, $p<.05$. This indicates that a greater number of BAS relevant events predicted less time in euthymia. Furthermore, diagnostic group and time spent in euthymia were significantly positively correlated, B=7.904, $r=.39$, $p<.001$. Normal control participants spent more time in a euthymic state than did bipolar individuals.

A bootstrapping approach (Shrout & Bolger, 2002) to mediation was used here. Tests of simple indirect effects indicated that the relationship between diagnostic group and euthymia was not significantly mediated by BAS activation-relevant events, $p >.05$. However, this bootstrapping operation assumes normality of the standard error and is not preferred. Thus, we examined the bootstrap results for the indirect effect. This also

indicated that the mediator was not significant, as the 95% confidence interval includes zero (.0056, -.0072). Both the preferred and non-preferred tests for mediation are in agreement that BAS activation-relevant events do not significantly mediate the relationship between diagnostic group and euthymia.

Hypothesis 5

It was hypothesized that individuals with a predominantly depressive course of bipolar disorder would experience a greater number of BAS deactivation-relevant events than those with a predominantly manic/hypomanic course. Conversely, those individuals with a predominantly hypomanic/manic course of bipolar disorder would experience a greater number of BAS activation-relevant events than those with a predominantly depressive course. Similarly, the number of BAS-activation and –deactivation relevant events would predict the proportion of the number of hypomanic/manic vs. depressive episodes and the proportion of days with hypomanic/manic vs. depressive symptoms.

Based on episode data, 108 participants experienced at least 1 mood episode and of those, 73 participants (68%) were determined to have experienced a depressive course of bipolar disorder and 35 participants (32%) experienced a hypomanic course of bipolar disorder. Based on the days in episodes, 90 participants were determined to have experienced a depressive course of bipolar disorder and 18 participants (17%) experienced a hypomanic course of bipolar disorder.

T-tests were conducted to determine group differences in the number of BAS deactivation-relevant events and BAS activation-relevant events experienced by individuals with a predominantly hypomanic versus depressive course of illness. T-tests revealed a significant difference between hypomanic and depressive episode course of

illness for BAS activation-relevant events, $t(95) = 1.677$, p (1-tailed)<.05, $r = .17$, with individuals with a depressive course experiencing more BAS activation-relevant events. There were no significant differences between the groups on the number of BAS deactivation-relevant events and total BAS-relevant events. When using the days in episode course of illness, there were no significant group differences in BAS activation- or deactivation-relevant events, or total BAS-relevant events.

Utilizing linear regression, results showed that BAS activation-relevant events significantly predicted the percentage of days spent in depression, $B = .22$, $F(1, 196) = 8.682$, $p<.01$, such that as BAS activation-relevant events increased, so did the percentage of days in depression (see Table 5 for a summary of these results). BAS activation-relevant events also significantly predicted the proportion of depressive episodes to total episodes, $B = .17$, $F(1, 196) = 5.546$, $p<.05$, such that as BAS activation-relevant events increased, so did the proportion of depressive episodes to total episodes. However, these effects were not significant when controlling for treatment status and comorbidity. BAS deactivation-relevant events significantly predicted the percentage of days spent in depression, B=.210, $F(1, 196) = 9.128$, $p<.01$, such that as BAS deactivation-relevant events increased, so did the percentage of days in depression. However, this effect was not significant when controlling for treatment status and comorbidity. All other analyses were not significant.

Hypothesis 6

It was hypothesized that individuals in a depressive episode would be less likely than individuals in a manic/hypomanic episode to create or select goal-striving or goal-attainment events.

Table 5. Hypothesis 5. Linear Regression Using Number of BAS Activation- and BAS Deactivation-Relevant Life Events to Predict Course of Illness.

Predictor Variable	*B*	*SEB*	*β*	R^2	ΔR^2	ΔF
Overall Model Predicting Days in Hypomania				.06	.04	.11
Treatment Status	.00	.00	.08			
Comorbidity	.02	.01	.20*			
BAS Activation Events	.00	.00	-.03			
Overall Model Predicting Days in Hypomania				.06	.04	.03
Treatment Status	.00	.00	.08			
Comorbidity	.02	.01	.20*			
BAS Deactivation Events	.00	.00	-.01			
Overall Model Predicting Proportion of Episodes of Hypomania				.13	.11	.261
Treatment Status	.07	.02	.22**			
Comorbidity	.15	.05	.22**			
BAS Activation Events	.00	.00	-.04			
Overall Model Predicting Proportion of Episodes of Hypomania				.13	.11	.108
Treatment Status	.07	.02	.22**			
Comorbidity	.15	.05	.22**			
BAS Deactivation Events	.00	.00	-.02			
Overall Model Predicting Days in Depression				.14	.13	3.66
Treatment Status	.02	.01	.13			
Comorbidity	.06	.02	.23**			
BAS Deactivation Events	.00	.00	.14			
Overall Model Predicting Days in Depression				.14	.12	2.991
Treatment Status	.02	.01	.13			
Comorbidity	.06	.02	.24**			
BAS Activation Events	.00	.00	.13			
Overall Model Predicting Proportion of Episodes of Depression				.07	.06	2.804
Treatment Status	.01	.03	.02			
Comorbidity	.18	.07	.20*			
BAS Activation Events	.01	.00	.13			
Overall Model Predicting Proportion of Episodes of Depression				.06	.04	.362
Treatment Status	.02	.03	.04			
Comorbidity	.18	.07	.21*			
BAS Deactivation Events	.00	.01	.05			

NOTE.*$p < .05$, **$p < .01$

Logistic regression was used here, and Table 6 presents a summary of the findings. Results showed that greater days spent in a hypomanic episode, both with and without controlling for treatment status and comorbidity, significantly predicted a greater likelihood of a subsequent BAS activation-relevant or goal-attainment event after an episode of hypomania. Additionally, a greater number of hypomanic episodes experienced, controlling for treatment status and comorbidity, significantly predicted a greater likelihood of subsequent BAS activation or goal attainment-relevant events after an episode of hypomania. Also, the overall model including number of hypomanic episodes experienced, treatment status, and comorbidity, significantly predicted the likelihood of subsequent BAS activation or goal attainment-relevant events after an episode of major depression. However, the number of hypomanic episodes was not a significant predictor in this model.

Furthermore, greater days spent in a depressive episode, while controlling for treatment status and comorbidity, significantly predicted a greater likelihood of a subsequent BAS activation-relevant or goal-attainment event after an episode of major depression. In addition, a greater number of depressive episodes experienced, both with and without controlling for treatment status and comorbidity, significantly predicted a greater likelihood of a subsequent BAS activation-relevant or goal-attainment relevant event after an episode of either major or minor depression. The number of depressive episodes alone was a significant predictor of events after a minor depression, but not after a major depression.

Utilizing t tests, results indicated that, on average, individuals experienced a higher number of BAS activation and goal attainment-relevant events after an episode of

Table 6. Logistic Regression Predicting BAS and Goal-Relevant Events in Month After Onset of Mood Episodes

	B(SE)	Wald	Odds Ratio	X^2	df
			Prediction of BAS or GA Events after Hypomania		
Overall Model				19.11**	5
Treatment Status	-.56(.60)	.88	.57		
Comorbidity	-.21(.52)	.17	.81		
Days in Hypomania	20.43(7.38)**	7.66	7.45		
Overall Model				7.13	5
Treatment Status	-.49(.57)	.74	.61		
Comorbidity	-.40(.48)	.70	.67		
Days in Depression	.83(1.41)	.353	2.30		
Overall Model				61.82***	4
Days in Study	.00(.00)	2.38	.99		
Treatment Status	-.07(.30)	.05	.94		
Comorbidity	.00(.75)	.00	1.00		
Hypomania Episodes	1.73(.40)***	18.72	5.61		
Overall Model				8.26	4
Days in Study	.00(.00)	.52	1.00		
Treatment Status	.23(.20)	1.40	1.25		
Comorbidity	.39(.49)	.63	1.47		
Depressive Episodes	.11(.08)	1.70	1.11		
			Prediction of BAS or GA Events after Major Depression		
Overall Model				10.44	5
Treatment Status	-.35(.66)	.28	.71		
Comorbidity	-1.71(.71)*	5.86	1.14		
Days in Hypomania	.14(6.12)	.00	1.15		
Overall Model				24.51***	5
Treatment Status	-.19(.75)	.07	.83		
Comorbidity	-1.54(.75)*	4.24	.22		
Days in Depression	6.38(1.97)***	10.50	591.18		
Overall Model				9.49*	4
Days in Study	.00(.00)	.36	1.00		
Treatment Status	.10(.23)	.19	1.11		
Comorbidity	1.73(.70)*	6.08	5.62		
Hypomania Episodes	.00(.05)	.00	1.00		
Overall Model				13.76*	4
Days in Study	.00(.00)	.00	1.00		
Treatment Status	.11(.22)	.26	1.12		
Comorbidity	1.89(.77)*	6.03	6.60		
Depressive Episodes	.08(.05)	3.34	1.09		

Table 6 *(continued).*

	B(SE)	Wald	Odds Ratio	X^2	df
Prediction of BAS or GA Events after Minor Depression					
Overall Model				1.23	5
Treatment Status	-.45(.56)	.624	.64		
Comorbidity	.03(.46)	.01	1.03		
Days in Hypomania	2.78(4.59)	.37	16.15		
Overall Model				7.97	5
Treatment Status	-.32(.60)	.29	.73		
Comorbidity	.25(.49)	.27	1.29		
Days in Depression	3.94(1.61)*	5.99	51.40		
Overall Model				4.09	4
Days in Study	.00(.00)	.44	1.00		
Treatment Status	.10(.20)	.25	1.10		
Comorbidity	.02(.47)	.00	1.02		
Hypomania Episodes	.06(.06)	1.97	1.06		
Overall Model				41.67***	4
Days in Study	.00(.00)	.00	1.00		
Treatment Status	-.04(.26)	.03	.96		
Comorbidity	-.87(.63)	1.89	.42		
Depressive Episodes	.99(.23)***	18.23	2.68		

NOTE.*$p < .05$, **$p < .01$, ***$p < .001$

hypomania (M = .55, SE = .10) than after an episode of major depression (M = .30, SE = .09). This difference was significant $t(97) = 5.337$, p (1-tailed) <.001. Similarly, on average, individuals experienced a smaller number of BAS activation and goal attainment-relevant events after an episode of hypomania than after an episode of minor depression (M = .68, SE = .12). This difference was significant $t(97) = 5.337$, p (1-tailed)<.001.

Hypothesis 7

It was hypothesized that the interaction of an individual's BAS sensitivity with the number of BAS activation-relevant events would predict the number of hypomania/mania episodes over time. Relatedly, the interaction of BAS sensitivity with the number of BAS deactivation-relevant events would predict the number of episodes of depression over time. These effects would be stronger for individuals with a diagnosis in the bipolar spectrum, as compared to normal controls. In addition, the interaction of an individual's BAS-relevant cognitive styles with the number of congruent positive events would predict the number of hypomania/mania episodes over time. Relatedly, the interaction of BAS-relevant cognitive styles with the number of congruent negative events would predict the number of depressive episodes over time.

BAS Model

Prediction of hypomanic episodes.

Results indicated that whereas the overall model including the interaction of BAS sensitivity and BAS activation-relevant events, and all main effects, significantly predicted the number of hypomanic episodes, the main effects of BAS sensitivity and

BAS activation events and their interaction were not significant predictors in the model (see Table 7).

Prediction of depression episodes.

Results indicated that the overall model including the interaction of BAS sensitivity and BAS deactivation-relevant events, and all main effects, significantly predicted the number of depressive episodes (see Table 8). However, the main effect of BAS sensitivity was the only significant predictor in the model. The BAS subscales were also examined. The model including the interaction of Funseeking and BAS deactivation-relevant events, and all main effects, significantly predicted the number of depressive episodes. The Funseeking subscale was the only significant predictor. All other regressions involving the Drive and Reward subscales were not significant.

Group differences.

In order to determine group differences, a regression was conducted to determine the effect of the 3-way interaction between group, BAS sensitivity, and BAS activation-relevant events in the prediction of hypomanic episodes. The 3-way interaction was significant, $B = -.29$, $p<.05$. Post hoc probing found that, among the normal controls, the BAS x BAS activation-relevant events interaction term was not significant in predicting hypomanic episodes ($B =-.22$, $p > .05$). Similarly, among the bipolar group, the BAS x BAS activation-relevant events interaction term was not significant in predicting hypomanic episodes ($B =-.27$, $p > .05$). As the effect sizes are in the small, but reasonable range, it is likely that we do not have sufficient power to detect significant differences. However, it should be noted that the effect of the interaction was larger in the bipolar group than among the normal controls.

Table 7. Hypothesis #7. Hierarchical Linear Regression Using BAS Sensitivity and BAS-Relevant Cognitive Vulnerability Scores to Predict Hypomanic Episodes.

Predictor Variable	*B*	*SE B*	*β*	R^2	ΔR^2	*F*
		BAS Model				
Overall Model				.29	.02	5.564***
Days in Study	.01	.00	.42***			
Treatment Status	1.13	.64	.19			
Comorbidity	1.87	1.41	.14			
BAS	.09	.10	.09			
BAS-A Events	.01	.01	.10			
BAS x BAS-A Events	.00	.00	-.28			
		Cognitive Vulnerability Model				
Overall Model				.26	.06	9.686***
Days in Study	.00	.00	.33***			
Treatment Status	1.10	.35	.24**			
Comorbidity	.85	.73	.09			
DAS-PE	.49	.34	.11			
BAS-A Events	.01	.01	.07			
DAS-PE x BAS-A Events	.02	.00	.41***			
Overall Model				.26	.07	9.840***
Days in Study	.00	.00	.33***			
Treatment Status	1.10	.35	.24**			
Comorbidity	.85	.73	.09			
DAS-PE	.49	.34	.11			
PosGoal Events	.00	.01	.01			
DAS-PE x PosGoal Events	.02	.01	.26***			
Overall Model				.27	.08	10.507***
Days in Study	.00	.00	.33***			
Treatment Status	1.10	.35	.24**			
Comorbidity	.85	.73	.09			
DAS-PE	.49	.34	.11			
PosAchEvents	.00	.01	.02			
DAS-PE x PosAch Events	.05	.01	.93***			
Overall Model				.22	.01	8.048***
Days in Study	.00	.00	.32***			
Treatment Status	1.09	.34	.23**			
Comorbidity	.90	.72	.09			
SAS-A	.06	.02	.17*			
BAS-A Events	.01	.01	.08			
SAS-A x BAS-A Events	.00	.00	.09			

Table 7 *(continued).*

Predictor Variable	*B*	*SEB*	*β*	R^2	ΔR^2	*F*
			Cognitive Vulnerability Model			
Overall Model				.21	.00	7.482***
Days in Study	.00	.00	.32***			
Treatment Status	1.09	.34	.23**			
Comorbidity	.90	.72	.09			
SAS-A	.06	.02	.17*			
PosGoal Events	.00	.01	.02			
SAS-A x PosGoal Events	.00	.00	.03			
Overall Model				.21	.00	7.531***
Days in Study	.00	.00	.32***			
Treatment Status	1.09	.34	.23**			
Comorbidity	.90	.72	.09			
SAS-A	.06	.02	.17*			
PosAchEvents	.01	.01	.04			
SAS-A x PosAch Events	.00	.00	.03			
Overall Model				.22	.02	7.732***
Days in Study	.00	.00	.33***			
Treatment Status	1.11	.35	.24**			
Comorbidity	.84	.75	.08			
DEQ-SC	.52	.33	.13			
BAS-A Events	.01	.01	.08			
DEQ-SC x BAS-A Events	.01	.00	.15			
Overall Model				.22	.02	7.845***
Days in Study	.00	.00	.33***			
Treatment Status	1.11	.35	.24**			
Comorbidity	.84	.75	.08			
DEQ-SC	.52	.33	.13			
PosGoal Events	.00	.01	.02			
DEQ-SC x PosGoal Events	.01	.01	.16*			
Overall Model				.23	.03	8.198***
Days in Study	.00	.00	.33***			
Treatment Status	1.11	.35	.24**			
Comorbidity	.84	.75	.08			
DEQ-SC	.52	.33	.13			
PosAch Events	.01	.01	.03			
DEQ-SC x PosAch Events	.03	.01	.18**			

NOTE. All variables are centered. *p < .05, **p < .01, ***p <.001, BAS = BAS sensitivity, BAS-A = BAS activation-relevant events, DAS-PE = Dysfunctional Attitudes Scale-Performance Evaluation Subscale, PosGoal Events = Positive Goal-Relevant Events, PosAch Events = Positive Achievement Events, SAS-A = Sociotropy-Autonomy Scale Autonomy Subscale, DEQ-SC = Depressive Experiences Questionnaire – Self-Criticism Subscale.

Table 8. Hypothesis #7. Hierarchical Linear Regression Using BAS Sensitivity and BAS-Relevant Cognitive Vulnerability Scores to Predict Depressive Episodes.

Predictor Variable	*B*	*SEB*	*β*	R^2	ΔR^2	*F*
		BAS Model				
Overall Model				.15	.00	2.311*
Days in Study	.00	.00	.28**			
Treatment Status	-.27	.69	-.05			
Comorbidity	1.83	1.51	.14			
BAS	.22	.10	.23*			
BAS-D Events	.00	.01	.01			
BAS x BAS-D Events	.00	.00	-.06			
		Cognitive Vulnerability Model				
Overall Model				.13	.00	3.992***
Days in Study	.00	.00	.27***			
Treatment Status	.12	.37	.03			
Comorbidity	1.16	.77	.12			
DAS-PE	.79	.36	.18*			
BAS-D Events	.01	.01	.10			
DAS-PE x BAS-D Events	.00	.01	.07			
Overall Model				.12	.00	3.615**
Days in Study	.00	.00	.27***			
Treatment Status	.12	.37	.03			
Comorbidity	1.16	.77	.12			
DAS-PE	.79	.36	.18*			
NegGoal Events	-.02	1.06	-.00			
DAS-PE x NegGoal Events	.31	1.05	.02			
Overall Model				.14	.00	4.545***
Days in Study	.00	.00	.27***			
Treatment Status	.12	.37	.03			
Comorbidity	1.16	.77	.12			
DAS-PE	.79	.36	.18*			
NegAchEvents	.06	.03	.17*			
DAS-PE x NegAch Events	.01	.02	.04			
Overall Model				.11	.01	3.538**
Days in Study	.00	.00	.27***			
Treatment Status	.09	.36	.02			
Comorbidity	1.25	.76	.13			
SAS-A	.01	.03	.03			
BAS-D Events	.01	.01	.12			
SAS-A x BAS-D Events	.00	.01	.10			

Table 8. *(continued).*

Predictor Variable	*B*	*SEB*	*β*	R^2	ΔR^2	*F*
Cognitive Vulnerability Model						
Overall Model				.09	.00	2.836*
Days in Study	.00	.00	.27***			
Treatment Status	.09	.36	.02			
Comorbidity	1.25	.76	.13			
SAS-A	.01	.03	.03			
NegGoal Events	-.02	1.08	.00			
SAS-A x NegGoal Events	-.05	.12	-.05			
Overall Model				.13	.01	4.289***
Days in Study	.00	.00	.27***			
Treatment Status	.09	.36	.02			
Comorbidity	1.25	.76	.13			
SAS-A	.01	.03	.03			
NegAchEvents	.07	.03	.20*			
SAS-A x NegAch Events	.00	.00	.11			
Overall Model				.15	.00	4.762***
Days in Study	.00	.00	.27***			
Treatment Status	.10	.37	.02			
Comorbidity	1.19	.79	.12			
DEQ-SC	1.04	.34	.25**			
BAS-D Events	.01	.10	.10			
DEQ-SC x BAS-D Events	.00	.01	.02			
Overall Model				.14	.00	4.525***
Days in Study	.00	.00	.27***			
Treatment Status	.10	.37	.02			
Comorbidity	1.19	.79	.12			
DEQ-SC	1.04	.34	.25**			
NegGoal Events	-.28	1.07	-.02			
DEQ-SC x NegGoal Events	-.23	.78	-.02			
Overall Model				.16	.00	5.371***
Days in Study	.00	.00	.27***			
Treatment Status	.10	.37	.02			
Comorbidity	1.19	.79	.12			
DEQ-SC	1.04	.34	.25**			
NegAch Events	.06	.03	.17*			
DEQ-SC x NegAch Events	.00	.03	-.00			

NOTE. All variables are centered. *p < .05, **p < .01, ***p <.001, BAS = BAS sensitivity, BAS-D = BAS deactivation-relevant events, DAS-PE = Dysfunctional Attitudes Scale-Performance Evaluation Subscale, NegGoal Events = Negative Goal-Relevant Events, NegAch Events = Negative Achievement Events, SAS-A = Sociotropy-Autonomy Scale Autonomy Subscale, DEQ-SC = Depressive Experiences Scale – Self-Criticism Subscale.

Similar analyses were conducted to predict depressive episodes. The 3-way interaction between group, BAS sensitivity, and BAS deactivation-relevant events significantly predicted depressive episodes, B = -.37, p <.05. Post hoc probing was conducted and considered the interactions between BAS sensitivity and BAS deactivation-relevant events for individuals with bipolar disorder as compared to the normal controls. This interaction was not significant among the bipolar group, which may be due to insufficient power. Among normal controls, the BAS x BAS deactivation-relevant events interaction term predicted depressive episodes (B = 2.02, p < .05). For high BAS sensitivity, the slope was significantly different from zero (B = -.67, t(51) = -2.393, p < .05), as was the slope for low BAS sensitivity (B = .93, t(51) = 3.309, p <.01). Among individuals with both high and low BAS sensitivity, more BAS deactivation-relevant events were associated with more depressive episodes.

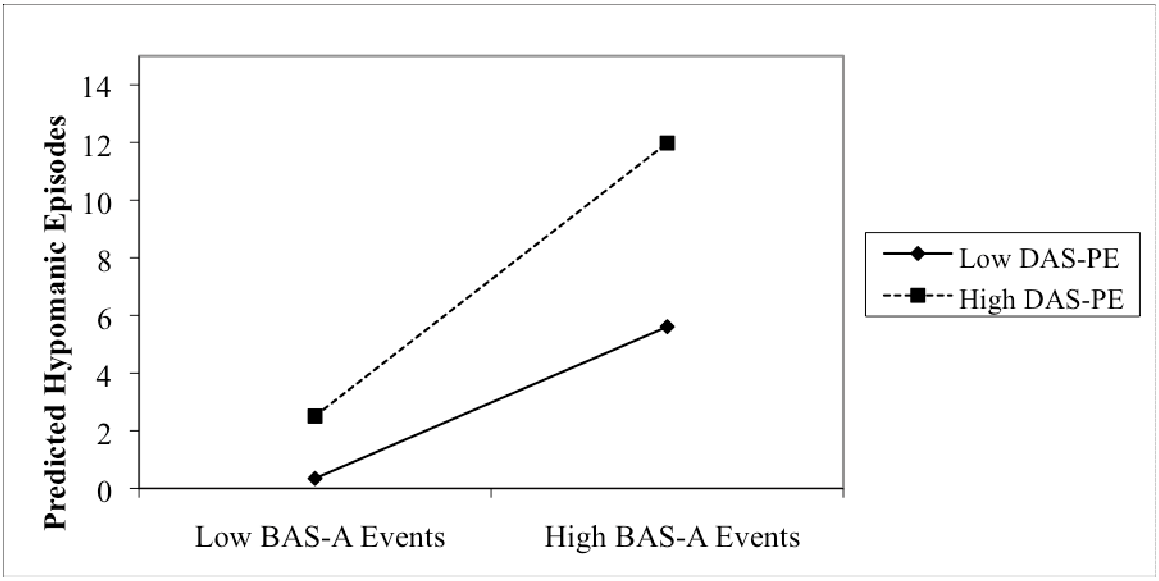
Cognitive Vulnerability Model

Prediction of hypomanic episodes.

Results for the BAS-relevant cognitive styles indicated that the model including the interaction of DAS-PE and BAS activation-relevant events, and all main effects, significantly predicted the number of hypomanic episodes (see Table 7). The interaction was significant in this model (see Figure 1). Planned contrasts revealed that BAS activation-relevant events had a slightly stronger association with hypomanic episodes for individuals with high DAS-PE scores (B=.03), as compared to individuals with low DAS-PE scores, (B=.004).

Similar results were obtained when including positive goal-relevant events and positive achievement-relevant events in the equation instead of BAS activation-relevant

Figure 1. Hypothesis #7: Interaction Between DAS-PE and BAS-A (BAS activation-relevant) Events Predicts Hypomanic Episodes.



events. The interaction between DAS-PE and positive goal-relevant events was also significant (see Figure 2). Planned contrasts revealed that positive goal-relevant events had a greater association with hypomanic episodes for individuals with high DAS-PE scores (*B*=.03), as compared to individuals with low DAS-PE scores, (*B*=.004). Also, the interaction between DAS-PE and positive achievement-relevant events was significant (see Figure 3). Planned contrasts revealed that positive achievement-relevant events had a greater relationship with hypomanic episodes for individuals with high DAS-PE scores (*B*=.05), as compared to individuals with low DAS-PE scores, (*B*=.01). Similarly, the model including the interaction of SAS-A and BAS activation-relevant events, and all main effects, significantly predicted the number of hypomanic episodes. However, only the main effect of SAS-A events significantly contributed to the model. Similar results were obtained when using positive goal-relevant and positive achievement-relevant events.

Lastly, the model including the interaction of DEQ-SC and BAS activation-relevant events, and all main effects, significantly predicted the number of hypomanic episodes. The interaction approached significance, p =.053 (see Figure 4). Planned contrasts revealed that BAS activation-relevant events had a slightly greater association with hypomanic episodes for individuals with high DEQ-SC scores (*B*=.02), as compared to individuals with low DEQ-SC scores, (*B*=.01).

Similar results were obtained when including positive goal-relevant events and positive achievement-relevant events in the equation instead of BAS activation-relevant

Figure 2. Hypothesis #7: Interaction Between DAS-PE and Pos Goal (Positive Goal-Attainment Relevant) Events Predict Hypomanic Episodes.

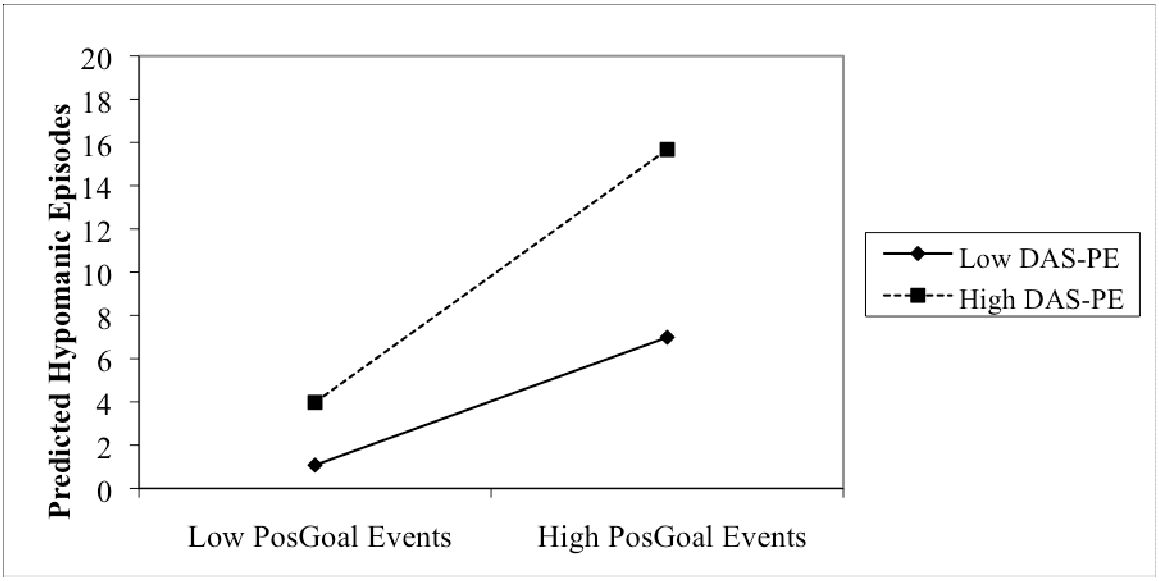


Figure 3. Hypothesis #7: Interaction Between DAS-PE and PosAch (Positive Achievement-Relevant) Events Predict Hypomanic Episodes.

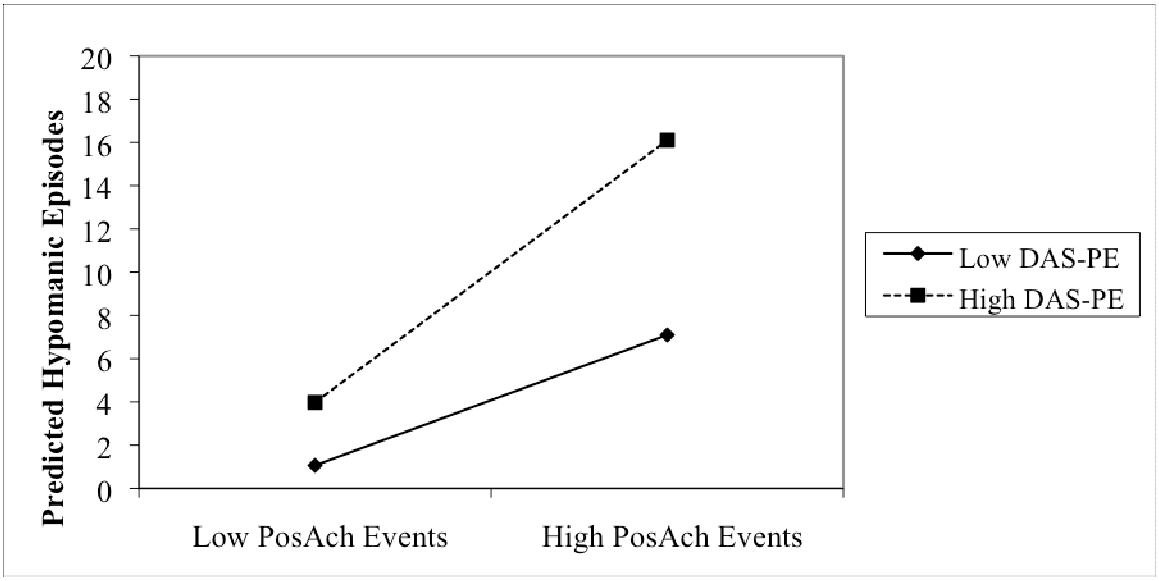
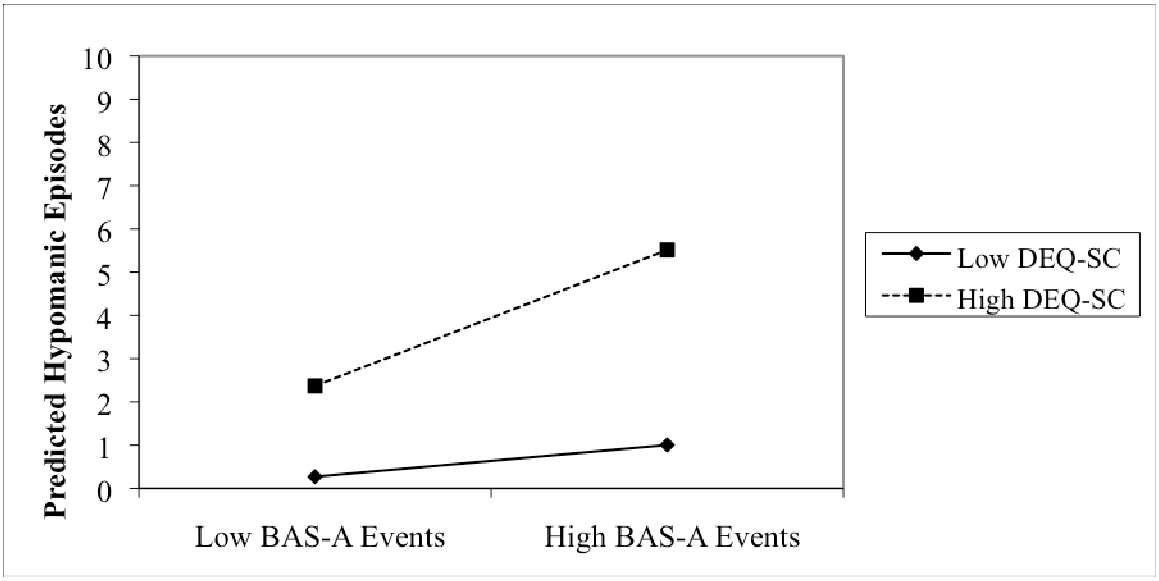


Figure 4. Hypothesis #7: Interaction Between DEQ-SC and BAS-A (BAS Activation-Relevant) Events Predict Hypomanic Episodes.



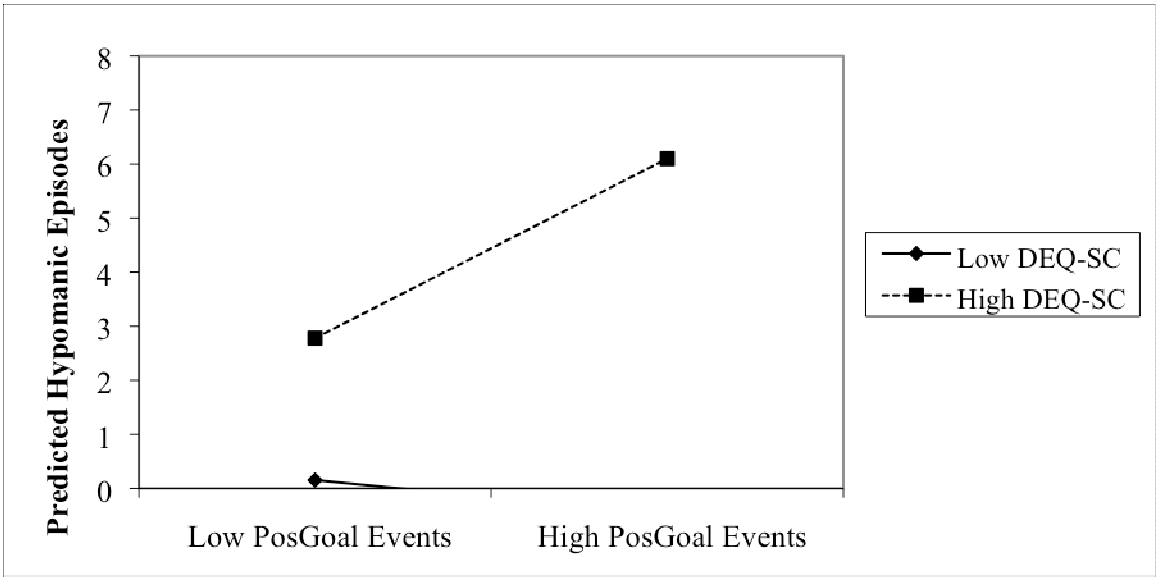
events. The interaction between DEQ-SC and positive goal-relevant events was significant (see Figure 5). Planned comparisons revealed that positive goal-relevant events had a greater relationship with hypomanic episodes for individuals with high DEQ-SC scores, (*B*=.03), as compared to those with low DEQ-SC scores, (*B*=.01). The interaction between DEQ-SC and achievement-relevant events was also significant (see Figure 6). Planned comparisons revealed that positive achievement-relevant events had a greater association with hypomanic episodes for individuals with high DEQ-SC scores, (*B*=.07), as compared to those with low DEQ-SC scores, (*B*=.01).

Results for the BAS-irrelevant cognitive styles indicated that the model including the interaction of DAS-ABO and positive interpersonal life events, and all main effects, significantly predicted hypomanic episodes (see Table 9). The interaction was significant here (see Figure 7). Planned comparisons revealed that positive interpersonal-relevant events had a greater association with hypomanic episodes for individuals with high DAS-ABO scores, (*B*=.04), as compared to individuals with low DAS-ABO scores, (*B*=.01).

Similarly, the model including the interaction of SAS-S and positive interpersonal life events, and all main effects, significantly predicted hypomanic episodes. The interaction approached significance here, p =.097 (see Figure 8). Planned comparisons revealed that positive interpersonal-relevant events had a greater relationship with hypomanic episodes for individuals with high SAS-S scores, (*B*=.04), as compared to individuals with low SAS-S scores, (*B*=.02).

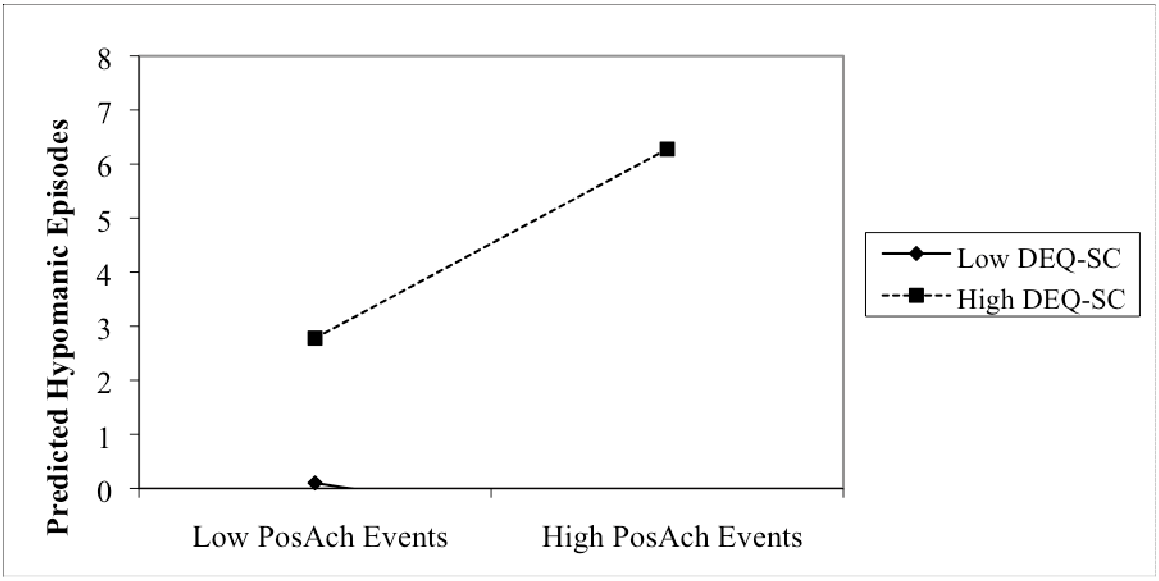
Lastly, the model including the interaction of DEQ-DEP and positive interpersonal life events, and all main effects, did not significantly predict hypomanic episodes.

Figure 5. Hypothesis #7: Interaction Between DEQ-SC and PosGoal (Positive Goal-Relevant) Events Predicts Hypomanic Episodes.[3]



[3] Note that PosGoal Events is positively skewed and has a high kurtosis value, indicating that data may not be normally distributed, leading to a negative slope in the interaction figure.

Figure 6. Hypothesis #7: Interaction Between DEQ-SC and PosAch (Positive Achievement-Relevant) Events Predicts Hypomanic Episodes[4].



[4] Note that PosAch Events is positively skewed and has a high kurtosis value, indicating that data may not be normally distributed, leading to a negative slope in the interaction figure.

Figure 7. Hypothesis #7: Interaction Between DAS-ABO and PosInt (Positive Interpersonal-Relevant) Events Predict Hypomanic Episodes.

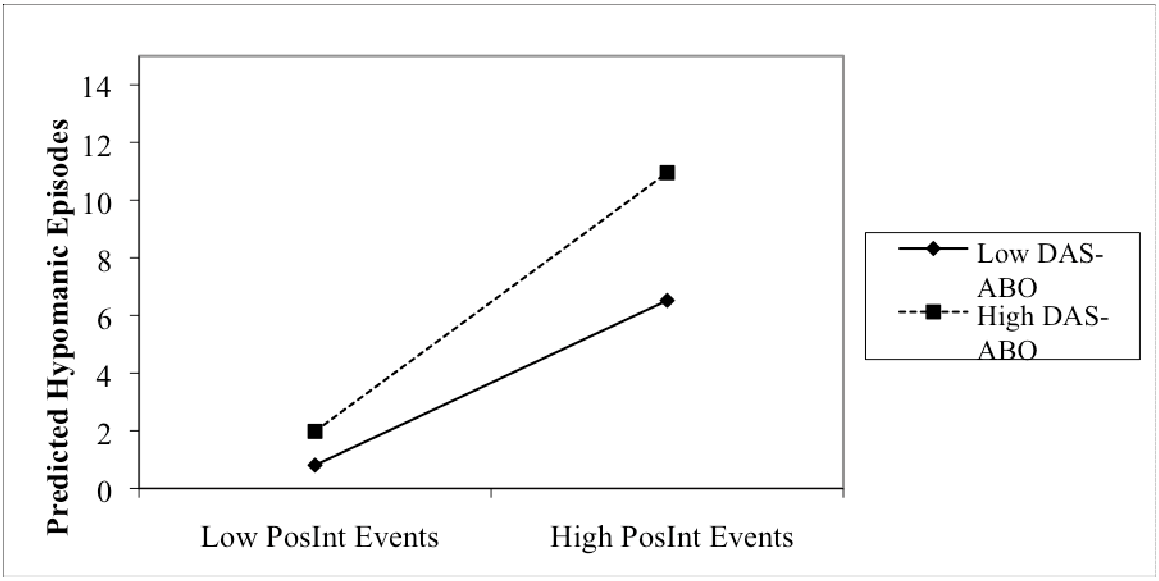
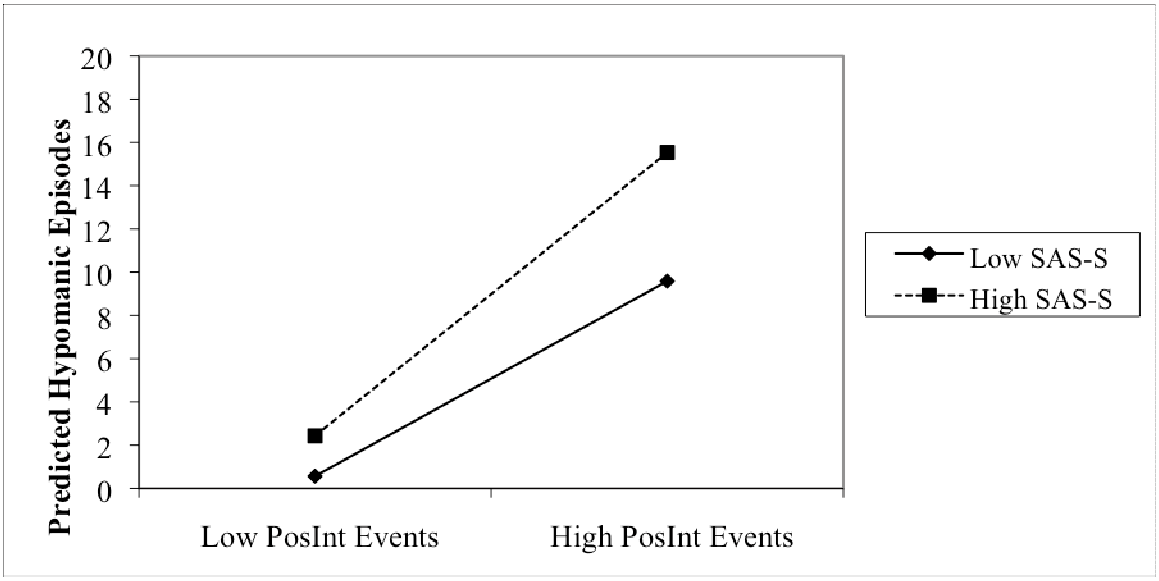


Figure 8. Hypothesis #7: Interaction Between SAS-S and PosInt (Positive Interpersonal-Relevant) Events Predict Hypomanic Episodes.



Prediction of depressive episodes.

Results indicated that the overall model including the interaction of DAS-PE and BAS deactivation-relevant events, and all main effects, significantly predicted the number of depressive episodes (see Table 8). However, only DAS-PE significantly contributed to the model. Similar results were obtained when using negative goal-relevant events. When using negative achievement-relevant events, DAS-PE and negative achievement events as main effects were the only significant predictors.

The model including the interaction of SAS-A and BAS deactivation-relevant events, and all main effects, did not significantly predict the number of depressive episodes. Similar results were obtained when using negative goal-relevant events. When using negative achievement events, the overall model was significant, but negative achievement events were the only significant predictor.

Similarly, the model including the interaction of DEQ-SC and BAS deactivation-relevant events, and all main effects, significantly predicted the number of depressive episodes. DEQ-SC was the only significant predictor. Similar results were obtained when using negative goal-relevant events instead. When using negative achievement-relevant events, both DEQ-SC and negative achievement events were significant predictors.

Results for the BAS-irrelevant cognitive styles indicated that the model including the interaction of DAS-ABO and negative interpersonal life events, and all main effects, did not significantly predict depressive episodes. Similar results were obtained when examining the interaction of DEQ-DEP and negative interpersonal life events. Lastly, the model including the interaction of SAS-S and negative interpersonal life events, and all

Table 9. Hypothesis #7. Hierarchical Linear Regression Using BAS-Irrelevant Cognitive Vulnerability Scores to Predict Hypomanic and Depressive Episodes.

Predictor Variable	*B*	*SE B*	*β*	R^2	ΔR^2	*F*
Prediction of Hypomanic Episodes						
Overall Model				.22	.03	7.809***
Days in Study	.00	.00	.33***			
Treatment Status	1.10	.35	.24**			
Comorbidity	.85	.73	.09			
DAS-ABO	.05	.34	.01			
PosInt Events	.01	.01	.08			
DAS-ABO x PosInt Events	.03	.01	.17*			
Overall Model				.21	.01	7.565***
Days in Study	.00	.00	.32***			
Treatment Status	1.09	.34	.23**			
Comorbidity	.90	.72	.09			
SAS-S	.02	.02	.09			
PosInt Events	.02	.01	.09			
SAS-S x PosInt Events	.00	.00	.12			
Overall Model				.20	.00	6.703***
Days in Study	.00	.00	.33***			
Treatment Status	1.11	.35	.24**			
Comorbidity	.84	.75	.08			
DEQ-DEP	.20	.37	.04			
PosInt Events	.01	.01	.08			
DEQ-DEP x PosInt Events	.01	.01	.06			
Prediction of Depressive Episodes						
Overall Model				.12	.00	3.898***
Days in Study	.00	.00	.27***			
Treatment Status	.12	.37	.03			
Comorbidity	1.16	.77	.12			
DAS-ABO	.69	.36	.15			
NegInt Events	.02	.01	.14			
DAS-ABO x NegInt Events	.00	.01	-.02			
Overall Model				.14	.00	4.645***
Days in Study	.00	.00	.27***			
Treatment Status	.10	.36	.02			
Comorbidity	1.25	.76	.13			
SAS-S	.05	.02	.21**			
NegInt Events	.02	.01	.14			
SAS-S x NegInt Events	.00	.00	.00			

Table 9. *(continued).*

Predictor Variable	*B*	*SEB*	*β*	R^2	ΔR^2	*F*
Prediction of Depressive Episodes						
Overall Model				.12	.00	3.693**
Days in Study	.00	.00	.27***			
Treatment Status	.10	.37	.02			
Comorbidity	1.19	.79	.12			
DEQ-DEP	.62	.38	.12*			
NegInt Events	.01	.01	.13			
DEQ-DEP x NegInt Events	.00	.01	-.01			

NOTE. All variables are centered. *p < .05, **p < .01, ***p <.001, BAS = BAS sensitivity, BAS-D = BAS deactivation-relevant events, DAS-ABO = Dysfunctional Attitudes Scale-Approval by Others Subscale, PosInt Events = Positive Interpersonal events, SAS-S = Sociotropy-Autonomy Scale Sociotropy Subscale, DEQ-DEP = Depressive Experiences Questionnaire – Dependency Subscale, NegInt Events = Negative Interpersonal Events.

main effects, did significantly predict depressive episodes. However, the only significant predictor was SAS-S.

Hypothesis 8

It was hypothesized that the interaction of an individual's BAS sensitivity with the number of BAS-relevant events would predict the time period between episodes; increasing numbers of BAS-relevant events would predict less time between episodes for individuals with a more sensitive BAS. These effects would be stronger for individuals with a diagnosis in the bipolar spectrum.

Results of the hierarchical regression indicated that the model including BAS sensitivity, BAS activation-relevant events, and their interaction significantly predicted time between episodes $F(5, 87) = 7.191$, $p<.001$. However, only BAS sensitivity, B =-.01 (.00), significantly contributed to the model. Another model with BAS sensitivity, BAS deactivation-relevant events, and their interaction also significantly predicted time between episodes $F(5, 87) = 7.728$, $p <.001$. Again, only BAS sensitivity significantly contributed to the model, B =-.01 (.001).

The 3-way interactions including BAS activation-relevant or BAS deactivation-relevant events were not significant, indicating that there were no significant group differences here.

CHAPTER 4

DISCUSSION

Cognitive, psychosocial, and biological approaches to bipolar disorder seek to both describe the course of and identify individuals vulnerable to bipolar disorder. Cognitive approaches, guided by cognitive models of unipolar depression (Alloy, Abramson, Walshaw, Keyser, et al., 2006), have focused on cognitive vulnerability-stress models in which individuals with maladaptive thinking styles are more likely to develop episodes of depression and/or mania when they experience stressful life events. Psychosocial approaches to bipolar disorder have focused on the role of social support and stressful life events in the disorder (see Johnson, 2005b for a review). Recently, some psychobiological approaches to the disorder have focused on the Behavioral Approach System (BAS), an approach/reward motivational system in the brain that may be dysregulated in individuals with bipolar disorder (Depue & Iacono, 1989).

Each model offers somewhat different predictions for the course of bipolar disorder. The BAS model suggests that extreme fluctuations in activation and deactivation of the BAS in response to environmental events may lead to episodes of mania, hypomania, and depression, characteristic of bipolar disorder (Alloy et al, 2008; 2009; Urosevic et al., 2008). The cognitive vulnerability-stress model suggests that maladaptive thinking styles interact with congruent stressful life events to lead to episodes of depression, hypomania, and mania. It is important to compare these approaches with respect to their ability to predict the course of bipolar disorders, including the amount, frequency, and type of mood episodes.

Summary of Hypotheses and Results

There was little support for this study's most central hypothesis, that the interaction of BAS sensitivity and BAS-relevant life events predicts the course of bipolar disorder. Specifically, this model was not significant when predicting episodes of hypomania, and only BAS sensitivity was significant when predicting episodes of depression. More support was found for the role of BAS sensitivity and BAS relevant events as individual predictors of the course of bipolar disorder. BAS sensitivity significantly predicted depressive episodes and BAS relevant events significantly predicted time spent in euthymia. These findings lend some support to the expanded BAS Dysregulation Model (Urosevic et al., 2008; Alloy et al., 2009). They are consistent with the results from several studies that found that individuals with a diagnosis in the bipolar spectrum tend to experience stressful life events (Alloy, Abramson, Neeren, et al., 2006; Alloy, Abramson, et al., 2005; Alloy, Reilly-Harrington, et al., 2005; Johnson & Kizer, 2002), and in particular, goal-attainment and goal-striving events (Johnson, Sandrow, et al., 2000; Nusslock et al., 2007), prior to the onset of episodes of the disorder.

The first hypothesis examined the relationship between age of onset and BAS sensitivity, both with and without controlling for family history of bipolar disorder. We found no significant relationship between these variables. The lack of significant findings here may be attributable to insufficient statistical power in the bipolar group.

The second hypothesis examined the relationship between BAS sensitivity and euthymia. Results suggested that higher BAS sensitivity was associated with less time in euthymia. This is consistent with a logical extension of the BAS dysregulation model; as the BAS becomes more dysregulated, individuals should exhibit more mood episodes.

However, this result did not hold for the bipolar group alone, probably because of insufficient statistical power given that the magnitude of the correlation between BAS sensitivity and time spent in euthymia was the same for the bipolar group alone as for the whole sample.

The third hypothesis examined predictors of depressive or hypomanic course of bipolar disorder. We found that higher BAS sensitivity correlated with a higher number of hypomanic episodes, greater % of days spent in hypomania, and greater % of days spent in depression. In addition, BAS sensitivity predicted greater % of days spent in a hypomanic episode and a higher number of depressive episodes, controlling for length of time in study, treatment status, and comorbidity. Several measures of BAS-relevant cognitive styles (DAS-PE, SAS-A, and DEQ-SC) also correlated with a higher number of hypomanic episodes. In addition, DEQ-SC significantly predicted greater % of days spent in hypomania, controlling for time in study, treatment status, and comorbidity.

For the fourth hypothesis, we found that increased BAS-relevant events were associated with less time spent in euthymia. However, using stringent bootstrapping techniques, BAS-relevant events did not significantly mediate the relationship between diagnostic group and time spent in euthymia. This suggests that other factors also contribute to this relationship, possibly including BAS-relevant cognitive styles and initial mood symptom levels.

The fifth hypothesis examined the relationship between BAS relevant events and predominant hypomanic vs. depressive course of bipolar disorder. We found that individuals with a depressive course of bipolar disorder experienced more BAS activation-relevant events than individuals with a hypomanic course of bipolar disorder.

Similarly, BAS activation-relevant events (and BAS deactivation-relevant events) predicted more days spent in depression.

The sixth hypothesis tested whether individuals were more likely to experience a BAS activation-relevant or goal attainment event in the month following the onset of a hypomanic, major depressive, or minor depressive episode. Results showed that more days spent in a hypomanic episode and a higher number of hypomanic episodes predicted a greater likelihood that individuals had a BAS activation or goal attainment-relevant event after an episode of hypomania. Similarly, more days spent in a depressive episode and a higher number of depressive episodes predicted a greater likelihood that individuals had a BAS activation or goal attainment-relevant event after an episode of major depression. Although it is likely that the more episodes (either hypomanic or depressive) individuals have, the more likely they are to have a particular type of life event following the episode, it was also the case that days in a depressive episode led to more BAS activation and goal attainment events. It could be that individuals with more days in depression and more BAS activation and/or goal attainment events have some shared vulnerabilities, including BAS sensitivity.

Furthermore, additional tests revealed that individuals had more BAS activation and goal attainment-relevant events after an episode of hypomania than after an episode of major depression. However, individuals had fewer BAS activation and goal attainment-relevant events after an episode of hypomania than after an episode of minor depression. This provides somewhat mixed support for the initial hypothesis that individuals in a depressive episode would be less likely than individuals in a hypomanic episode to create or select a BAS activation-relevant or goal-attainment event. It may be

the case that individuals in a minor depression may be less depressed than those in a major depression and may have more ability to create or select such goal-striving or goal-attainment life events to "pull themselves out of an episode." Individuals in a major depression may be too hopeless, helpless, or anhedonic to be able to create or select these types of life events.

The seventh hypothesis tested the interaction between BAS sensitivity and BAS relevant events in predicting the number of each type of bipolar mood episode. There was some support for the BAS model in predicting depressive episodes, although the interaction of BAS sensitivity and BAS deactivation-relevant events was not significant here. Post hoc probing was used to consider the interactions between group, BAS sensitivity, and BAS relevant events in predicting mood episodes. Among individuals with both high and low BAS sensitivity, more BAS deactivation-relevant events were associated with more depressive episodes. The BAS model predictions did not significantly predict hypomanic episodes. Overall, there were no significant interactions between BAS sensitivity and BAS relevant events in predicting mood episodes.

As compared to the BAS model, there was more support for the cognitive vulnerability-stress model in predicting the number and type of mood episodes. BAS-relevant cognitive styles, in interaction with congruent life events, significantly predicted hypomanic episodes. Specifically, DAS-PE and DEQ-SC in interaction with congruent positive life events, predicted hypomanic episodes. The nature of these interactions was such that congruent life events were more strongly associated with the occurrence of hypomanic episodes for individuals who were more cognitively vulnerable. There was

some support for BAS-relevant cognitive styles alone predicting depressive episodes. Specifically, DAS-PE and DEQ-SC alone significantly predicted depressive episodes.

There was also some support for BAS-irrelevant cognitive styles predicting hypomania in interaction with congruent life events. Both DAS-ABO and SAS-S, in interaction with positive interpersonal events, predicted hypomanic episodes.

The last hypothesis examined the relationship between BAS sensitivity, BAS relevant-events, and time between mood episodes. We found that the BAS model significantly predicted time between mood episodes, but BAS sensitivity was the only significant predictor. Higher BAS sensitivity predicted shorter time between episodes.

Key Findings

The most notable findings in this study involved the cognitive vulnerability-stress model's prediction of hypomanic and depressive episodes, along with the inability of the BAS model to predict the same course variables. The interaction of BAS-relevant cognitive styles and congruent positive events, along with both main effects, significantly predicted the number of hypomanic episodes for several cognitive style measures. There was no evidence that the interaction of BAS sensitivity and BAS activation-relevant events predicted hypomanic episodes, nor was there evidence that the interaction of BAS sensitivity and BAS deactivation-relevant events predicted depressive episodes. Several cognitive styles and negative life events, alone but not in interaction, did predict depressive episodes.

An examination of the significant interactions in these analyses shed further light on the relationships between BAS-relevant cognitive styles, congruent life events, and mood episodes. Specifically, in the prediction of hypomanic episodes, the effect of

congruent life events was greater for individuals with high cognitive vulnerability. Furthermore, there was little evidence that BAS-irrelevant cognitive styles, in interaction with congruent events, predicted bipolar mood episodes. This lends support to the cognitive vulnerability x stress model; specifically, the transactional part of the model suggests a two-hit model in which individuals with maladaptive cognitive styles not only react more strongly to relevant life events, but also are exposed to such events more frequently, which, in turn, precipitates bipolar mood episodes. These findings also suggest that an amalgam of the BAS dysregulation and cognitive models may be in order, inasmuch as it was primarily cognitive styles with BAS-relevant content that predicted mood episodes in combination with congruent life events (including BAS-relevant events).

These findings are also consistent with other studies that find support for the cognitive vulnerability x stress model in general, and BAS relevant cognitive styles specifically, as applied to bipolar disorder. Research shows that individuals with bipolar disorder tend to exhibit dysfunctional cognitive styles with BAS-relevant features, such as goal-striving, drive, and incentive motivation (Goldberg et al., 2008; Lam et al., 2004; Rosenfarb et al., 1998; Scott et al., 2000). Most recently, Alloy, Abramson, Walshaw et al. (2009) found that individuals with a diagnosis in the bipolar spectrum significantly differed from normal controls on BAS-relevant, but not BAS-irrelevant, cognitive styles and that only BAS-relevant cognitive styles predicted onset of hypomanic/manic and depressive episodes prospectively.

Furthermore, Alloy, Reilly-Harrington, et al. (1999) found that the interaction of cognitive style with congruent life events predicted an increase in mood symptoms.

More recently, Francis-Raniere et al. (2006) found that BAS-relevant cognitive styles, in interaction with congruent positive events, predicted increases in hypomanic symptoms and in interaction with style-congruent negative events, predicted increases in depressive symptoms. In a more severe population, Lozano and Johnson (2001) found that an achievement-striving cognitive style predicted manic, but not depressive, symptoms in a 6-month follow-up of individuals with bipolar I disorder.

Surprisingly, in contrast to the study's hypothesis, there was little evidence supporting predictions made by the BAS Dysregulation theory (Urosevic et al., 2008) about the course of bipolar disorder. Only BAS sensitivity predicted depressive episodes, and there were no significant predictors for hypomanic episodes. However, it should be noted that we had insufficient power to detect a medium effect size in any analysis using BAS sensitivity. It is possible that the interaction of BAS sensitivity with BAS-relevant life events would predict the course of bipolar mood episodes when the data from both sites of the LIBS Project combined are available and statistical power is greater. However, it is also possible that a BAS-relevant cognitive vulnerability-stress model is a better predictor of the course of bipolar disorder than the BAS model.

Although the interactions between BAS sensitivity and BAS-relevant events were not significant, BAS-relevant events alone predicted several aspects of the course of bipolar disorder. Individuals with a hypomanic course of bipolar disorder, as compared to individuals with a depressive course, differed significantly on the total number of BAS activation-relevant events experienced. Also, BAS activation-relevant events and BAS deactivation-relevant events both predicted the percentage of days spent in depression, and BAS activation-relevant events alone predicted the proportion of depressive episodes

to total episodes. BAS-relevant events were also negatively correlated with time spent in euthymia, indicating that as the number of BAS-relevant events increased, time spent in euthymia decreased. However, it was surprising that neither type of life event predicted episodes of hypomania. It might be that as hypomania episodes tend to be much shorter than depressive episodes, there was less ability to predict them accurately.

Strengths and Limitations

The most notable strength of this study was the use of a prospective, longitudinal design and naturalistic follow-up that provides a more thorough test of the BAS dysregulation model and cognitive vulnerability-stress model as applied to the course of bipolar disorders. In previous studies of the course of bipolar disorder, many of the participants have been previously treated with pharmacotherapy or psychotherapy that could ameliorate, de-activate, or otherwise reduce the likelihood of reporting negative cognitions (Alloy et al., 1999) or BAS hypersensitivity. Yet, these previous studies did not control for treatment status. Other important strengths include the use of several ways of measuring the course of bipolar disorder, including episodes, days in episodes, and time between episodes. Additionally, the study utilized standardized diagnostic interviews and criteria, interviewers blinded to BIS/BAS and cognitive style scores, and extension of prior findings to a non-clinical, bipolar spectrum sample.

However, this study was limited in several ways. The sample consisted solely of undergraduates with bipolar spectrum disorders, which although ethnically and socioeconomically diverse, may not be representative of community or clinical samples. Replication of our findings in a community sample with individuals with bipolar spectrum disorders and in samples with more severe bipolar diagnoses is important.

However, as bipolar II and cyclothymia tend to be understudied relative to bipolar I disorder and are often risk factors for the progression to bipolar I disorder (Shen et al., 2008), the present study is of great value. Second, cognitive styles and BAS sensitivity were assessed with self-report measures only. Although the self-report measures utilized in this study are reliable and valid assessments, future studies may benefit from the use of task-based measures of cognition and BAS sensitivity as well. Specifically, the BIS/BAS scales may be more sensitive to assessing responses to BAS activation-relevant cues than to deactivation-relevant cues. Thus, further instrument development is warranted. Additionally, although the BIS/BAS scales have been validated against both behavioral (Heponiemi, Keltikangas-Jarvinen, Puttonen, & Ravaja, 2003; Zinbarg & Mohlman, 1998) and neurobiological (Harmon-Jones & Allen, 1998; Sutton & Davidson, 1997) indices of BAS activity, future studies would benefit from the use of multiple indicators of BAS (e.g., EEG). Finally, the sample size for this study, and the bipolar spectrum group in particular, may have been too small to detect significant effects, particularly interaction effects which tend to be smaller in magnitude than main effects, in prediction of the bipolar course variables.

Clinical Implications

Given that current interventions for bipolar disorder seem to be much more promising in reducing levels of depression, as opposed to mania (Scott, 2004), new treatment approaches based on the BAS model and the cognitive vulnerability-stress model are needed and might be particularly helpful in targeting hypomania/mania. If, as predicted by the BAS dysregulation theory, excessive goal pursuit is closely tied to the onset or course of hypomania/mania symptoms, this process is ripe for clinical

intervention. Such interventions could help individuals with bipolar disorder understand the relationship between ambitious goal-setting and the onset of manic/hypomanic episodes (Nusslock, Abramson, Harmon-Jones, Alloy, & Coan, 2009).

There is growing consensus that cognitive-behavioral therapists should target prodromes, or early signs and symptoms of a disorder that signal a full episode, in individuals with bipolar disorder. As the BAS model would suggest, cognitive prodromes of manic/hypomanic episodes are characterized by extreme goal-setting and increased expectations of success in the achievement domain (Nusslock et al., 2009), similar to BAS-relevant cognitive styles. Monitoring goal-attainment events, such as promotions and new romances, could allow individuals to counter the impact of these events. Thus, behavioral deactivation strategies including 'modifying high activities,' 'restraining oneself,' and 'engaging in calm activities' may be especially helpful in dealing with the prodromes of mania (Lam & Wong, 1997). Relatives should also be incorporated into the treatment plan to assist the individual with bipolar disorder in identifying and regulating prodromal symptoms (Nusslock et al., 2009). Furthermore, clinicians could develop behavioral interventions to help individuals with bipolar disorder monitor their expectations for success and to limit excessive goal pursuit (Johnson, 2005b). These interventions could help individuals test for the accuracy of confidence and realism of goal setting.

To address this need for new treatment approaches based on the BAS model, Johnson and Fulford (2009) recently developed a mania prevention treatment program. The authors conducted a small, open controlled trial of 10 individuals with bipolar I disorder who were currently euthymic. The program included five modules; one module

involved psychoeducation on bipolar disorder and four modules targeted goal-regulation variables shown to relate to the course of mania. These included (a) emotional reactivity to positive stimuli, (b) high goal-setting, (c) increases in confidence after success, and (d) goal pacing. Each module involved an assessment piece, motivational interviewing strategies, and specific CBT strategies. Results showed that mean levels of manic symptoms decreased significantly from baseline to termination. Although these results are encouraging, this program did not address depression or suicidal ideation. Future research should include randomized-controlled trials of the mania prevention program, as well as integrating this program with other CBT treatments for bipolar disorder.

Conclusion and Future Research Directions

The results of this study suggest that both the BAS model and cognitive vulnerability-stress model predict aspects of the course of bipolar disorder. The most striking finding was that BAS-relevant cognitive styles, in interaction with congruent events, predicted hypomanic episodes. There was no evidence that the interaction of BAS sensitivity and BAS activation-relevant events predicted hypomania. Neither model did a good job of predicting depressive episodes in this sample.

The results of this study were consistent with some of those from past research and inconsistent with others. To replicate these findings and reconcile differences from past research, as well as to extend this research, future research should use more advanced and thorough designs. This study suggests that researchers examining this topic should utilize multiple methods of assessment, such as self-report, behavioral measures, neuroimaging of the brain, interviews, and examine these constructs at

multiple points over time. In addition, future research should extend these findings to more severe populations, including individuals with a diagnosis of bipolar I disorder.

Future research should also examine potential mediators of the relationships described in this study. Specifically, research should examine possible mediators of the relationship between BAS-relevant cognitive styles, congruent life events, and hypomania. Such mediators might include self-focused attentional processes, such as "basking," and cognitions such as hope and self-efficacy that promote goal striving and attainment (Alloy, Abramson, Walshaw, Keyser et al., 2006).

Another model that has been applied to the course of bipolar disorder is the Social Zeitgebers/Circadian Rhythms Model (Aschoff, 1981; Ehlers, Frank, & Kupfer, 1988). The model suggests that many seemingly benign life events (e.g., skipping breakfast, exercising at night instead of in the morning) that are associated with changes in daily routines place considerable stress on the body's attempt to maintain a synchronized sleep-wake, appetite, energy, and alertness rhythm (Frank, 2007). Researchers refer to the environmental factors that set the circadian clock as zeitgebers. The primary and most powerful zeitgeber is the rising and setting of the sun. However, today where light is available 24 hours a day, social factors including the timing of work, timing of meals, and social contact can have an important influence on circadian rhythms. Researchers suggest that changes in such social cues can lead to disruptions in circadian rhythms in all individuals. However, for individuals vulnerable to bipolar disorder, researchers suggest that it is more difficult to adapt to such changes, and these individuals tend to get stuck in the somatic and cognitive state associated with disrupted circadian rhythms. This can lead vulnerable individuals to go on to develop full-blown episodes of depression and/or

mania. Indeed, research has shown that life events characterized by disruptions in daily routines are associated with the onset of depression, and in particular, mania (Malkoff-Schwartz et al. 2000, Malkoff-Schwartz et al. 1998).

Future research should examine the predictions made from the Social Zeitgebers/Circadian Rhythms model as applied to the course of bipolar disorder. For example, research may examine the role of life events characterized by disruptions in daily routines in predicting the number, duration, and frequency of bipolar mood episodes. Furthermore, it would be of interest to compare the Social Zeitgebers/ Circadian Rhythms model to the BAS model and Cognitive Vulnerability-Stress model in predicting aspects of the course of bipolar disorder. Researchers should also investigate how these models may interact in predicting the course of bipolar disorder; it may be the case that individuals with a more sensitive BAS are also more sensitive to life events that disrupt daily routines.

Finally, both the BAS dysregulation model and Cognitive Vulnerability-Stress models have clinical implications for bipolar disorder. As previously mentioned, CBT for bipolar disorder should be updated to include aspects of the BAS and cognitive-vulnerability stress approach. Future research should examine outcome studies of an updated CBT protocol for bipolar disorder.

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