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An Assessment of Emotional Reactivity to Frustration of Goal Pursuit in Euthymic Bipolar I Disorder

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Abstract
Affective disturbance is a central feature of bipolar disorder. Many investigators have hypothesized that euthymic people with bipolar disorder might display elevated emotional reactivity, but laboratory studies of emotional reactivity have had mixed results. Drawing on theories of bipolar disorder that emphasize dysregulation of goal pursuit, we hypothesized that people with bipolar disorder might be emotionally hyperreactive to frustration of goal pursuit. Forty-seven euthymic participants with bipolar disorder and 43 control participants played a computer game for a monetary reward. To induce frustration, we programmed the game to respond inconsistently to user input during two periods. The frustration induction was successful as measured by self-report, physiological responding, and facial behavior, but contrary to the hypothesis of emotional hyperreactivity in bipolar disorder, the bipolar and control groups were equally reactive to frustration. Future studies will benefit from more specific hypotheses about how emotion might be altered in bipolar disorder.

Keywords
bipolar disorder, emotion, emotional reactivity, goal pursuit, mania

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Bipolar I disorder is defined by the presence of a single manic episode. Manic episodes, in turn, are defined by the presence of either elevated or irritable mood (American Psychiatric Association, 2000). Because affective disturbance is a central feature of bipolar disorder, psychologists studying bipolar disorder have focused on emotion (for review, see Gruber, 2011a; Johnson, Gruber, & Eisner, 2007). Several theories suggest that emotional disturbance is a primary driver of bipolar disorder symptoms (e.g., Strakowski et al., 2012; Townsend & Altshuler, 2012). Given the primacy of affect in many neurobiological and psychological conceptualizations of bipolar disorder, thorough characterization of affective responding in bipolar disorder is a priority.

Emotional reactivity—the degree or intensity of a relatively short-term emotional response to a stimulus—is one important component of affective responding. In this study, we test whether euthymic people with bipolar disorder are more emotionally reactive than control participants. In particular, we test whether people with bipolar disorder might be more emotionally reactive to frustration of goal pursuit, as measured via self-report, physiology, or behavior. As we explain later, we focus on anger in response to frustration of goal pursuit because it offers an underutilized opportunity to study approach-related affect—which, for many reasons, is an interesting target for study in Bipolar I disorder—in a context in which people with and without bipolar disorder may face similar pressure to regulate their emotions.

Suggestions that people with bipolar disorder might display elevated emotional reactivity come from clinical experience (see M'Bailara et al., 2009) as well as from empirical findings that show that people with bipolar disorder are more likely to experience manic episodes after life events that involve goal attainment (Johnson et al.,

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2000; Johnson et al., 2008; Nusslock, Abramson, Harmon-Jones, Alloy, & Hogan, 2007). People with bipolar disorder report being more affectively labile and experiencing more intense affect than do control participants during euthymic periods (Henry et al., 2008; Kesebir et al., 2005), and some experience-sampling studies have suggested that individuals at risk for or diagnosed with bipolar disorder show higher or more variable affect across time (Hofmann & Meyer, 2006; Knowles et al., 2007; Myin-Germeys et al., 2003; but for different results, see Havermans, Nicolson, Berkhof, & deVries, 2011; Lovejoy & Steuerwald, 1995). Finally, some—but not all—neuroimaging studies of emotion processing in bipolar disorder have suggested that euthymic bipolar disorder is associated with increased activity in areas associated with emotional reactivity during viewing and labeling of emotional faces (for review, see Delvecchio et al., 2012; Phillips & Swartz, 2014; Townsend & Altshuler, 2012). Although suggestive, these lines of evidence do not establish whether euthymic people with bipolar disorder are more emotionally reactive than are control participants. To answer this question, researchers have turned to laboratory studies using standardized emotion inductions.

Laboratory Studies of Emotional Reactivity in Bipolar Disorder

Studies of emotional reactivity in bipolar disorder can be divided into studies of negative and of positive affect. Most studies of negative affect have used sad or aversive stimuli and have not shown reactivity differences between euthymic people with bipolar disorder and control participants (Aminoff, Jensen, Lagerburg, Andreassen, & Melle, 2011; Cuellar, Johnson, & Ruggero, 2009; Gruber, Hay, & Gross, 2014; Mansell & Lam, 2006; Ruggero & Johnson, 2006; Townsend et al., 2013; Wright, Lam, & Newsom-Davis, 2005; but see Pavlova, Uher, Dennington, Wright, & Donaldson, 2011, for an exception).[1]

Despite the lack of group differences in reactivity to negative stimuli, there are at least two reasons to predict that euthymic people with bipolar disorder might be more reactive to positive stimuli. First, elevated mood is a cardinal symptom of mania, which suggests disruptions in positive affect that may persist during euthymia. Second, reactivity to positive stimuli is a form of approach-related affect. Interest in approach-related affect stems from psychological theories of mania based on the behavioral approach system (BAS; for review, see Johnson, Edge, Holmes, & Carver, 2012; Urošević, Abramson, Harmon-Jones, & Alloy, 2008). The BAS is conceptualized as a system that guides the organism in the pursuit of goals by integrating and responding to cues of reward. Several lines of evidence suggest that BAS sensitivity is elevated in Bipolar I disorder, including the correspondence of mania symptoms with BAS outputs, self-reports of BAS sensitivity, the tendency for mania to occur after progress toward important goals, higher valuation of goals among people with bipolar disorder, and increases in confidence and effort after initial success in bipolar disorder (Johnson et al., 2012; Urošević et al., 2008). If BAS sensitivity is elevated in Bipolar I disorder, it is natural to predict that reactivity to positive emotional stimuli might also be elevated.

But findings regarding emotional reactivity to positive stimuli have been deeply mixed, with some evidence for heightened positive emotional reactivity in euthymic bipolar disorder (Gruber, Harvey, & Purcell, 2011; Pavlova et al., 2011), other studies finding no difference between people with bipolar disorder and control participants (Farmer et al., 2006; Gruber et al., 2014; Hayden et al., 2008; Mansell & Lam, 2006; Wright et al., 2005), and at least one study finding diminished reactivity in bipolar disorder (Lomax & Lam, 2011). The pattern of mixed results for positive emotional reactivity is not explained by sample size, mode of emotional responding measured, or the type of procedure used for emotion induction.

One possible explanation for these mixed findings is that elevated positive emotional reactivity in individuals with bipolar disorder is masked by heightened motivation to regulate positive emotions. As a consequence of the major life disruptions that accompany mania, people with bipolar disorder report being motivated to downregulate positive emotions (Edge et al., 2012). If control participants are not motivated to downregulate positive emotions or are motivated to upregulate positive emotions, then a difference in reactivity may be cancelled by an opposing difference in motivation to regulate.

With these considerations in mind, what sort of emotion should one use to test the theory that euthymic people with bipolar disorder are more emotionally reactive than are control participants? To test the theory, one might seek an emotion that is related to bipolar symptoms, that is approach related, and that people with and without bipolar disorder face similar pressures to regulate. We argue that anger—especially anger in response to frustration of goal pursuit—is such an emotion.

Anger as a Key Emotion in Bipolar Disorder

Elevated or positive mood may be the most widely appreciated symptom of mania, but it is not the only cardinal symptom of mania—irritable mood is an equally central part of the disorder. Although elevated and irritable

moods have differing valences, they are both forms of approach-related affect. Anger—the emotion most closely related to irritable mood—is classified as an approach-related affect both because it can be generated when goal pursuit is frustrated and because electroencephalography asymmetry and personality studies reveal similarities between anger and other approach-related affects (Carver & Harmon-Jones, 2009). BAS models of mania suggest that anger in response to frustration of goal pursuit might be elevated in bipolar disorder. In support of this model, self-report and experience-sampling research has suggested that people with bipolar disorder are sensitive to frustration of goal pursuit (Wright, Lam, & Brown, 2008).

Like positive emotion, inappropriate anger or irritation can be problematic for people with Bipolar I disorder. Unlike positive emotion, though, which people without bipolar disorder experience as pleasant and desirable, anger can cause problems for people without bipolar disorder in social, achievement, and health domains (e.g., Quinn, Rollock, & Vrana, 2014). Thus, people with and without bipolar disorder are likely to experience anger as a potentially problematic emotion requiring regulation in many contexts.

To date, there have been no laboratory studies of affective reactivity in response to frustration of goal pursuit in euthymic adults with Bipolar I disorder, but two studies in related populations are suggestive. First, Harmon-Jones et al. (2002) asked 67 undergraduates to listen to a speech in favor of tuition increases and found that risk for bipolar disorder, as measured by the Hypomanic Personality Scale (Eckblad & Chapman, 1986), was correlated with greater electroencephalography-measured left frontal activity, a measure of approach motivation (Harmon-Jones & Allen, 1998; Sutton & Davidson, 1997). Second, Rich et al. (2010) studied youths with pediatric bipolar disorder and control participants by using rigged feedback during an attention task to induce frustration. Compared with control participants, youths with pediatric bipolar disorder reported a larger increase in negative affect after negative feedback and showed increased theta power in right anterior cingulate cortex, which is associated with emotional processing.

The Present Study

In this study, we examined the hypothesis that euthymic adults with Bipolar I disorder might be more emotionally reactive to frustration of goal pursuit than members of a well-matched control group. To test this hypothesis, we developed a video game to serve as an engaging emotion induction. In our game, participants navigate a vehicle down a corridor, earn money for colliding with some objects, and lose money for colliding with obstacles. To induce anger, we programmed the game's controls to fail intermittently to respond during two periods of game play. Our task allowed us to assess both positive and negative approach-related affective reactivity using self-report, facial behavior, and autonomic physiology. In particular, to assess positive approach-related reactivity, we examined increases in happy/amused facial expressive behavior and self-reported enthusiasm during periods of the task in which the game's controls functioned normally and goal pursuit was unimpeded. To assess negative approach-related reactivity, we examined angry facial behavior, excessive key pressing, heart rate increases, and self-reported frustration during periods of the task in which the game's controls intermittently failed and goal pursuit was frustrated. To our knowledge, this is the first laboratory study of emotional reactivity to frustration of goal pursuit in adults with bipolar disorder.

Method

Participants

Ninety-four people participated in this study, 51 of whom met criteria for Bipolar I disorder as assessed by the Structured Clinical Interview for *DSM–IV* Axis I Disorders (SCID; First, Spitzer, Gibbon, & Williams, 1997). The remaining 43 participants had no history of mood disorder, including Bipolar I disorder, Bipolar II disorder, cyclothymia, major depressive disorder, or dysthymia. Participants were community members from the San Francisco Bay Area recruited by online advertisements, flyers in mood disorder clinics, and outreach through support groups.

All participants were between 18 and 60 years of age and fluent in English. Exclusion criteria included substance or alcohol abuse or dependence in the past year, primary psychotic disorder, general medical condition of the central nervous system, history of head injury with loss of consciousness greater than 1 hr across the lifetime or greater than 5 min in the past year, or developmental disability that could interfere with informed consent or study measures.

Participants completed informed consent procedures and were compensated for their participation. All procedures associated with this study were approved by University of California Berkeley's Committee for the Protection of Human Subjects. Data were gathered as part of a broader study (Ng & Johnson, 2013).

To ensure that participants in the bipolar group were euthymic at the time of the session, we had them complete the Modified Hamilton Rating Scale for Depression (MHRSD; I. W. Miller, Bishop, Norman, & Maddever, 1985) and the Young Mania Rating Scale (YMRS; Young, Biggs, Ziegler, & Meyer, 1978) monthly until participants

recovered. Sessions were postponed for participants who scored above 7 on the MHRSD or the YMRS (Chengappa et al. 2003; Thompson et al. 2005). Remission status was verified no more than 48 hr before sessions. One participant was excluded from analysis for incorrectly responding to more than 5 out of 10 "catch" items included in the questionnaire battery. (An example catch item might ask participants to "please answer this question with '3.'") Three participants were excluded from analysis for scoring below 0 on the retro runner task (described in the following section) on the lowest difficulty level setting. The final sample includes 47 bipolar participants and 43 control participants for analyses of self-report data.

Materials

Experimental task. Our video game was based on a game previously used to induce frustration (Kaiser, Wehrle, & Edwards, 1994). Participants navigated a vehicle through a corridor during which they avoided obstacles and collected "power-ups." Participants earned money that was added to their compensation for the session. When participants collected a power-up, a pleasant sound was played and a message that indicated the amount of money earned (either $0.05 or $0.07) was briefly displayed. In contrast, when participants collided with an obstacle, an unpleasant sound was played and a message that indicated the amount of money lost ($0.10) and said "Use L-R keys to steer" was displayed. In an effort to make the game as simple as possible, we presented the game using minimal vector-based graphics, music was omitted, and participants needed to use only the left and right arrow keys to control their vehicle. In addition to the vehicle and the course, a running count of participants' winnings was displayed.

Participants played for 5 min. During two 30-s periods (at 3:00–3:30 min and at 4:30–5:00 min into the task), the game was programmed to respond only intermittently to participants' key presses so that participants were unable to avoid obstacles and, thus, lost money.

All events within the game were automatically logged, including key presses, collisions with obstacles, and collection of power-ups. Key-pressing frequency was analyzed as a proxy for engagement with the task.

Measurement of emotional responding. We measured participants' self-reported affect, autonomic responding, and facial behavior. Autonomic physiology and facial behavior recording were added to the protocol after the first participants completed the study. As a result, we report more data for self-reported affect ratings than for physiology and more data for physiology than for facial behavior.

Affect ratings. At several points, participants endorsed adjectives relevant to enthusiasm ("Enthusiastic," "Excited") and anger ("Frustrated," "Irritated") along with several other adjectives that were not analyzed ("Serene," "Content," "Sad," "Nervous," "Confident") on a 5-point scale ranging from *very slightly or not at all* to *extremely*. Internal consistency (α) ranged from .79 to .90 for enthusiasm and from .80 to .88 for anger. Correlations (*r*s) between the self-rated enthusiasm and anger indices ranged from –.30 to –.05 across the five time points. As described in the Procedure section, participants were asked to report their current affect three times and to report their retrospective affect twice (see Fig. 1 for a schematic showing timing of the practice period, task, and affect ratings).

Heart rate. Heart rate, a measure of autonomic arousal, tends to accelerate during anger (Kreibig, 2010). Thirty-one bipolar participants and 41 control participants had valid physiological data. Several bipolar participants were recruited for the study but excluded from psychophysiological analyses for use of medications that influence sympathetic responding. We placed pregelled silver electrocardiogram electrodes on the left collarbone and below the right lower rib. A third electrode was placed below the lower left rib as a ground. Electrocardiogram data were acquired using BioLab acquisition software from MindWare and processed and cleaned using MindWare's heart rate variability analysis suite.

Facial behavior. Video recordings of facial displays were coded using the emotional expressive behavior coding system (Gross & Levenson, 1993). The coder was unaware of diagnostic status. Facial displays of happiness/amusement and anger were coded on a scale from 0 (*none*) to 3 (*strong*) on a second-by-second basis. Sums of the intensity ratings were calculated for four periods of the task: from 0:00 to 3:00 min when the keys worked, from 3:00 to 3:30 min when the keys stopped working, from 3:30 to 4:30 min when the keys worked again, and from 4:30 to 5:00 min when the keys stopped working again. For both happiness/amusement and anger, the sum of the intensity ratings in each task period was used as an index of expressive behavior.

To assess reliability, we had a second coder (also unaware of participants' diagnostic status) rate a subset of 25 participant videos. Our analysis revealed the following intraclass correlation coefficients (ICCs): aggregate anger index for each participant, ICC(3, 1) = .70; aggregate happiness/amusement index for each participant, ICC(3, 1) = .96 (Shrout & Fleiss, 1979). The results reported here are based on the ratings of the coder who rated all 62 videos (34 bipolar and 28 control videos).

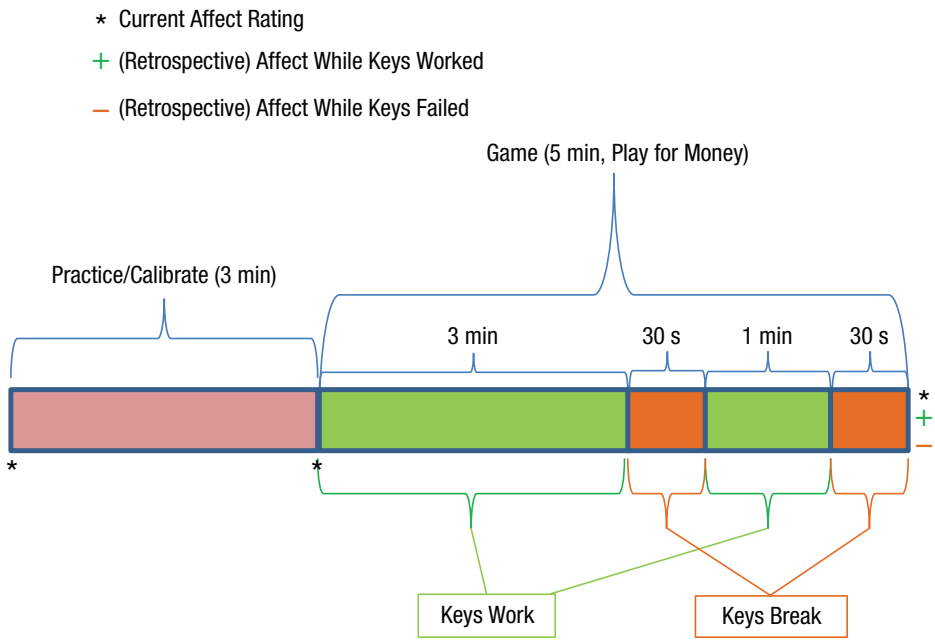

Fig. 1. Schematic showing timing of the practice period, task, and affect ratings. At the last affect rating, participants were asked to rate their current affect as well as their retrospective affect during the parts of the task when the keys responded appropriately and during the parts of the task when the keys failed to respond.

Measurement of clinical status and covariates

SCID. The SCID is a well-validated interview designed for assessment of *DSM–IV–TR* Axis I diagnoses (First et al., 1997). Before administering the SCID, interviewers completed extensive training and established reliability. To evaluate interrater reliability of SCID diagnoses, we had four judges independently rate 10 randomly selected audiotaped interviews. Interrater reliability of all diagnostic categories was excellent as evaluated using ICCs for ordinal data with absolute agreement as the criterion. ICCs ranged from .880 to .889 for current manic episode, lifetime manic episode, and lifetime major depressive episode. The ICC for current major depressive episode was .995.

Medication coding. Participants were interviewed about medication regimens and adherence using the Somatotherapy Index (Bauer et al., 1997). Medication doses were adjusted for nonadherence. We converted dosages of antidepressants to imipramine equivalents, and we converted atypical neuroleptics to a dose equivalency for Risperidol. All mood-stabilizing medications were scaled by dividing dose by maximum recommended dose, and overall mood-stabilizer adequacy was computed as the sum of these lithium, valproate, carbamazepine, and atypical neuroleptic scores. Antidepressant dose equivalency scores were examined separately.

MHRSD. The MHRSD (I. W. Miller et al., 1985) was used to assess depressive symptoms in the bipolar group. The MHRSD is a 14-item interview with scores ranging from 0 to 52. Scores of 7 or lower indicate recovery from depression. Scores on the MHRSD are correlated with other measures of depression and sensitive to changes in clinical status (I. W. Miller et al., 1985). The MHRSD uses standardized probes and behavioral anchors for each rating point, which enhances reliability.

YMRS. The YMRS (Young et al., 1978) was used to assess manic symptoms in the bipolar group. The YMRS is an 11-item interview measure that spans cognitive, affective, and behavioral symptoms of mania. Scores range from 0 to 60, with scores of 7 or lower indicating remission. Items cover affective, behavioral, and cognitive symptoms of mania. Scores are correlated with other mania rating scales, clinician ratings, and treatment (Young et al., 1978).

Before administering symptom severity measures (MHRSD and YMRS), interviewers completed extensive training and demonstrated reliability with gold-standard recordings. Reliability was checked through ratings of audiotaped interviews on an ongoing basis. Interrater reliability of our team, as assessed by three raters reviewing four randomly selected tapes, was high—YMRS: ICC = .999; MHRSD: ICC = .99.

Beck Depression Inventory–Short Form (BDI-SF). The BDI-SF (Beck & Steer, 1993) is a 13-item version of the Beck Depression Inventory. It consists of the cognitive

and affective items from the inventory and excludes items related to somatic symptoms. It has been validated as a measure of depression severity (Furlanetto, Mendlowicz, & Romildo Bueno, 2005), and it has good internal consistency (α = .85 in this sample).

Altman Self-Rating Mania Scale (ASRM). The ASRM (Altman, Hedeker, Peterson, & Davis, 1997) is a self-rated measure of manic symptom severity. Five items cover happiness, self-confidence, talkativeness, activity, and decreased sleep and are rated on a 5-point Likert scale. Scores on the ASRM are correlated with other mania severity ratings (Altman, Hedeker, Peterson, & Davis, 2001). In this sample, internal consistency was acceptable (α = .76).

Computer questionnaire. Participants answered six questions to assess comfort with computer use and video games. With regard to both general computer use and video games specifically, we asked participants how much time they spent per week engaged in the activity, how confident they were in their ability to engage in the activity, and how much they enjoy the activity. Each question was rated on a 7-point Likert scale. We used maximum likelihood to extract two factors with eigenvalues higher than 1 and conducted a varimax rotation. The first factor included our three questions with respect to video or computer games (loadings of 0.68, 0.66, and 0.94 for time spent playing, confidence regarding, and enjoyment of video games, respectively; all other loadings were below 0.35), and the second factor included our three questions with respect to computer use in general (loadings of 0.83, 0.62, and 0.43 for time spent using, confidence regarding, and enjoyment of computers, respectively; all other loadings were below 0.3). For this reason, we computed an index of comfort with video games (α = .81) and an index of comfort with computers (α = .67). These two indices were correlated (r = .39).

Procedure

Potential participants were interviewed by phone to assess exclusion criteria. Participants deemed potentially eligible on the basis of the phone interview were invited to the university for the first session of the study. At the first session, participants provided informed consent and completed the SCID. At the second session, participants completed the computer questionnaire and other tasks not described here.

On arriving at the third session, participants were prepped for physiological recording and a baseline recording of 5 min was taken. Subsequently, participants completed other tasks, including the BDI-SF, the ASRM, and other procedures not described here. Before introducing the video game, we asked participants to complete an affect rating. The experimenter then provided instructions for playing the game.

Participants were given 3 min to practice. Performance in the practice period was used to assign participants to a corresponding difficulty level for the main task. (Difficulty levels differed by virtue of how quickly the vehicle proceeded down the corridor.) After allowing participants to practice, we asked them to complete another set of affect ratings. They were then reminded that in the next version of the task, they would play for money.

After participants had finished the task, we asked them to complete another affect rating. After participants had rated their current affect, they were asked to retrospectively rate their affect during the parts of the task in which the keys responded and during the parts of the task in which the keys failed to respond. Because retrospective and concurrent self-report of affect may access distinct processes (Robinson & Clore, 2002), we conducted two sets of analyses parallel to those presented herein, one in which we excluded the retrospective reports and another in which we used only the retrospective reports. The results—not reported herein—did not differ from the analyses that included all self-reports (see Fig. 1 for task timing).

Analytic strategy

All analyses were performed in R. Each index of emotional reactivity was measured repeatedly within participants. To accommodate correlations between the repeated observations from the same participant, we used generalized estimating equations (GEEs) with exchangeable correlation matrices. Choosing an alternative unstructured correlation matrix did not alter any of the results reported here. For most variables reported, normal-family GEEs were used. For the facial coding data and the self-reported frustration data, Poisson-family GEEs were used to accommodate increased variance during the periods in which the keys failed to respond. The models for the facial coding data included an offset term to account for the differing lengths of task segments. All GEEs were fit using the R package geepack (Højsgaard, Yan, & Halekoh, 2005) with Huber sandwich standard errors. For our indices of frustration, we viewed the interaction between time or task period and diagnostic status as the key analysis for identifying group differences in reactivity. In particular, we were interested in increases in self-reported frustration, key pressing, heart rate, and angry facial expressions during periods in which the game's controls responded intermittently as indices of negative approach-related affective reactivity.

Several of our dependent variables' distributions did not accord with model assumptions. For example, the facial coding data were overdispersed and zero inflated

Table 1. Sample Characteristics

Characteristic	Bipolar I ($N = 47$)	Control ($N = 43$)	Group difference
Age	33.4 (10.3)	31.7 (12.3)	$t(82.2) = 0.7$
Gender (% female)	57	51	$\chi^2(1) = 0.1$
U.S. census race (% White)	72	56	$\chi^2(1) = 2.0$
Years of education	15.1 (1.8)	15.4 (1.8)	$t(86.7) = -0.8$
Currently employed (%)	45	56	$\chi^2(1) = 0.7$
Lifetime anxiety disorder (%)	60	2	$\chi^2(1) = 31.1$***
Lifetime substance or alcohol disorder (%)	64	9	$\chi^2(1) = 26.1$***
BDI-SF	3.6 (3.6)	1.0 (1.3)	$t(58.2) = 4.7$***
ASRM	3.2 (2.8)	2.9 (2.6)	$t(87.9) = 0.5$
Comfort with computers (range = 1–7)	5.9 (1.0)	5.9 (0.9)	$t(87.9) = 0.1$
Comfort with computer or video games (range = 1–7)	3.5 (1.5)	4.1 (1.6)	$t(87.1) = -1.6$
Enjoyment of computer or video games (range = 1–7)	3.9 (1.8)	4.8 (1.7)	$t(86.9) = -2.5$*
Difficulty level assigned (range = 1–5)	2.5 (0.9)	2.8 (1.0)	$t(85.2) = -1.5$
Task earnings	$2.47 ($1.12)	$2.68 ($1.20)	$t(86) = -0.9$
Baseline heart rate	71.1 (12.6)	71.2 (9.7)	$t(54.8) = -0.04$
YMRS	2.0 (2.2)	—	—
MHRSD	2.3 (1.8)	—	—
Taking a mood stabilizer (%)	68	—	—
Taking an antidepressant (%)	32	—	—

Note: Unless noted otherwise, the table presents means for each measure. Standard deviations are shown in parentheses. BDI-SF = Beck Depression Inventory–Short Form; ASRM = Altman Self-Rating Mania; YMRS = Young Mania Rating Scale; MHRSD = Modified Hamilton Rating Scale for Depression. All *t* tests are Welch's *t* tests with adjusted degrees of freedom shown.
*$p < .05$. **$p < .01$. ***$p < .001$.

compared with Poisson expectations. Although GEEs tend to be robust to various forms of model misspecification (Hubbard et al., 2010; Ziegler, Kastner, & Blettner, 1998), we ran permutation tests to compute nonparametric *p* values for our main hypothesis tests involving diagnostic status and indicators of reactivity to frustration. Specifically, we permuted our participants' diagnostic labels 1,000 times, recalculated the GEE each time, and saved the Wald test statistics associated with the main effect of diagnosis and with the interaction of diagnosis and task timing. This provided an approximate distribution of test statistics under the null hypothesis that the joint distribution of responses across the task is the same in the bipolar and control groups (Ernst, 2004). We compared our sample test statistics with the distribution attained via this permutation procedure.

We include a power analysis in the appendix. We find that our study is powered to detect small-to-moderate group differences in reactivity to frustration across the modes of responding we consider.

Results

Sample characteristics

Table 1 shows descriptive statistics for demographic and illness variables in both groups. The groups did not differ on age, gender, years of education, or current mania symptoms. Bipolar participants reported more depressive symptoms than did control participants, though their symptoms were not in the clinical range (I. W. Miller et al., 1985; Young et al., 1978). Participants in the bipolar group, not surprisingly (Krishnan, 2005), were more likely to meet criteria for anxiety, substance-use, or alcohol-use disorders. The bipolar group reported a relatively severe history of bipolar disorder symptoms, with a median of 5 manic episodes and 5 depressive episodes. Because groups differed on these variables, we considered depressive symptoms, history of anxiety and substance disorders, and mood-stabilizer and antidepressant dosages as potential covariates in comparisons between the bipolar and control groups. The analyses reported in the following sections do not include covariates. For each analysis, parallel analyses were performed including the set of candidate covariates that were at least weakly associated ($p < .1$) with the dependent variable either as a main effect or as part of an interaction with time. When included in the model, covariates were entered in the model along with their interactions with task timing. The results of these parallel analyses are noted only if they differ from the unadjusted results.[2] We consider the unadjusted analyses to be our primary results because the adjusted results may alter the meaning of the primary construct under study: Bipolar I diagnosis (G. A. Miller & Chapman, 2001).

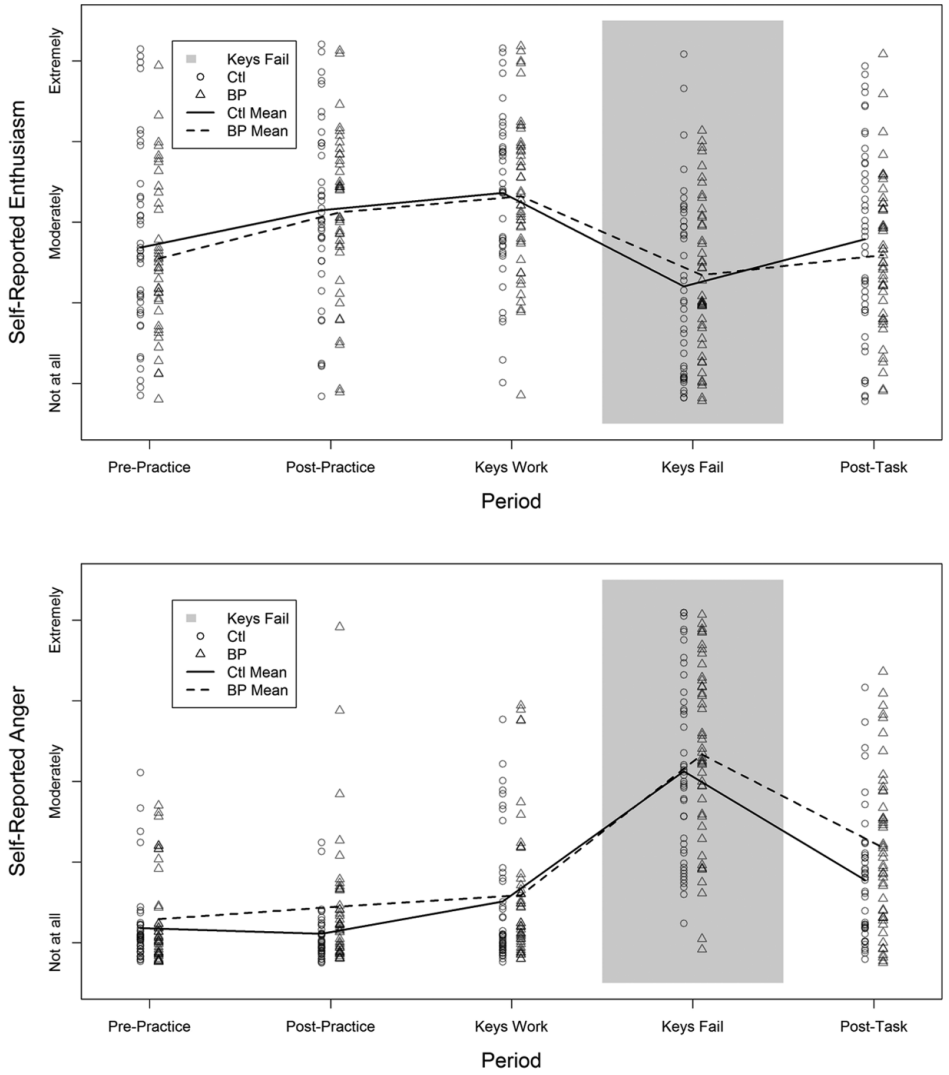

Fig. 2. Results: self-reported enthusiasm and anger across the task in the bipolar and control groups (n = 90). Because many data points overlap, a random number between –0.5 and 0.5 was added to each data point to aid visualization of the number of overlapping points. Ctl = control group; BP = bipolar group.

Task performance (n = 90)

The groups did not differ on comfort with computers or video games as measured by the computer questionnaire (see Table 1). However, the control group reported significantly greater enjoyment of video games than did the bipolar group. Reported enjoyment of video games was considered as a potential covariate in comparisons between the bipolar and control groups, along with the illness variables listed earlier. The groups did not differ in their performance on the task, either during practice, as assessed by the difficulty level at which they were assigned to play, or during the actual task, as assessed by the payment they earned.

When the keys responded, control participants pressed the keys approximately 35 times per 30-s period, β = 35.0, SE = 1.4. When the keys were not responding, control participants pressed the keys approximately 13 extra times per 30-s period, β = 13.3, SE = 2.3, $p < .001$. The groups did not differ in how frequently they pressed the keys overall, β = 3.7, SE = 2.4, p = .12, permutation p = .57. There was no interaction between whether the keys were functioning and diagnostic status, β = –0.80, SE = 3.3, p = .81, permutation p = .90.

Self-reported emotional reactivity (n = 90)

Enthusiasm. Figure 2 shows participants' self-reported enthusiasm across the task by diagnostic status. We used a normal-family GEE with the five time periods (before practice, after practice, while the keys responded

[retrospective], while the keys failed to respond [retrospective], and after the task) as a within-subjects factor and diagnostic status as a between-subjects factor. Enthusiasm varied significantly across the five measurements, Wald $\chi^2(4, N = 90) = 118.0$, $p < .001$. In particular, compared with the prepractice rating, participants reported (on a 5-point Likert scale) increased enthusiasm after practice, $\beta = 0.47$, $SE = 0.12$, $p < .001$, and while the keys were responding, $\beta = 0.77$, $SE = 0.13$, $p < .001$, as well as less enthusiasm when the keys failed to respond, $\beta = –0.47$, $SE = 0.14$, $p < .001$. However, the groups did not differ in self-reported enthusiasm, $\beta = –0.08$, $SE = 0.24$, $p = .72$, permutation $p = .90$, nor did the pattern of changes in enthusiasm across time vary by group, Wald $\chi^2(4, N = 90) = 3.5$, $p = .48$, permutation $p = .52$.

Anger. Figure 2 also shows participants' self-reported anger across the task by diagnostic status. As with enthusiasm, we considered five separate time periods, the effect of diagnostic status, and the interaction of diagnostic status and time. Use of Poisson-family GEE improved the homoscedasticity of Pearson residuals because time points with higher mean anger had proportionally greater variance. Anger varied significantly across the five measurements, Wald $\chi^2(4, N = 90) = 508.0$, $p < .001$. Specifically, compared with the prepractice period, participants retrospectively reported increased anger during the parts of the task in which the keys responded, $\beta = 0.24$, $SE = 0.085$, $p = .01$, and the parts of the task in which the keys did not respond, $\beta = 0.96$, $SE = 0.070$, $p < .001$. They also reported increased anger after the task ended, $\beta = 0.40$, $SE = 0.08$, $p < .001$. There was no main effect of diagnostic status, $\beta = 0.07$, $SE = 0.09$, $p = .41$, permutation $p = .52$, nor was there an interaction between diagnostic status and time, Wald $\chi^2(4, N = 90) = 7.0$, $p = .12$, permutation $p = .46$. When reported enjoyment of computer games, lifetime history of substance abuse, and mood-stabilizer dosage were included as covariates, the interaction between diagnostic status and time approached but did not reach significance, Wald $\chi^2(4, N = 90) = 9.0$, $p = .054$. On the basis of this suggestive result, we probed the comparisons that would provide clearest evidence of self-reported anger reactivity. Namely, we fit one GEE using just the reports occurring immediately after the practice and immediately after the task, and we fit another GEE using just the retrospective reports comparing the periods during which the keys worked and the periods during which they failed. In neither case was there a significant interaction of diagnostic status with time, regardless of whether covariates were included (all ps > .4).

*Heart rate (*n = 72*)*

As with key presses, we used a GEE to analyze heart rate in each of the ten 30-s periods of the task to examine diagnostic status, whether the keys were responding, and the interaction of these two variables. However, for this model, we transformed heart rate values to differences from the participants' baseline mean, and we added participants' mean heart rate during the baseline period as a covariate, $\beta = –0.28$, $SE = 0.06$, $p < .001$. Because heart rate responds to metabolic demand, we added participants' change in key-pressing frequency from the first period as a covariate to adjust for physical activity, $\beta = 0.026$, $SE = 0.013$, $p = .06$.

During the periods in which the keys failed to respond, participants' heart rates increased compared with the period in which the keys responded, $\beta = 0.76$, $SE = 0.38$, $p = .04$. When these periods were examined separately, a significant increase was found for the second period in which the keys broke, $\beta = 1.5$, $SE = 0.66$, $p = .03$, but not for the first period, $\beta = 0.29$, $SE = 0.67$, $p = 0.66$, relative to the periods in which the keys responded. Diagnostic status was not associated with a greater increase in heart rate from baseline to the parts of the task when the keys responded, $\beta = –1.8$, $SE = 1.3$, $p = .16$, permutation $p = .36$, nor was it associated with a greater increase in heart rate associated with the keys' failing to respond, $\beta = –0.01$, $SE = 0.62$, $p = .99$, permutation $p = .96$.

*Facial expression (*n = 62*)*

Happiness/amusement. Figure 3 shows participants' happiness expression indices across the task by diagnostic status. When the keys failed to respond, happy/amused facial behavior increased marginally, $\beta = 0.20$, $SE = 0.12$, $p = .09$. The bipolar group displayed less happiness and amusement overall, $\beta = –0.83$, $SE = 0.33$, $p = .01$, but the degree to which their happiness and amusement displays increased when the keys failed to respond was greater than the control group's increase, $\beta = 0.62$, $SE = 0.21$, $p = .004$. However, neither of these group differences were significant in our permutation test (main-effect permutation $p = .43$, interaction permutation $p = .38$). When BDI-SF score, lifetime anxiety disorder, and lifetime substance/alcohol-use disorder were included as covariates, both the main effect of diagnostic status, $\beta = –0.55$, $SE = 0.42$, $p = .19$, and the interaction of diagnostic status and key responsiveness, $\beta = 0.24$, $SE = 0.35$, $p = .49$, dropped below significance. It is possible that the main effect of diagnostic status on happy/amused expressiveness is better explained by history of substance-related disorders, which was associated with less displayed happiness/amusement,

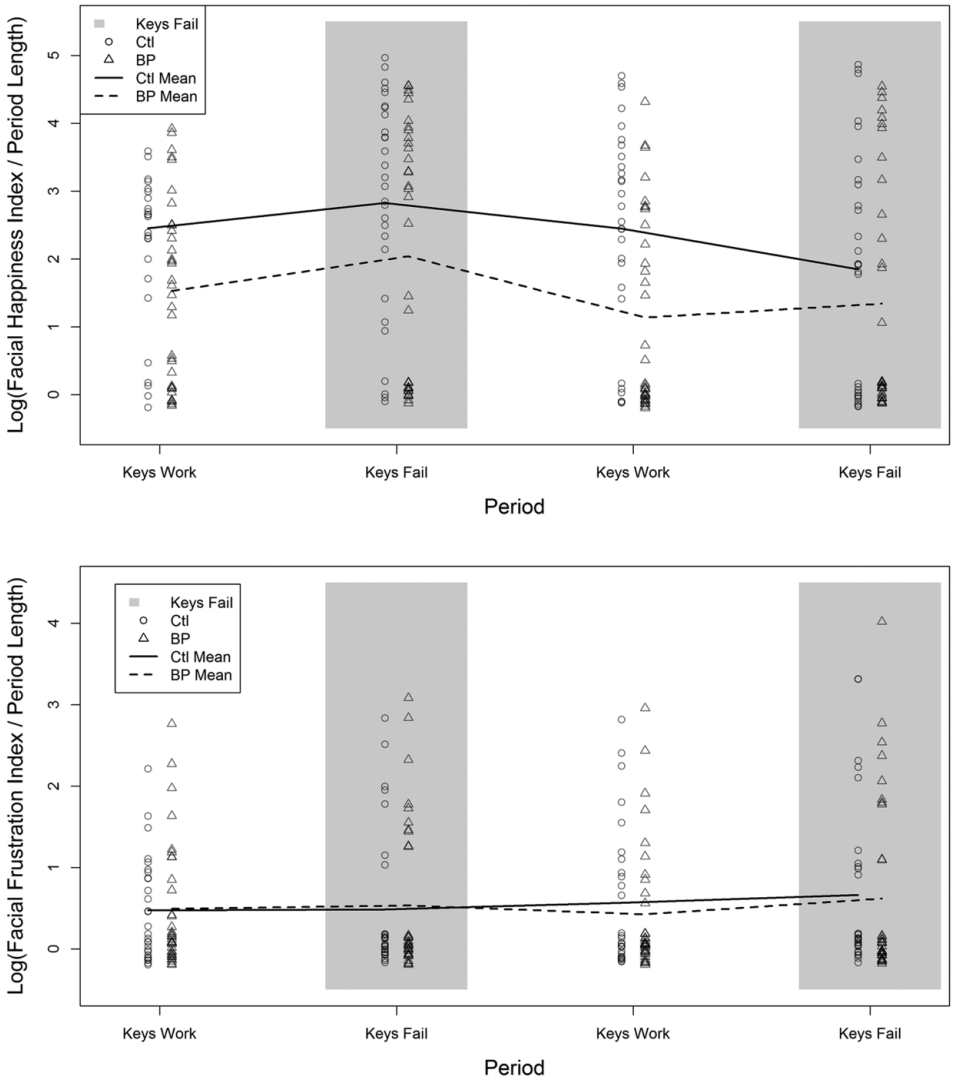

Fig. 3. Results: facial displays of happiness and frustration across the task in the bipolar and control groups (n = 62). Many participants in each period had the same value for the facial display indices (e.g., an absence of amusement or anger). A random number between –0.2 and 0.2 was added to each data point to aid visualization by decreasing the number of overlapping points. Ctl = control group; BP = bipolar group.

β = –0.47, *SE* = 0.22, p = .03, but not with the change in displayed happiness/amusement across the task, β = 0.20, *SE* = 0.14, p = .17.

Anger. Figure 3 also shows participants' frustration displays across the task by diagnostic status. Angry facial expressions increased when the keys failed to respond, though this effect fell just short of significance, β = 0.68, *SE* = 0.35, p = .051. There was no main effect of diagnosis, β = 0.29, *SE* = 0.43, p = .50, permutation p = .67, nor was there an interaction between diagnosis and whether the keys responded, β = –0.07, *SE* = 0.50, p = .89, permutation p = .92. When BDI-SF score and mood-stabilizer dosage were included as covariates, the increase in displayed anger when the keys failed to respond reached significance, β = 0.78, *SE* = 0.35, p = .03.

Discussion

We hypothesized that euthymic people with Bipolar I disorder would be more emotionally reactive in response to frustration of goal pursuit than would control participants. The task we used to induce emotion succeeded in changing self-reported affect, autonomic physiology, and facial behavior for both euthymic bipolar and control participants. In particular, when the keys failed to respond and participants were unable to control the vehicle, participants pressed the keys more frequently and displayed

more angry expressions. Participants' heart rates increased—though this increase occurred only the second time the keys failed to respond—even after we adjusted for physical activity. Immediately after the task, participants reported more anger and less enthusiasm than before the task, and when asked to retrospectively rate their experience, they reported greater anger and less enthusiasm when the keys failed. These results suggest that the manipulation used here successfully induced anger in participants.

Nonetheless, the bipolar group did not display greater reactivity than did the control group in terms of self-report, heart rate, or facial behavior. Thus, the hypothesis that euthymic people with Bipolar I disorder would be more emotionally reactive to frustration of goal pursuit than would control participants was not supported. This result accords with most studies on emotional reactivity in bipolar disorder. Our study extends previous results on emotional reactivity to the study of frustration of goal pursuit, a context that is salient with respect to well-established disturbances of goal pursuit in bipolar disorder. Considering the present study and the prior literature, euthymic bipolar disorder does not seem to be associated with generally greater reactivity to a wide variety of emotion inductions.

We did find some evidence that the bipolar group displayed less happiness and amusement across the task than did the control group, though this result was not significant when we used a permutation test rather than the parametric test provided by the GEE. Even with the bipolar group's larger increase in happy and amused displays when the keys failed to respond consistently (shown in Fig. 3), they still displayed less happiness and amusement than did the control group when the keys failed to respond. This finding contrasts with previous studies that have suggested that compared with control participants, euthymic people with bipolar disorder report more positive emotion and show elevated respiratory sinus arrhythmia across emotional contexts of varying valence (Gruber et al., 2011). At the same time, it is consistent with some previous experience-sampling studies that have shown diminished positive affect among people with bipolar disorder (Myin-Germeys et al., 2003).

We note several methodological limitations. First, the sample size was too small to allow reliable detection of small differences in reactivity to frustration. At the same time, we note that our sample size was larger than all previous multimodal studies of emotional reactivity in bipolar disorder and adequate for assessment of moderate group differences (see the appendix for power analyses). Second, the bipolar group reported less enjoyment of video games, and although we adjusted for enjoyment of video games in analyses, it is possible that individual differences in attitudes toward video games led to effects that cannot be eliminated through statistical adjustment. Nevertheless, our induction was successful in generating emotional responses to frustration across experiential, behavioral, and physiological channels in both groups. Third, like other investigators in this area, we asked participants to report their affect frequently—this study involved three current and two retrospective affect ratings within a 15-min period. It is possible that frequent self-report measurement called participants' attention to affect and altered their processing of emotional stimuli (Lieberman et al., 2007). Given that people with bipolar disorder may experience more concern about emotionality (Edge et al., 2012), increased attention to emotion may affect the emotional responses of participants with bipolar disorder differently than it affects the responses of control participants. Fourth, although we adjusted for the medication dosage in the analyses, it is important to note that most of our bipolar sample reported taking psychoactive medications, and these medications may blunt reactivity.

Finally, it remains possible that bipolar disorder is related to elevated emotional reactivity in other contexts, in response to ideographically defined stimuli, or during symptomatic states. Although these hypotheses merit further study, they are distinct from the hypothesis we tested—that increased emotional reactivity is a core feature of bipolar disorder that can be documented in the euthymic state in response to standardized stimuli relevant to goal pursuit.

What, then, of this hypothesis? Our study provides no evidence for increased emotional reactivity to frustration of goal pursuit in self-report, autonomic, or behavioral channels among euthymic adults with Bipolar I disorder, in accord with most of the previous literature. It is possible to suggest refined hypotheses about emotional reactivity differences in bipolar disorder that remain tenable, but it may also be time to consider the import of the failure of strong versions of the hypothesis of emotional hyperreactivity in euthymic bipolar disorder. We consider implications for both the BAS model of mania and the study of affect in bipolar disorder more generally.

The lack of approach-related emotional hyperreactivity in bipolar disorder contrasts with one reasonable prediction from the BAS model of mania. The BAS model has several successes to its name—it explains features of the symptoms of mania and correctly predicts, for example, the types of life events that precede mania, higher valuation of goals among people with bipolar disorder, and more ambitious goals among people with mania (Johnson et al., 2012). At the same time, not every prediction of the BAS model has been supported. People with bipolar disorder may have pronounced responses to goal-relevant stimuli in some dimensions of BAS responding, such as increases in energy, effort, and goal setting, but not in all dimensions of BAS responding (Duek,

Osher, Belmaker, Bersudsky, & Kofman, 2014; Johnson, Ruggero, & Carver, 2005; Mansell & Lam, 2006; Roiser et al., 2009; Ruggero & Johnson, 2006; Stern & Berrenberg, 1979; see Johnson et al., 2012, for review).

We suggest that affective scientists interested in bipolar disorder move beyond the investigation of emotional reactivity differences in euthymia. Resources for studying psychological aspects of bipolar disorder are limited, and the data suggest that any disruptions in affective reactivity in people vulnerable to mania are not large or consistent enough to figure prominently in explanations of risk for mania.

This is not to say that research on affect in bipolar disorder should stop—on the contrary, we agree with many other researchers that the centrality of affect in the disorder's symptoms is enough to justify intensive study of affect in bipolar disorder. Studies of self-reported trait emotionality (Henry et al., 2008 Kesebir et al., 2005) and of emotional responses in daily life (Havermans et al., 2011; Hoffman & Meyer, 2006; Knowles et al., 2007; Lovejoy & Steuerwald, 1995; Myin-Germeys et al., 2003) suggest that some features of affective responding in bipolar disorder are disrupted even during euthymia. Affective reactivity does not seem to be one of these features, but there are other aspects of affect that warrant further study. For example, people with bipolar disorder may interpret ambiguous stimuli more positively (Dutra et al., 2014; Piff, Purcell, Gruber, Hertenstein, & Keltner, 2012) and may show higher levels of positive affect—but not necessarily higher positive affective reactivity—across contexts (Gruber 2011a, 2011b).

Along these lines, more effort should be devoted to an understudied feature of affect in bipolar disorder—duration of affective responses. A few studies have suggested that bipolar disorder may be associated with longer affective responses (Farmer et al., 2006; Talbot, Hairston, Eidelman, Gruber, & Harvey, 2009; Wright et al., 2008), and prolonged affective responding could explain some of the cross-sectional and experience-sampling results on affect in bipolar disorder, such as the finding that people with bipolar disorder think of themselves as having more pronounced affective responses than control participants do (Henry et al., 2008; Kesebir et al., 2005). Furthermore, duration of affective responding has been a fruitful target of study in other mood disorders—longer affective responses have been observed in people with a history of unipolar depression (Gilboa & Gotlib, 1997), and in interaction with life stress, duration of affective response is prospectively associated with increases in dysphoria after 7 weeks (Beevers & Carver, 2003). Nonetheless, there have been no standardized laboratory studies of duration of affective responding in euthymic bipolar disorder in which researchers have assessed multiple indices of affective responding, including behavior, physiology, and self-report. Nor have there been any studies in which the duration of responses to personally engaging, approach-related affect inductions was assessed. We now know much more about affective reactivity in euthymic bipolar disorder than we do about duration of affective responding. Rather than test increasingly refined hypotheses about a difference in reactivity that may not exist, we should examine other aspects of affect that remain largely unexplored. Research on affect in bipolar disorder, though still young, has reached a maturity that calls for models that go beyond reactivity.

Appendix: Power Analysis

We conducted power analyses using the approach given by Donohue, Edland, and Gamst (2013) for interactions of group and time in a two-group longitudinal study with an exchangeable covariance structure. The Donohue et al. formula is a special case of formulas found in Diggle, Liang, and Zeger (1994) and in Liu and Liang (1997). Assume that the data are produced by the linear model

$$Y_{ij} = \beta_0 + \beta_1 g_i + \beta_2 t_{ij} + \beta_3 g_i t_{ij} + \varepsilon_{ij},$$

where Y_{ij} is the response of participant i at time j, g_i is the group membership of participant i (here, $g_i = 1$ for participants in the bipolar group and $g_i = 0$ for participants in the control group), t_{ij} indicates whether frustration is being induced ($t_{ij} = 1$ if the keys fail to work in period j; otherwise, $t_{ij} = 0$.), and ε_{ij} is an error term. Assume that the ε_{ij} are jointly normally distributed with mean 0, variance 1, and correlation ρ if the two observations are from the same participant and 0 otherwise; that is, $corr(\varepsilon_{ij}, \varepsilon_{ik}) = \rho$ for $j \neq k$ and $corr(\varepsilon_{ij}, \varepsilon_{lk}) = 0$ for all $i \neq l$. If we further assume that the study has equal numbers of participants in both groups and that all participants are measured at the same times ($t_{ij} = t_{kj} = t_j$ for all i, j, and k), then the number of participants needed in each group to achieve power θ with Type I error rate α in a two-sided test is given by

$$m = \frac{2\left(z_{\alpha/2} + z_{1-\theta}\right)^2 (1-\rho)^2}{n s_x \beta_3^2}.$$

Here, $s_x = \Sigma_{j=1}^{n}(t_i - \bar{x})/n$, n is the number of times the participants are measured, $\bar{x}$ is the mean of the t_js, and z_x is the xth quantile of the standard normal distribution (Donohue et al., 2013).

In this framework, there are two interpretations for β_3 that will be familiar to psychologists. First, β_3 is the size of the group difference in response to the frustration

induction measured in units of the standard deviation of the errors. Second, we can transform β_3 slightly to get η_p^2. If p is the proportion of participants in the bipolar group and q is the proportion of measurements taken when frustration is being induced, then

$$\frac{\beta_3^2 pq(1-pq)}{1+\beta_3^2 pq(1-pq)} = \frac{\sigma_b^2}{\sigma_e^2+\sigma_b^2} = \eta_p^2,$$

where σ_b^2 is the variance accounted for by the interaction and σ_e^2 is the residual variance, which we have set to 1. One can show that $\sigma_b^2 = \beta_3^2 pq(1-pq)$ using the law of total variance.

In interpreting our power analyses, some caution is warranted because our data violate some of the assumptions of this model. Some of our data are skewed right, most of our data have differing variances by task period, and we do not have exactly the same number of participants in each diagnostic group. Nonetheless, we use this model because it is simple, has a clear interpretation, and can be used to build intuition about the types of effects we can detect given our sample size, the correlation structure of our data, and the number of measurements we have per outcome. For our main four frustration-relevant outcomes—self-reported frustration, angry facial expressions, heart rate, and key presses—we fit exchangeable generalized estimating equations using time as the only independent variable to estimate the correlation parameter. We used these estimated correlations, an assumed Type I error rate of $\alpha = .05$, the sample sizes for each outcome variable, and the t_j for each outcome to identify the minimum β_3 and η_p^2 we can detect with power $\theta = 0.8$. For self-reported frustration, our sample size is 90, the estimated exchangeable correlation is .6, and we can detect $\beta_3 > 0.2$ and $\eta_p^2 > .006$. For angry facial expressions, our sample size is 62, the estimated correlation is .3, and we can detect $\beta_3 > 0.45$ and $\eta_p^2 > .036$. For heart rate, our sample size is 72, the estimated correlation is .76, and we can detect $\beta_3 > 0.11$ and $\eta_p^2 > .001$. For key presses, our sample size is 90, the estimated correlation is .58, and we can detect $\beta_3 > 0.18$ and $\eta_p^2 > .003$. We emphasize that this model is scaled so that the error variance is 1; the units of β_3 here do not correspond to the units used in the Results section.

Author Contributions

M. D. Edge and S. L. Johnson developed the study concept, designed the study, and assembled the materials. S. J. Lwi performed the facial coding, and M. D. Edge processed the behavioral and physiological data. M. D. Edge analyzed the data and wrote the first draft of the manuscript. All authors contributed to revisions of the manuscript. S. L. Johnson supervised all phases of the project. All authors approved the final version of the manuscript for submission.

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Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

Notes

1. We summarize the results of previous studies with respect to emotional reactivity as defined here—group differences in the degree of change in self-reported emotional experience, physiological responding, or expressive behavior relative to a baseline condition (Nelson, Shankman, Klein, & Olino, 2011). Some studies use differing definitions of *emotional reactivity* that do not require change from a baseline condition. One example is the study of M'Bailara et al. (2009), which suggested that compared with control participants, euthymic people with bipolar disorder give higher ratings of pleasantness and arousal to neutral pictures—but not to positive or negative pictures.
2. When we adjusted only for covariates that were weakly associated with the dependent variable in the bipolar group alone (as opposed to the full sample), we obtained similar results.

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