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ORIGINAL ARTICLE

Reward and Punishment Sensitivity and Emotion Regulation Processes Differentiate Bipolar and Unipolar Depression

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Abstract

Bipolar disorder (BD) and major depressive disorder (MDD) cannot be reliably differentiated by depression symptom expression alone, suggesting a need to identify processes that may more effectively differentiate the two disorders. To explore this question, currently depressed adults with BD ($n = 30$) and MDD ($n = 30$), and healthy control participants with no history of psychiatric illness (CTL; $n = 30$), completed self-report measures of reward and punishment sensitivity (i.e., behavioral activation and inhibition) and emotion regulation processes (i.e., rumination and avoidance). Results revealed that constructs putatively linked to depression *across* the mood disorders (i.e., behavioral inhibition, negative rumination, dampening of positive affect, behavioral and experiential avoidance) were significantly higher in both mood disorder groups compared to CTLs. Yet there was also some specificity between mood disorder groups, such that the BD group reported significantly greater reward responsiveness and positive rumination, in addition to greater behavioral inhibition and avoidance, compared to the MDD group. These data suggest that patterns of affective responding previously linked to underlying risk for mania in BD may remain evident during a major depressive episode. Further, current models of reward sensitivity in BD may benefit from the inclusion of punishment sensitivity and behavioral avoidance, particularly with respect to bipolar depression.

Keywords Bipolar disorder · Major depressive disorder · Reward sensitivity · Punishment sensitivity · Emotion regulation

Introduction

Bipolar disorder (BD) remains one of the most debilitating illnesses worldwide (Whiteford et al. 2013) with significant morbidity (Judd et al. 2002) and mortality (Schaffer et al. 2015). Although a history of mania is the primary requirement for the diagnosis of BD, the severe and chronic disability in BD may be better accounted for by the depressive, rather than the manic, phase of illness (Judd et al. 2005). Unsurprisingly, initial misdiagnosis of major depressive disorder (MDD) is most common (Ghaemi et al. 2000), which may delay appropriate treatment. This underscores the importance of studying depression in BD and accurately differentiating in from depression in MDD.

Many studies have examined potential differences in the symptomatic expression of depression between BD and MDD, with the hope that such differences might aid in differential diagnosis and inform delivery of appropriate treatment (e.g., Cuellar et al. 2005). However, this literature has been quite mixed and confounded by heterogeneity across samples and research settings, variability in the selection of symptoms evaluated, and the lack of control for underlying depressive severity between groups (Weinstock et al. 2010b). Equating for underlying differences in depression severity, recent studies using large, epidemiologic samples have revealed surprisingly few symptom-level differences between bipolar and unipolar depression (Weinstock et al. 2009, 2010a), and are more consistent with arguments that BD and MDD cannot be differentiated based on depression symptom expression alone (Joffe et al. 1999; Smith and Craddock 2011). Moving beyond evaluation of differences in overt depression symptom endorsement, it is critical to identify mechanisms that may uniquely underlie and differentiate BD and MDD, and to validate such potential

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endophenotypic illness markers (Hasler et al. 2006). *Reward and punishment sensitivity* and processes of *emotion regulation* are particularly relevant, theory-driven constructs that have been implicated in the pathology of both BD and MDD, and that may provide a useful framework for investigation of shared versus distinct disorder mechanisms.

As two well-validated psychological indices of reward and punishment that encompass approach/appetitive and withdrawal/avoidance motivations, respectively (Depue and Iacono 1989; Gray 1981), research on the behavioral activation (BAS) and behavioral inhibition (BIS) systems has demonstrated that high BAS sensitivity is associated with risk for (Johnson and Carver 2006; Meyer et al. 1999) and history of (Meyer et al. 2001; Salavert et al. 2007) mania in euthymic BD samples. Elevated BAS sensitivity has also been shown to be predictive of first onset (Alloy et al. 2012) and recurrence (Alloy et al. 2008) of manic episodes in at-risk samples. In contrast, *decreased* BAS sensitivity has been associated with current (Kasch et al. 2002; Pinto-Meza et al. 2006) and remitted (Pinto-Meza et al. 2006) MDD, and elevated BIS sensitivity has been associated with greater depression severity in both MDD (Kasch et al. 2002; Pinto-Meza et al. 2006) and BD (Alloy et al. 2008; Meyer et al. 2001) samples. Altogether, these data suggest that heightened BAS—but not BIS—sensitivity may uniquely differentiate BD from MDD. Yet we are not aware of any published research that has directly examined whether BAS sensitivity does indeed differentiate both groups during a depressive episode.

Similarly, a growing literature has elucidated the central role of emotion dysregulation in mood disorders (e.g., Aldao et al. 2010). Yet few studies to date have systematically evaluated differences in emotion regulation processes between BD and MDD (Gilbert et al. 2013; Gruber et al. 2011; Johnson et al. 2008), and such studies have typically been conducted within euthymic samples. Two candidate emotion regulation processes may be especially relevant to the shared experience of depression between BD and MDD; namely, *rumination* (Nolen-Hoeksema 1991) and *avoidance* (Hayes et al. 1996; Lewinsohn 1974). There is a robust literature linking rumination on the content and causes of negative feelings (i.e., negative rumination) to depression in both MDD and BD (Johnson et al. 2008). Grounded in models that implicate perturbations in the positive valence system in BD, there is also an emerging literature focused on the potentially unique association between ruminative responses to positive affect (i.e., positive rumination) and BD, drawing from findings both in analogue (Feldman et al. 2008) and euthymic (Gruber et al. 2011; Johnson et al. 2008) BD samples. For example, in a euthymic sample, Shapero et al. (2015) found that individuals with BD differed from individuals with MDD and controls in emotion-focused positive rumination; dampening responses to positive affect also differentiated individuals with BD and controls, and showed a moderate, albeit not statistically significant, ability to discriminate between BD and MDD. It remains unclear whether these effects extend into periods of bipolar depression.

Often concurrent with negative rumination (Cribb et al. 2006; Dickson et al. 2012), avoidance appears to contribute to, and perpetuate, depression. Indeed, early behavioral conceptualizations of depression (Lewinsohn 1974) emphasized the role of avoidance behaviors that individuals may use to temporarily alleviate distress or escape unpleasant feelings, which may then maintain depression through a lack of response-contingent positive reinforcement. A subsequent literature has supported the associations between behavioral avoidance and depression (Trew 2011), and more recent conceptualizations have further incorporated a focus on experiential avoidance. As an emotion regulation strategy, individuals engage in experiential avoidance in an effort to escape certain aspects of negative and internal emotional experiences (Bond et al. 2011; Hayes et al. 1996). Yet the process of experiential avoidance has been shown to be associated with *increased* experiences of the avoided affect (Hayes et al. 2004), and a number of studies have revealed associations between experiential avoidance and increased depression (Cribb et al. 2006; Kashdan et al. 2010; Shahar and Herr 2011). Although one might presume that the processes of behavioral and experiential avoidance may be just as relevant to depression in BD, there is surprisingly no published literature of which we are aware evaluating behavioral or experiential avoidance and its role in depression within BD samples.

In an effort to integrate these literatures, the present investigation evaluated reward and punishment sensitivity and the emotion regulation processes of rumination and avoidance across the mood disorders spectrum, with the aim of identifying shared versus distinct mechanisms that may help differentiate bipolar from unipolar depression. To achieve these aims, currently depressed adults with BD type I and MDD, as well as healthy control participants without a history of psychiatric illness, were recruited to evaluate two primary sets of hypotheses: (1) With respect to *reward and punishment sensitivity*, we hypothesized that greater BAS sensitivity would differentiate BD from MDD, but that both diagnostic groups together would report significantly heightened BIS in comparison to healthy controls; and (2) With respect to *emotion regulation processes*, we hypothesized that both diagnostic groups would report greater negative rumination, dampening of positive affect, and behavioral and experiential avoidance in comparison to the healthy controls, but that the BD group only would report greater emotion-focused positive rumination in comparison to the MDD group. Taken together, we hypothesized that both mood disorder groups would share similar features in areas known to be associated with depression (i.e., behavioral inhibition, negative

Table 1 Descriptive characteristics and group comparisons for preliminary analyses

	BD ($n=30$)	MDD ($n=30$)	CTL ($n=30$)			Any Dx vs. CTL		BD vs. MDD	
	M (*SD*)	*M* (*SD*)	*M* (*SD*)			*F* (*df* = 1)	*p*	*F* (*df* = 1)	*p*
Age	42.4 (12.2)	39.7 (11.7)	32.3 (13.7)			**9.81**	**0.002**	0.70	0.407
QIDS-SR	17.1 (3.2)	16.3 (3.2)	1.7 (3.3)			**403.09**	**< 0.001**	1.00	0.320
ASRM	2.4 (2.7)	2.2 (2.7)	1.6 (2.4)			2.23	0.139	0.05	0.822
	n (%)	*n* (%)	*n* (%)	χ^2	*p*				
Sex (female)	19 (63)	22 (73)	18 (60)	3.24	0.518				
Race (White)	25 (83)	21 (70)	19 (63)	8.86	0.354				
Ethnicity (non-Hispanic)	30 (100)	24 (80)	26 (87)	6.70	0.153				

Bolded findings reflect results with a p value < 0.05

QIDS-SR Quick Inventory of Depressive Symptomatology-Self Report; *ASRM* Altman Self-Rated Mania Scale

rumination, avoidance), but that BD would be differentiated from MDD on features hypothesized to convey unique risk for mania (i.e., BAS sensitivity and emotion-focused positive rumination). Evaluation of such questions within the context of a depressive episode allowed for further elucidation of the potential specificity of these putative mechanisms across the mood disorders spectrum.

Methods

Participants

Participants ($N=90$) were recruited to participate in a study of affective responding across mood disorders, and included currently depressed adults with bipolar I disorder (BD; $n=30$) and MDD ($n=30$), as well as healthy controls with no lifetime history of DSM-IV-TR Axis I psychiatric illness (CTL; $n=30$). All participants were required to be 18 years or older and speak and read English sufficiently well to provide informed consent and complete study procedures. In addition, BD and MDD participants were required to meet DSM-IV-TR criteria (American Psychiatric Association 2000) for a current (i.e., past month) major depressive episode, as determined by the Structured Clinical Interview for DSM-IV-TR Axis I disorders (SCID-I; First et al. 2002). Exclusion criteria for all participants included: (1) current psychotic symptoms; (2) suspected alcohol or substance dependence as evidenced by a score > 10 on the Alcohol Use Disorders Identification Test (AUDIT; Babor et al. 2001) and/or a score ≥ 2 (for females) or ≥ 6 (for males) on the Drug Use Disorders Identification Test (DUDIT; Berman et al. 2003); and (3) self-reported history of major neurological injury or disease. Participants were recruited through numerous community sources (e.g., internet advertisements, flyers, brochures, clinician referrals). On average, participants were 38.2 (SD = 13.1) years old, 66% ($n=59$) female, 72% ($n=65$) White, and 89% ($n=80$) non-Hispanic (see Table 1).

Assessments

Diagnosis

Diagnostic status was determined by SCID-I (First et al. 2002) interview, administered by two trained bachelor's level clinical raters. Training consisted of a didactic workshop followed by several weeks of: (a) trainee review and practice scoring of gold standard assessment recordings, (b) supervised role plays, (c) trainee observation of assessments in real time, and (d) supervisor observation of trainee-conducted assessments in real time. All raters were required to achieve kappa = 0.80 with expert faculty ratings prior to conducting independent diagnostic assessments. SCID-I interviews were audio recorded and 20% of the interviews, selected randomly and distributed evenly across the 3 participant groups, were later scored separately by an independent rater blind to original diagnoses. Analyses of inter-rater reliability indicated perfect agreement for BD and MDD primary diagnoses, as well as for the absence of any lifetime psychiatric diagnosis in the CTL group (all kappas = 1.00).

Symptom Severity

The 16-item Quick Inventory of Depressive Symptomatology (QIDS; Trivedi et al. 2004) and the 5-item Altman Self-Rated Mania scale (ASRM; Altman et al. 1997) were used to assess current mood symptoms. Consistent with published reports (Altman et al. 1997; Trivedi et al. 2004), good internal consistency reliability was obtained for both the QIDS ($\alpha=0.93$) and ASRM ($\alpha=0.67$).

Sensitivity to Reward and Punishment

The 24-item self-report Behavioral Inhibition System/Behavioral Activation System scales (BIS/BAS; Carver and White 1994) were used to assess punishment and reward sensitivity, respectively. Whereas the BIS was developed to assess behavioral inhibition in response to aversive or threatening stimuli, the BAS was developed to assess the tendency to experience strong positive affect or behavioral approach in response to incentive cues. The BAS is further comprised of three subscales that assess the inclination to seek out novel, rewarding situations (i.e., BAS fun seeking), pursuit toward appetitive goals (i.e., BAS drive), and tendency to experience positive affect/excitability in response to a desired event or potential reward (i.e., BAS reward responsiveness; Ross et al. 2002). In the current study, adequate internal consistency reliability was obtained for the BIS ($\alpha = 0.81$) and the BAS fun seeking ($\alpha = 0.55$), drive ($\alpha = 0.75$) and reward responsiveness ($\alpha = 0.70$) subscales.

Emotion Regulation Processes

Rumination about negative emotion (i.e., negative rumination) was assessed with the widely used 5-item Brooding subscale of the Response Styles Questionnaire (RSQ; Nolen-Hoeksema 1991). Internal consistency reliability of the Brooding subscale was high in the current study ($\alpha = 0.90$). Rumination about positive emotion (i.e., positive rumination) was assessed using the 17-item responses to positive affect (RPA; Feldman et al. 2008) questionnaire. Factor analysis has supported the use of three RPA subscales, including emotion-focused (e.g., "Think about how happy you feel") and self-focused (e.g., "Think about how proud you are of yourself") positive rumination as well as dampening (e.g., "Remind yourself that these feelings won't last"; Feldman et al. 2008). In the current study, good internal consistency reliability was obtained for all subscales ($\alpha = 0.81$, 0.71, 0.90, respectively).

The 9-item Behavioral Activation for Depression Scale-Short Form (BADS-SF; Manos et al. 2011) was used to assess degree of behavioral avoidance. The BADS-SF contains two subscales measuring activation (e.g., "I engaged in many different activities") and avoidance (e.g., "Most of what I did was to escape from or avoid something unpleasant"), with higher scores reflecting greater evidence of the behaviors assessed in each domain. In the current study, internal consistency reliability was good for both the activation ($\alpha = 0.91$) and avoidance ($\alpha = 0.78$) subscales.

Experiential avoidance was assessed using the 10-item Acceptance and Action Questionnaire-II (AAQ-II; Bond et al. 2011). In the time since original data collection for the current study, recommendations emerged supporting the use of only the seven items of the AAQ-II that are not reverse scored (Bond et al. 2011). Thus, current study scores were based on the 7-item version of this questionnaire. The AAQ-II demonstrates strong concurrent and discriminant validity as well as internal consistency reliability in both clinical and nonclinical samples. Lower scores reflect greater acceptance of unwanted private events and higher scores reflect greater experiential avoidance. Internal consistency reliability of the AAQ-II was high in the current study ($\alpha = 0.96$).

Procedure

Identified through community advertisements (e.g., internet advertisements, flyers, brochures) and local clinician referral, individuals were invited to participate in an IRB-approved study (Butler Hospital IRB#1005-001) on affective responding and depression. Informed consent was obtained from all individual participants included in the study. After providing informed consent, participants completed an initial diagnostic assessment to determine eligibility. If determined to be eligible following this initial assessment, participants completed all remaining study assessments, including the self-report questionnaires of reward and emotion dysregulation. All assessments were conducted on an outpatient basis, in a university-affiliated hospital research clinic. Participants were compensated $35 for their participation in the broader study.

Data Analytic Plan

Descriptive data were evaluated, and preliminary multiple regression and Chi square analyses were used to evaluate potential sociodemographic differences between groups. Any sociodemographic differences identified were used as covariates in all subsequent analyses. Examination of primary study aims relied upon a set of multiple regression analyses, using an orthogonal set of Helmert contrast codes (Judd et al. 2009), to evaluate potential group differences on variables of interest. Groups were coded such that study analyses evaluated differences between CTL versus any diagnosis, and BD versus MDD. By reducing the total number of analyses by two-thirds, the use of Helmert coding provided a more streamlined analytic approach than the use of pairwise comparisons, yet nevertheless allowed for evaluation of the primary questions of interest. Because this analytic plan still resulted in testing the set of orthogonal contrast codes within 11 regression models (i.e., one for each of the outcomes assessed), we used the Benjamini–Hochberg procedure (Benjamini and Hochberg 1995) to correct for multiple comparisons, reduce Type I error, and restrict the false discovery rate (FDR) to 0.05. Corresponding Cohen's *d* statistics were calculated to provide estimates of overall effect size for group differences, and were interpreted using standard guidelines (Cohen 1988).

Table 2 Results from multiple regression analyses of group differences, adjusted for age

	BD ($n=30$)	MDD ($n=30$)	CTL ($n=30$)	Any Dx vs. CTL			BD vs. MDD		
	M (*SD*)	*M* (*SD*)	*M* (*SD*)	*F* (*df* = 1)	*p*	Cohen's d	F (*df* = 1)	*p*	Cohen's d
BAS fun seeking	11.0 (2.3)	10.0 (2.3)	10.4 (2.4)	0.06	.814	0.04	2.70	.104	0.44
BAS drive	10.2 (2.4)	9.0 (2.4)	9.2 (2.4)	0.62	.433	0.17	3.88	.052	0.51
BAS reward responsiveness	16.6 (2.5)	15.2 (2.4)	16.3 (2.5)	0.55	.461	−0.16	**5.59**	**.020**	**0.58**
BIS	24.9 (3.4)	22.9 (3.3)	18.6 (3.5)	**45.15**	**< .001**	**1.58**	**5.77**	**.018**	**0.61**
RSQ brooding	11.1 (3.1)	10.0 (3.0)	2.8 (3.1)	**116.77**	**< .001**	**2.56**	1.88	.174	0.37
RPA emotion-focus	14.2 (3.2)	12.0 (3.2)	12.2 (3.3)	1.44	.234	0.28	**7.57**	**.007**	**0.70**
RPA self-focus	9.5 (2.8)	8.4 (2.7)	8.6 (2.9)	0.31	.579	0.13	2.21	.141	0.41
RPA dampening	20.1 (5.3)	19.8 (5.2)	11.2 (5.4)	**52.84**	**< .001**	**1.67**	0.06	.803	0.06
BADS activation	15.2 (5.8)	15.3 (5.7)	22.2 (5.9)	**26.68**	**< .001**	**−1.21**	0.00	.973	−0.02
BADS avoidance	12.1 (3.8)	9.1 (3.8)	2.4 (3.9)	**86.56**	**< .001**	**2.16**	**9.51**	**.003**	**0.80**
AAQ-II	38.3 (6.5)	34.7 (8.7)	12.0 (5.6)	**221.83**	**< .001**	**3.64**	4.06	.047	0.47

BAS Behavioral Activation System scale (Fun Seeking, Drive, and Reward Responsiveness subscales); *BIS* Behavioral Inhibition Scale; *RSQ* Response Styles Questionnaire (Brooding subscale); *RPA* Responses to Positive Affect scale (Emotion-Focus, Self-Focus, and Dampening subscales); *BADS* Behavioral Activation for Depression Scale (Activation and Avoidance subscales); *AAQ-II* Acceptance and Action Questionnaire II. Bolded findings survived a false-discovery rate correction for multiple comparisons

Results

Preliminary Analyses

Preliminary analyses (see Table 1) revealed no differences in sex [χ^2 (4, $N=90$) = 3.24, $p=0.518$], race [χ^2(8, $N=90$) = 8.86, $p=0.354$], or ethnicity [χ^2(4, $N=90$) = 6.70, $p=0.153$] across study groups. Although there was no difference in age between BD and MDD groups [$F(1,59)=-0.70$, $p=0.407$], CTL participants were younger than the BD and MDD groups together [$F(1,89)=9.81$, $p=0.002$]. Thus, age was used as a covariate in all subsequent analyses. Age-adjusted means and standard deviations for all study measures, as well as group differences, are presented in Table 2. Consistent with the study design, the BD and MDD participants endorsed comparable and significantly higher depressive symptom severity than CTLs, with average scores for both diagnostic groups falling within the severely depressed range of the QIDS-SR (Trivedi et al. 2004). There was no difference between BD and MDD in QIDS-SR depression symptom severity. Also consistent with the study design, all three groups evidenced minimal to no ASRM manic symptom severity at the time of study participation, and did not differ significantly from one another.

Reward and Punishment Sensitivity

Consistent with study hypotheses, the BD group scored higher on BAS reward responsiveness [$F(1,59)=5.59$, $p=0.020$] when compared to the MDD group, with an effect that fell within the medium effect size range (Cohen's $d=0.58$). There was a non-significant trend towards the BD group scoring higher on BAS drive when compared to the MDD group [$F(1,59)=3.88$, $p=0.052$; Cohen's $d=0.51$]. Also consistent with study hypotheses, the BD and MDD groups together scored higher on the BIS compared to CTLs, with a large effect for this difference [$F(1,89)=45.15$, $p<0.001$; Cohen's $d=1.58$]. Though not originally hypothesized, analysis also revealed that the BD group endorsed higher BIS than the MDD group [$F(1,59)=5.77$, $p=0.018$; Cohen's $d=0.61$]. All of these findings, with the exception of trending group difference in BAS drive, survived FDR correction for multiple comparisons.

Emotion Regulation Processes

Consistent with study hypotheses, the BD and MDD groups endorsed greater use of negative rumination [$F(1,89)=116.77$, $p<0.001$; Cohen's $d=2.56$], dampening of positive affect [$F(1,89)=52.84$, $p<0.001$; Cohen's $d=1.67$], and behavioral [$F(1,89)=86.56$, $p<0.001$; Cohen's $d=2.16$] and experiential [$F(1,89)=221.83$, $p<0.001$; Cohen's $d=3.64$] avoidance in comparison to the CTL group, with large effects. Also consistent with study hypotheses, the BD group reported greater use of emotion-focused positive rumination [$F(1,59)=7.57$, $p=0.007$; Cohen's $d=0.70$] compared to the MDD group. Not originally hypothesized, additional analysis revealed that the BD group reported greater experiential [$F(1,59)=4.06$, $p=0.047$; Cohen's $d=0.47$] and behavioral [$F(1,59)=9.51$, $p=0.003$; Cohen's $d=0.80$] avoidance than the MDD group, with effect sizes ranging from medium to large. With

the exception of the initial difference between BD and MDD on the AAQ-II, these findings survived FDR correction for multiple comparisons.

Discussion

Although the literature on mood disorders, reward and punishment sensitivity, and processes of emotion regulation has grown significantly over the past decade (Aldao et al. 2010), this is the first study of which we are aware that has evaluated such processes concurrently in a sample comprised of depressed individuals with BD and MDD. By including clinical groups, this study was well-positioned to elucidate potential transdiagnostic processes associated with depression (i.e., independent of mood disorder diagnosis) from those that may be specific to BD or MDD. To achieve these aims, we evaluated reward and punishment sensitivity and two relevant emotion regulation processes, rumination and avoidance, in an outpatient adult sample. Overall, study results were largely consistent with a priori hypotheses. Specifically, we hypothesized that the diagnostic groups would share features of reward and punishment sensitivity and emotion dysregulation in areas known to be associated with depression, and that BD would further be differentiated from MDD on features purported to convey unique, underlying liability for mania. Indeed, with respect to those constructs hypothesized to be markers of depression *across* the mood disorders, those with BD and MDD together reported significantly greater behavioral inhibition, negative rumination, dampening of positive affect, behavioral avoidance, and experiential avoidance when compared to the CTLs. The magnitude of these differences all fell within the large effect size range, and suggest that such constructs may potentially reflect robust, transdiagnostic markers of depression.

With respect to negative rumination and dampening of positive affect, in particular, current study findings in this depressed sample align with those reported between controls and euthymic individuals with MDD and BD (Shapero et al. 2015), suggesting that perturbations in these constructs may be relevant both during periods of active depressive symptomatology and when individuals are relatively asymptomatic. There has been some preliminary evidence that dampening of positive affect may further differentiate BD from MDD (Shapero et al. 2015), which was not supported in the current study. Such inconsistent findings between studies may be driven by the evaluation of group differences in an actively depressed versus euthymic sample (as in the Shapero et al. analysis). For example, one might suspect that there is an avoidance of positive affect during depressive episodes among adults with MDD, given attempts to maintain negative (mood-congruent) states and avoid positive (mood-incongruent) states (e.g., Millgram et al. 2015). Hence, it may be that those with unipolar depression might engage in strategies aimed to minimize positive affect, at a level similar to that reported by those with bipolar depression, but it may be that the function of this behavior is different (i.e., maintenance of mood-congruence in MDD versus protection against mania in BD; Johnson et al. 2008). Yet it may also be possible that dampening of positive affect in BD may serve a different function in a euthymic state (i.e., to protect against mania) than during a depressive episode (i.e., similar to that in MDD). Future research to replicate these effects and explore the underlying function of positive affect dampening in unipolar relative to bipolar depression would further advance this line of inquiry.

Over and above the shared mechanisms of depression elucidated above, we further hypothesized that there would be differences between BD and MDD on self-reported constructs believed to reflect some liability toward BD, but had heretofore not been evaluated in BD samples during periods of active depressive symptomatology. First, with respect to the behavioral activation system, and consistent with study hypotheses, current study participants with BD reported significantly greater reward responsiveness when compared to those with MDD. The reported differences fell into the medium effect size range, and support the perspective that heightened BAS sensitivity may indeed be specific to BD, even during periods of active depression.[1] Although future research will be necessary to replicate and further unpack this pattern of results, current study findings nevertheless expand prior research on BAS sensitivity (Alloy et al. 2012, 2008; Meyer et al. 2001; Salavert et al. 2007) and ambitious goal striving (Shapero et al. 2015) and risk for mania in BD, even if reported levels in the current study were somewhat dampened relative to levels observed in euthymic (Meyer et al. 2001; Salavert et al. 2007) or at-risk (Alloy et al. 2012; Johnson and Carver 2006; Meyer et al. 1999) samples.

Also consistent with study hypotheses was the finding that self-reported emotion-focused positive rumination was significantly higher in the BD versus MDD group. Similar

[1] Although we did not have any specific *a priori* hypotheses about the BAS subscale comparisons for the combined diagnostic group versus the CTLs, it might be helpful interpret study findings within the context of these comparisons. Upon closer examination, the lack of a significant difference between the diagnostic groups and the CTLs on the BAS subscales may have been driven by a pattern of scores from the BD subsample that were somewhat similar to those reported by the CTLs (see Table 2). In comparison to prior research demonstrating significantly greater BAS sensitivity in at-risk or remitted individuals with BD versus healthy controls (Johnson and Carver 2006; Salavert et al. 2007), these findings point to a potential dampening of BAS sensitivity for BD when in a depressive episode, to levels similar to those reported by CTLs, but not as low as those reported by individuals with MDD. Future research will be necessary to further explore this possibility.

to the findings described above reflecting BAS sensitivity, these data point to a mechanism that is potentially unique to risk for BD, as argued previously (Johnson et al. 2008) and demonstrated in prior studies of remitted BD (Gruber et al. 2011; Shapero et al. 2015), that may remain evident during periods of a major depressive episode.

Over and above findings that those with BD and MDD together reported significantly greater behavioral inhibition and avoidance when compared to CTLs, there was additional evidence that these constructs may be particularly robust markers of bipolar depression, as those with BD reported even greater BIS and behavioral avoidance when compared to those with MDD. Together with the BAS findings, these findings suggest that individuals with BD may be particularly sensitive to both rewarding and aversive stimuli, which may be accompanied by the use of behavioral avoidance as an emotion regulation strategy. This pattern of findings is consistent with the reward hypersensitivity model of BD (Alloy et al. 2015), yet also suggests further elaboration on the role of BIS in its conceptualization. That is, the reward hypersensitivity model emphasizes the role of approach-activation events such as goal-striving and attainment (i.e., "BAS-activating events") in risk for mania in BD, and emphasizes the role of approach deactivation events such as failure or nonattainment of goals (i.e., "BAS-deactivating events") as being implicated in risk for depression in BD (Alloy et al. 2015). Current study data suggest that this conceptualization may merit expansion to also include the potential role of a hypersensitive punishment system (i.e., high BIS sensitivity and behavioral avoidance) in the larger reward hypersensitivity model. Further work should also be conducted in an effort to distinguish between low BAS/BAS-deactivating events and high BIS/BIS-activating events with respect to risk for bipolar depression, specifically.

Current study findings should be interpreted within the context of several limitations. First, we note the relatively small sample size utilized per group; however, this group size is comparable with other experimental research that has relied upon similarly severe clinical samples (Rottenberg 2017). Indeed, in the current study, the MDD and BD groups both reported average QIDS-SR scores in the severe depression range. Nonetheless, replications with larger samples are warranted. Another limitation was that our findings were based upon cross-sectional, self-report measures. Recent data on the AAQ-II suggests that it may be better conceptualized as a measure of overall negative affect rather than experiential avoidance (Rochefort et al. 2017), which may have limited our ability to examine differences between bipolar and unipolar depression on this construct in the current study. We also note that the internal consistency reliability estimate for the BAS-Fun Seeking subscale was low, potentially limiting an ability to detect group differences on this particular facet of reward sensitivity. Future research utilizing more ecologically valid assessment paradigms, across prospective assessment periods, would further advance this line of study.

Relevant to next steps, we note a number of recent neuroimaging studies that have utilized experimental paradigms of the constructs of interest to this study, and have elucidated differential neural phenotypes associated with reward processing and emotion regulation in BD and MDD (De Almeida and Phillips 2013). For example, individuals with BD have been shown to evidence decreased activation in reward processing brain regions such as the nucleus accumbens and ventrolateral prefrontal cortex relative to individuals with MDD in response to and during the anticipation of rewards (Chase et al. 2013; Redlich et al. 2015). Given the BIS and behavioral avoidance findings from the current study, future neuroimaging studies could also use paradigms focused on punishment sensitivity and avoidance of aversive stimuli to possibly differentiate BD from MDD. Continued investigation identifying endophenotypes will be important and valuable.

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Compliance with Ethical Standards

Conflict of Interest Lauren M. Weinstock, Tina Chou, Cintly Celis-deHoyos, Ivan W. Miller, and June Gruber declare that they have no conflicts of interest.

Informed Consent All procedures were conducted in accordance with the ethical standards of the institutional review committees of Butler Hospital and Brown University, Providence, RI, USA, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Animal Rights No animal studies were carried out by the authors for this article.

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