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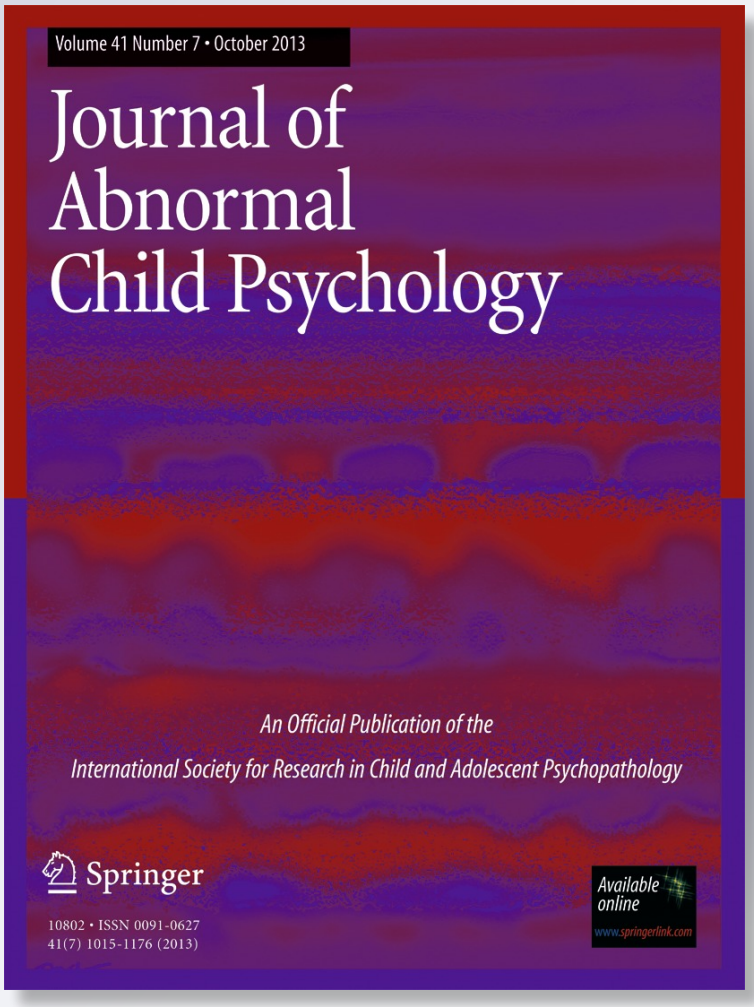

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Abstract Research on bipolar spectrum disorders (BPSD) in adolescence has burgeoned in the last decade, but continued work is needed to identify endophenotypic markers associated with illness onset and course. The present study examined reward dysregulation—measured via the behavioral activation system (BAS)—as one putative marker of BPSD in adolescence. A diverse group of 425 outpatient adolescents between 11 and 17 years of age (52 % male) completed the Behavioral Inhibition and Activation Scale (BIS-BAS) scale to measure reward dysregulation. Semi-structured interviews determined diagnoses and severity of mood symptoms. Parent-reported BAS was associated with increased symptoms of mania, and parent and adolescent-reported BAS were associated with symptoms of depression. Parent-reported BIS scores were associated with increased symptoms of mania. Results held independent of diagnostic status. Furthermore, parent BIS/BAS reports were stronger predictors for manic symptoms compared to adolescent-reports. Results extend work in adults with BPSD, suggesting a transdiagnostic association between reward dysregulation and mood symptom severity in adolescence.

Keywords Bipolar disorder · Mania · Depression, reward · Behavioral activation system · Adolescent

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Bipolar spectrum disorders (BPSD) are chronic and impairing psychiatric conditions (American Psychiatric Association 2000) affecting up to 4 % of the general population over the course of a lifetime (e.g., Kessler et al. 2005) and roughly 2 % of adolescents world-wide (Van Meter et al. 2011). BPSD broadly construed ranks among the top ten causes of medical disability worldwide (Coryell et al. 1993; Lopez et al. 2006) and is associated with the highest suicide rate compared to all other psychiatric disorders (Isometsa 1993; Simpson and Jamison 1999). In many affected individuals, clear manifestations of BPSD do not appear until adolescence (Merikangas et al. 2007). During this period, maturational and environmental events occur that can trigger latent dysfunctions inherent in the neurodevelopmental diathesis of BPSD (Goodwin and Jamison 2007; Johnson and McMurrich 2006). Thus, it is important to examine this crucial period of peak risk for BPSD in adolescence to identify mechanisms that trigger symptom onset and to identify and validate potential endophenotypic markers (Gottesman and Gould 2003; Hasler et al. 2006). Although research on BPSD in adolescence has expanded in the last decade (e.g., Geller and Luby 1997; Youngstrom et al. 2008), continued efforts to identify such mechanisms are needed. These research efforts yield promise to improve risk assessment and early, targeted treatment (e.g., Miklowitz and Chang 2008; Youngstrom et al. 2005a).

One promising endophenotypic marker associated with BPSD is reward dysregulation (e.g., Johnson 2005). By "reward dysregulation" we refer to two components including: (1) striving to pursue or attain pleasurable stimuli, also referred to as approach motivation (Harmon-Jones 2003) and anticipatory pleasure (Berridge et al. 2009); and (2) heightened response to positive or reward-laden cues, also referred to as reward hypersensitivity (Alloy et al. 2009; Ernst et al. 2004) or positive emotion reactivity (Gruber 2011; Johnson et al. 2007). In adult samples, research has

demonstrated that those at putative risk for developing BPSD report greater excitement at the possibility of earning rewards compared to healthy controls (Meyer et al. 1999, 2001) and striving for rewarding goals (Nusslock et al. 2007). Similarly, young adults at risk for developing BPSD exhibit heightened reactivity to positive stimuli compared to healthy controls across psychophysiological (Gruber et al. 2008; Sutton and Johnson 2002), cognitive (Johnson et al. 2005), life event (Johnson et al. 2000) and neuroimaging (Lawrence et al. 2004; Phillips and Vieta 2007) paradigms. Heightened reward pursuit in adults diagnosed with BPSD also demonstrates clinical significance, predicting increases in manic symptom severity longitudinally over time (Alloy et al. 2008; Lozano and Johnson 2001).

Comparatively, the adolescent BPSD literature remains less developed than that for adults. Existing findings on reward dysregulation and BPSD diagnosis and mood symptoms in adolescence are mixed. On the one hand, differential reward learning tasks demonstrate no group differences between adolescents with BPSD from controls (Rau et al. 2008). On the other hand, adolescents with BPSD do exhibit impairment in tasks assessing the ability to adapt to changing reward contingencies (Dickstein et al. 2004, 2007; Gorrindo et al. 2005). Although one reward selection task (i.e., wheel-of-fortune task) involving probabilistic monetary decision making trials demonstrated no differences between youths with and without BPSD, those youths with BPSD endorsed greater dissatisfaction when they did not win the money (Ernst et al. 2004). An important next step thus involves clarifying the nature of reward dysregulation during the adolescent developmental period in BPSD.

The present study seeks to begin to address this empirical gap. Specifically, we focus on one well-validated psychobiological index of reward dysregulation; namely, the behavioral activation system (BIS/BAS; Depue and Iacono 1989; Gray 1981). The behavioral activation system (BAS) regulates approach and appetitive motivation and is related to sensitivity to reward. By contrast, the behavioral inhibition system (BIS) regulates withdrawal behaviors and avoidance of punishment and is related to negative affect and anxiety. Applied to BPSD, symptoms of mania are conceptualized as the result of high BAS activity producing heightened reward sensitivity and positive affect, whereas symptoms of depression are associated with low BAS activity and decreased positive emotion (Depue and Iacono 1989). Research using the BIS/BAS scale as a basis for understanding BPSD in adults has demonstrated concurrent associations between increased self-reported BAS with a diagnosis of BPSD (Meyer et al. 2001; Salavert et al. 2007), cyclothymia (Urosevic et al. 2008), and risk for developing BPSD (Meyer et al. 1999). Additional work in adult BPSD populations demonstrates prospective associations between increased BAS and manic symptom severity (Alloy et al. 2008; Meyer et al. 2001). By contrast, both decreased BAS and increased BIS are associated with increased symptoms of depression in unipolar depressed patients (Kasch et al. 2002; Meyer et al. 2001). In sum, a growing body of work in adults reveals some associations between reward dysregulation and a diagnosis of, and symptoms associated with, BPSD.

Although such work is promising, several limitations exist. First, the findings reviewed above typically compare patients with BPSD to healthy controls, leaving it unclear to what extent such observations are diagnostic-specific or reflect a possible transdiagnostic feature of mood disorders more generally. Second, few studies have examined reward dysregulation using the BIS/BAS scale in an adolescent sample. One study in this domain found associations between increased self-reported BAS sensitivity with decreased symptoms of mania in a sample of adolescents diagnosed with BPSD (Biuckians et al. 2007). However, that study had a small sample size and included only youth (and not parent) reported BIS/BAS scores and so caution in the interpretation of results based on youth reports is warranted. Indeed, parent reports of manic symptoms are considered a more robust and valid measure of mood symptom severity as compared with youth self-reports (Geller and Luby 1997; Youngstrom et al. 2005a). Hence, there is a crucial need for further research to better understand how reward dysregulation—obtained from multiple informants—relates to mood dysregulation in adolescent manifestations of BPSD and transdiagnostically across adolescents independent of diagnosis.

The Present Investigation

The present study examined whether reward dysregulation—as measured by both adolescent- and parent-reported BIS/BAS activity—represents an endophenotypic marker that contributes to BPSD diagnosis and mood symptom severity in adolescence. Given existing emphasis on examining psychopathology in general and mania specifically on a continuum (Prisciandaro and Roberts 2011), we examined these aims both with respect to the BPSD diagnosis grouping as well as dimensionally focusing on mood symptoms across a diverse adolescent patient sample. Three primary aims were examined. First, based on the supposition that reward sensitivity is associated with increased symptoms of mania and BPSD in adults (Alloy and Abramson 2010; Johnson 2005; Meyer et al. 2001; Urosevic et al. 2008), we tested whether elevated BAS is an endophenotypic marker of BPSD in adolescents by examining associations between BAS and a diagnosis of BPSD. Two competing hypotheses were tested. One hypothesis is that BAS is a trait marker of BPSD and such that a diagnosis of BPSD would uniquely predict increased BAS

scores, and that this would hold independent of current symptoms. To test this hypothesis, we first adjusted for symptoms of mania and depression, and then examined whether a diagnosis of BPSD predicted self and parent-reported BAS. The second hypothesis is that BAS scores are a state like marker of mania symptom severity. Thus, greater symptoms of mania, but not depression, should predict increased BAS scores across independent of diagnostic status across all study participants. To test this hypothesis, we examined whether concurrent symptoms of mania uniquely predicted self- and parent-reported BAS.

For our second aim, we examined whether associations between depression with decreased reward sensitivity and increased behavioral inhibition in adults (e.g., Davidson et al. 2002; Dillon and Pizzagalli 2010) extended to adolescents. Two competing hypotheses between BIS and depression in adolescence were tested. The first hypothesis is that decreased BIS scores are a trait marker of BPSD and as such diagnoses of BPSD would predict decreased BIS scores, and that this association should hold independent of current symptom severity. This hypothesis is grounded in the observation that both adult and adolescent patients with BPSD primarily experience severe and recurrent symptoms of depression as compared to both manic and mixed states (e.g., Birmaher et al. 2009; Judd et al. 2003). To test this hypothesis, we first adjusted for symptoms of mania and depression, and then examined whether a diagnosis of BPSD predicted decreased self- and parent-reported BIS scores. The second hypothesis is that BIS scores are a state marker of depression symptom severity. Thus, greater symptoms of depression, but not mania, will predict increased BIS independent of diagnostic status across all study participants. To test this hypothesis, we examined whether concurrent symptoms of depression uniquely predicted self and parent-reported BIS.

The third and final aim was to compare the efficiency of parent- and self-reported BIS-BAS in predicting concurrent depression and mania symptoms and a DSM-IV-TR diagnosis of BPSD in adolescents. Based on prior findings (e.g., Youngstrom et al. 2004; 2005), we hypothesized that parent reports would be stronger predictors of symptom severity and a bipolar spectrum diagnoses than self-reports.

Method

Participants

The present study is a secondary analysis of data gathered to examine the prevalence of bipolar spectrum disorders in youths seeking community mental health services, as well as to evaluate the diagnostic efficiency of different rating scales for discriminating bipolar disorder from all other disorders presenting to the clinic. The only exclusion criterion was that both youth and primary caregiver needed to be able to complete the interview and rating scales in English. All diagnoses presenting to the clinics were included. The institutional review boards of all institutions involved in the project reviewed and approved the procedures. All adolescents provided assent to participate. Participants were N=425 demographically diverse families seeking outpatient mental health services for adolescents between the ages of 11 and 17 years (M=13.52, SD=1.85). Families came to either an urban community mental health center serving predominantly low-income families, or to the urban academic outpatient clinic of a university affiliated hospital (see Tables 1 and 2).

The grant included the academic clinic to ensure that raters were calibrated consistently for evaluating mood disorder at both sites, creating a linking sample to prior investigations. Youths were 52 % male, and 25 % European American, 68 % African American, 2.1 % Hispanic 0.5 % Asian or Pacific Islander and 4.5 % identifying as other. Parental education ranged from 7 to 20 years (highest education completed: 4.7 % junior high school; 15.3 % partial high school; 31.1 % high school/GED; 34.6 % part college/trade school; 7.1 % college; 2.6 % part graduate school; 1.9 % graduate school; 2.8 % refused to answer). Self-reported family income averaged between $10,000 to $14,000, with 66.3 % reporting less than $20,000 per year.

Measures

DSM-IV-TR Diagnoses Diagnoses were based on a consensus conference following a semi-structured diagnostic interview using the Kiddie Schedule for Affective Disorders and Schizophrenia—Present and Lifetime version (KSADS-PL; Kaufman et al. 1997) with the mood disorders modules from the WASH-U version (Geller et al. 2001). Highly trained raters (criterion of κ>0.85 at the item level on five interviews conducted by a reliable rater, and then κ>0.85 on five interviews they led themselves) interviewed the youth and the parent sequentially, using clinical judgment and re-interviewing to resolve discrepancies. Kappas for both BPSD diagnosis (0.94) and any type of mood disorder (0.85) were good. Interviews then reviewed findings with a licensed clinical psychologist in a "Longitudinal Expert evaluation of All Data" (LEAD; Spitzer 1983) meeting that integrated developmental history, prior treatment history, and family mental health history to arrive at a final diagnosis. The interview generated DSM-IV diagnoses, with bipolar spectrum diagnoses including bipolar I disorder, bipolar II disorder, cyclothymic disorder, and bipolar disorder not otherwise specified (NOS). Bipolar NOS diagnoses were made in cases where the adolescent did not meet criteria for any other bipolar

Table 1 Demographic and clinical characteristics presented separately by site

Characteristic	Community Mental Health Center (n=297)	Academic Center (n=128)	Total (n=425)
Age (SD)	13.43 (1.82)	13.71 (1.90)	13.52 (1.85)
Ethnicity (% Caucasian)	6.1 %***	68.8 %	25 %
Gender (% Female)	47.8 %	48.4 %	48 %
KDRS (SD)	22.82 (9.39)***	26.84 (9.57)	24.03 (9.61)
KMRS (SD)	18.52 (8.05)***	25.04 (10.53)	20.48 (9.35)
BPSD (%)	39 (45)**	47 (54)	86
Depressed (%)	6 (75)	2 (25)	8
Manic (%)	3 (60)	2 (40)	5
Mixed (%)	25 (40)*	39 (60)	64
Remitted (%)	5 (55)	4 (44)	9
MDD (%)	118 (74)	41 (26)	159
Depressed (%)	87 (73)	32 (27)	119
Remitted (%)	24(72)	9(27)	33
Disruptive Disorder (%)	115 (39)*	31 (24)	146
Residual Disorder (%)	25 (8)	9 (1)	34
Medication Status Y/N (%)	149 (50)***	89 (70)	238 (56)

KDRS KSADS depression rating scale; *KMRS* KSADS mania rating scale; *BPSD* bipolar spectrum disorder; *NOS* not otherwise specified; MDD = Major Depressive Disorder Dysthymic Disorder, Depressive Disorder not otherwise specified; Disruptive = Attention Deficit Hyperactivity Disorder, Conduct Disorder, Oppositional Defiant Disorder and Disruptive Disorder Not otherwise specified; Residual = anxiety disorders, adjustment disorders, psychotic disorders, cognitive or general medical condition disorders

*p<0.05; **p<0.01, ***p<0.0001. Adjusted Residuals from Chi-square used for diagnostic status comparisons (Agresti 2002)

diagnosis, usually due to insufficient duration of the index hypomania or mania episode.

Mood Symptoms The same diagnostic interview also generated severity ratings for the youth's current and worst lifetime mood episodes, if any. The KSADS Mania Rating Scale (KMRS) and KSADS Depression Rating Scale (KDRS; Axelson 2002) provided severity ratings of all mood symptoms relevant to the DSM-IV criteria for mania and depression. The KMRS and KDRS scores showed excellent internal consistency (α=0.92 and 0.86 in this sample, respectively).

Table 2 Group differences between diagnostic categories in adolescent and parent reported BIS/BAS subscales

	BPSD (n=86)	MDD (n=159)	Disruptive (n=146)	Residual (n=34)	Statistic	Group comparisons
Adolescent						
BAS-Reward	15.61 (3.40)	15.01 (3.67)	15.79 (3.27)	16.65 (3.36)	2.89*	Residual > MDD
BAS-Drive	10.17 (3.11)	9.75 (3.25)	10.39 (3.14)	8.97 (2.95)	2.36	–
BAS-Fun	11.14 (2.64)	10.77 (2.59)	11.19 (2.71)	11.41 (2.90)	0.95	–
BIS & Residual	18.36 (3.87)	18.22 (3.95)	17.47 (3.61)	17.55 (3.64)	1.48	BPSD > MDD, Disruptive,
Parent						
BAS-Reward	16.73 (3.17)	15.72 (3.44)	16.55 (3.11)	17.12 (2.65)	3.29*	–
BAS-Drive	12.33 (3.27)	10.31 (3.37)	11.23 (3.33)	9.26 (3.66)	9.98*	BPSD > MDD, Residual Disruptive>Residual
BAS-Fun	12.13 (2.60)	10.92 (2.68)	11.68 (2.94)	10.68 (3.06)	4.86*	BPSD>MDD, Residual
BIS	19.18 (3.79)	17.78 (3.34)	17.55 (4.06)	16.79 (3.70)	4.87*	–

BPSD bipolar spectrum disorder; *MDD* major depressive disorder, Dysthymic Disorder, Depressive disorder not otherwise specified; Disruptive = Attention Deficit Hyperactivity Disorder, Conduct Disorder, Oppositional Defiant Disorder and Disruptive Disorder Not otherwise specified; Residual = anxiety disorders, adjustment disorders, psychotic disorders, cognitive or general medical condition disorders; *BAS* behavioral activation system; *BIS* behavioral inhibition system. Group comparisons are Tukey's multiple comparisons

*p<0.05

Reward Dysregulation The Behavioral Inhibition and Behavioral Activation Scale (BIS-BAS; Carver and White 1994) was used to measure adolescent and parent-reported reward dysregulation. BIS and BAS subscales were scored such that higher scores reflect greater behavioral inhibition or activation, respectively. The Parent BIS-BAS scale (referred to here as "P-BIS" and "P-BAS") generated four subscale scores: P-BIS ("I worry about making mistakes"; α=0.54 median corrected item-total, r=0.34); P-BAS-Reward ("When I get something I want, I feel energized and excited"; α=0.76; median corrected item-total, r=0.57); P-BAS-Fun Seeking ("I crave excitement and new sensations"; α=0.66; median corrected item-total, r=0.44); and P-BAS-Drive ("I go out of my way to get things I want"; α=0.84; median corrected item-total, r=0.69). Adolescents completed self-report versions of the same scales (referred to here as "A-BIS" and "A-BAS"), with notably lower internal reliability: A-BIS (α=0.52, median corrected item-total, r=0.38); A-BAS Reward (α=0.74; median corrected item-total, r=0.55); A-BAS Fun Seeking (α=0.56; median corrected item-total, r=0.39); A-BAS Drive (α=0.73; median-corrected item-total, r=0.54).[1] However, when subscales were combined into the A-BAS Total score, internal reliability was good (α=0.80, median corrected item-total, r=0.39) and is consistent with prior research in adolescent BPSD populations (Biuckians et al. 2007).

Procedure

Participants were chosen by random selection or a consecutive case series when referrals exceeded the capacity to complete research interviews. Families completed informed consent and then began the interviews. When the parent was engaged in the KSADS interview, the adolescent completed questionnaires or other study procedures with a second research assistant. The grant enrolled families with youths as young as age 5, but youths did not provide self report unless they were 11 years or older, consistent with norms on widely used behavior checklists (Achenbach and Rescorla 2001). Participants would then switch and the parent would fill out rating scales while the youth did the KSADS interview. All measures were completed in the same session. Missing data were minimal and listwise deletion was used for all analyses (i.e., 9 participants missing diagnostic group status, 5 missing parent BIS/BAS and 8 missing adolescent BIS/BAS scores, and 13 participants missing manic and depressive symptom scores). Families received $40 for participation.

[1] Due to low reliability of A-BIS/BAS scores, we removed adolescents indicated to be poor responders on self-report and interview data, and reliability coefficients did not significantly differ ($Z \leq -1.09$, $ps > 0.05$). Moreover, examining median corrected item total scores, all BIS/BAS values were within an acceptable range (> 0.35; Steiner and Norman 1995).

Data Analysis Strategy

In order to examine potentially confounding variables, we first assessed bivariate correlations between BIS/BAS (adolescent and parent-reported) scores and all demographic variables. Second, we assessed bivariate correlation between depressive and manic symptoms, as well as bivariate correlations between BIS/BAS scores (adolescent and parent-reported) and depressive and manic symptoms.

For our two main aims, we performed block-entry linear regression analyses; missing data were deleted listwise[2] and multicollinearity diagnostics showed tolerance statistics well below standards indicating bias in the models (no tolerance values below 0.1 or VIF values greater than 10.0; Myers 1990). Cook's distance and the standardized DFBeta for each predictor revealed no influential cases (Cook and Weisberg 1982). To examine our first hypothesis regarding the relationship between BAS scores with mood symptoms and a BPSD diagnosis, regression analyses were conducted with individual BAS subscales (i.e., BAS-Fun, BAS-Reward, BAS-Drive) as outcome variables. Block 1 included demographic control variables, including age, ethnicity (Caucasian = 0; Non-Caucasian = 1), gender (Male = 0; Female = 1) and site (Community center = 0, University outpatient = 1). Block 2 included current mood symptoms, simultaneously entering symptoms of depression (KDRS) and mania (KMRS).[3] Finally, Block 3 included diagnostic status (BPSD disorders = 1; All other diagnoses which included MDD, anxiety disorders, behavioral disorders, adjustment disorders, psychotic disorders, cognitive or disorders = 0) to examine the role of diagnosis controlling for demographic variables and symptom severity. Six separate regressions were run for each of the three BAS subscales separately for both parent- and adolescent-reports following recommendations (Carver and White 1994). To examine our second hypothesis regarding the relationship between BIS scores with mood symptoms and a BPSD diagnosis, parallel regression analyses were conducted with the total BIS score as the outcome variable. Two separate regressions were run for both parent- and adolescent-BIS reports. For both the first and second hypotheses, the overall model is reported when significant. We structured the analyses this way

[2] Fortunately, there were minimal missing data that made listwise deletion possible. There was no missing data for gender, age, and ethnicity, and very little missing for diagnostic group, parent and adolescent BIS/BAS scores, and KDRS/KMRS scores (< 3 %).

[3] We completed the same set of regressions using the Young Mania Rating Scale (YMRS) and Children's Depression Rating Scale (CDRS) in place of the KMRS and KDRS respectively, and obtained parallel results. Moreover, KMRS and KDRS scores correlated r=0.92 and r=0.93 with YMRS and CDRS severity ratings, respectively. Because the KMRS and KDRS provide more comprehensive coverage of DSM-IV symptoms of mania and depression (Axelson et al. 2003), we opted to present results using these symptom variables in the final analyses.

because it enabled us to tease apart more clearly the influence of symptoms from diagnosis with BAS, simultaneously account for manic and depressive symptoms, and achieve these aims in a parsimonious way.

To examine our third aim comparing differences between self- and parent-reported BIS/BAS scores in predicting symptom severity and a DSM-IV-TR diagnosis of BPSD. For symptom severity, we performed Steger's test of dependent correlation coefficients based on parent and adolescent self-reports to compare differences between the parent and adolescent correlations (Cohen and Cohen 1983). For BPSD diagnosis, Areas Under the Curve (AUCs) from receiver operating characteristic analyses quantified the extent to which BIS-BAS scores discriminated BPSD diagnosis from all other cases. Logistic regression analyses were performed in parallel to determine the individual contributions of each parent and adolescent self-reported BIS-BAS subscale score in predicting a diagnosis of BPSD.

Results

Preliminary Analyses

First, we examined whether BIS/BAS scores were significantly associated with demographic variables using two-tailed bivariate correlations. Here, results revealed that age was positively correlated with A-BAS-Drive (r=0.12, p< 0.05) and negatively correlated with P-BAS-Reward (r= −0.14, p<0.05. However, age was not correlated with A-BAS-Fun, A-BAS-Reward, A-BIS, P-BAS-Drive, P-BAS-Fun, or P-BIS (p's>0.05). For gender, females endorsed higher A-BIS scores compared with males, t(423)=−3.56, p<0.05. For ethnicity, Caucasians reported higher P-BAS-Drive, t(423)=2.88, p<0.05 compared to all other ethnicities. In order to control for these demographic variables, we included age, gender, and ethnicity in Block 1 of the subsequent regression models. We then assessed whether the two sites differed on demographic characteristics, mood symptoms, and BIS/BAS scores. As expected when comparing a community center with an outpatient clinic, the community center had significantly higher numbers of African American patients (χ^2=239.47, p<0.05) and fewer depressive symptoms, t(423)=−4.03 p<0.05, manic symptoms t(423)=−6.96 p<0.05, and diagnoses of BPSD t(423)= −5.75, p<0.05. P-BAS-Drive scores were also significantly lower in the community sample, t(423)=−3.05, p<0.05. Hence, we included site in Block 1 along with demographic variables. We also assessed differences between parent and adolescent BIS/BAS scores depending on medication status (yes/no) and found no significant differences (ps>0.05). However, we did find differences on rates of medication use between sites. Thus we ran all analyses with medication status included in Block 1, and it did not change results; so it was not included in further analyses.[4]

Second, bivariate correlations assessed the relationship between symptoms of mania (KMRS) and depression (KDRS). Not surprisingly, KDRS and KMRS scores were positively correlated (r=0.52, p<0.001). This is consistent with prior work demonstrating that adolescents with BPSD frequently exhibit mixed mood symptoms (Biederman et al. 2005; Youngstrom et al. 2008). Third, bivariate correlations assessed the relationship between BIS/BAS scores with KMRS and KDRS scores (see Table 3). For parent report, KMRS scores were associated with increased P-BAS-Drive, P-BAS-Fun, and P-BIS. KDRS scores were associated with decreased P-BAS-Reward and increased P-BIS. The only significant correlations for adolescent report were for the KDRS and decreased A-BAS-Reward and increased A-BIS. Fourth, a one-way ANOVA examined group differences across diagnostic categories for both the adolescent and parent reported BIS/BAS subscales. Results most consistently indicated that the BPSD category demonstrated elevated BIS and BAS scores compared with other diagnostic categories, and thus to keep with a priori hypotheses, we focused on this diagnostic category in further analyses.

Hypothesis 1 Results: Symptoms Severity and BPSD Diagnosis as Predictors of BAS

The first set of analyses examined the link between current KMRS and KDRS scores with a BPSD diagnosis with A-BAS subscale scores. As shown in Table 4, demographic variables entered in Model 1 were not significant predictors of A-BAS-Reward. When depression and mania symptoms were added in Model 2, KDRS scores negatively predicted A-BAS-Reward while KMRS scores positively predicted A-BAS-Reward (Model 2: F(2,418)=5.78, R^2=0.03, ΔR^2= 0.03; KDRS: β=−0.20; KMRS: β=0.13, p<0.05). Once diagnostic status was added in Model 3, depression symptoms continued to negatively predict A-BAS-Reward (β=−0.20, p<0.05). However, KMRS scores did not continue to predict A-BAS Reward (β=0.17 p>0.05) nor did a BPSD spectrum diagnosis predict A-BAS-Reward (β=−0.05 p>0.05). Examining A-BAS-Drive, none of the overall Models were significant, although the individual predictor of age was associated with higher A-BAS-Drive (age: β=0.12, p<0.05) and remained a significant predictor in Model 2 (β=0.14, p<0.05) and Model 3 (β=0.14,

[4] For the purposes of the current analyses, yes/no medication status was included because more detailed analysis of individual medications is beyond the scope of this paper. However, in an ideal world, research should aim to include matching and/or random assignment of participants on medication types and dosages. Because the present sample consisted of youths receiving services in the community, there is a lot of heterogeneity in the choice and combination of medications used.

Table 3 Correlations of BIS/BAS and mood symptoms in adolescent and parent report and comparisons between adolescent and parent coefficients

	KMRS			KDRS		
	Adolescent *r*	Parent *r*	Comparison	Adolescent *r*	Parent *r*	Comparison
BAS-Reward	0.03	0.07	$t(422)=-0.73$	−0.11*	−0.10*	$t(422)=-0.16$
BAS-Drive	0.05	0.24*	$t(422)=-3.01$+	−0.04	0.08	$t(422)=-1.86$
BAS-Fun	0.04	0.17*	$t(422)=-1.94$*	−0.02	−0.03	$t(422)=0.15$
BIS	0.05	0.13*	$t(422)=-1.22$	0.10*	0.12*	$t(422)=-0.29$

KMRS KSADS mania rating scale; *KDRS* KSADS depression rating scale; *BAS* behavioral activation system; *BIS* behavioral inhibition system. *r*-values reflect bivariate correlation coefficients. Comparison is Stagers test of dependent correlation coefficients

*$p<0.05$; +$p<0.10$

$p<0.05$). Additionally, KDRS scores in Model 2 predicted decreased A-BAS-Drive ($\beta=-0.13$, $p<0.05$) and remained significant in Model 3 ($\beta=-0.13$, $p<0.05$) after controlling for a BPSD spectrum diagnosis. None of the overall models or individual predictors significantly predicted A-BAS-Fun (ps>0.05). In sum, KDRS scores predicted decreased A-BAS-Reward and decreased A-BAS-Drive, KMRS scores predicted elevated A-BAS-Reward only when a diagnosis of BPSD was not entered, and a BPSD diagnosis did not significantly predict any A-BAS scores.

We next examined P-BAS subscales as outcome variables in three separate regressions, using the same predictor variables. In the first regression, predicting P-BAS-Reward, demographic variables were entered in Model 1 and younger age ($\beta=-0.15$ $p<0.05$) was a significant predictor ($F(4,420)=2.59$, $\Delta R^2=0.02$, $p<0.05$) and remained significantly associated with P-BAS-Reward in Model 2 ($\beta=-0.12$ $p<0.05$) and Model 3 ($\beta=-0.12$ $p<0.05$). When KDRS scores were added in Model 2, they negatively predicted P-BAS-Reward ($F(2,418)=6.04$, $\Delta R^2=0.03$; $\beta=-0.17$ $p<0.05$), and continued to predict decreased P-BAS-Reward after BPSD spectrum diagnostic status was entered in Model 3 ($\beta=-0.17$ $p<0.05$). KMRS scores also predicted increased P-BAS-Reward scores in Model 2 ($\beta=0.17$, $p>0.05$) and remained a significant predictor in Model 3 ($\beta=0.18$, $p>0.05$). A BPSD diagnosis also did not predict P-BAS-Reward in Model 3 ($\beta=0.01$ $p>0.05$). Examining P-BAS-Drive, the overall Model 1 ($F(4,421)=2.67$, $\Delta R^2=0.03$; $\beta=0.14$ $p<0.05$) was significant, although none of the individual demographic predictors were significant predictors. The addition of KMRS scores in Model 2 ($F(2,418)=10.86$, $\Delta R^2=0.05$, p<0.05; $\beta=0.26$, $p<0.05$) predicted increased P-BAS-Drive and also remained significant in Model 3 ($\beta=0.25$, $p<0.05$). KDRS scores in Model 2 ($\beta=-0.07$, $p>0.05$) or a BPSD spectrum diagnosis in Model 3 ($\beta=-0.02$; $p>0.05$) did not significantly predict P-BAS-Drive scores. P-BAS-Fun was not predicted by any demographic variables across Model 1, 2, or 3 (ps>0.05). However, Model 2 was significant (F(2,418)=7.77, $\Delta R^2=0.04$, $p<0.05$), revealing that the KMRS predicted increased P-BAS-Fun ($\beta=0.23$, $p<0.05$) while the KDRS predicted decreased P-BAS-Fun ($\beta=-0.13$, $p<0.05$), findings which remained significant in Model 3 for both KMRS ($\beta=0.23$, $p<0.05$) and KDRS ($\beta=-0.13$, $p<0.05$) scores. BPSD diagnosis did not predict P-BAS-Fun in Model 3 ($\beta=-0.01$, $p>0.05$). In sum, KDRS scores predicted decreased P-BAS Reward and P-BAS-Fun, and KMRS predicted increased P-BAS-Reward and P-BAS-Fun.. However, only KMRS scores predicted increased P-BAS-Drive. These results held independent of BPSD diagnosis, and BPSD diagnosis did not significantly predict any P-BAS scores. We note that parallel results emerged when specifically focusing on the BPSD I subset of participants.

Hypothesis 2 Results: Symptoms Severity and BPSD Diagnosis as Predictors of BIS

To examine our second hypothesis, we performed two block entry linear regressions with adolescent and parent reported BIS as outcome variables (see Table 4). For A-BIS, Model 1 was significant ($F(4, 420)=3.37$, $\Delta R^2=0.03$, $p<0.05$), indicating that females demonstrated elevated BIS scores compared to males ($\beta=0.17$, $p<0.05$). For P-BIS, the overall Model 2 was significant ($F(2,418)=4.77$, $\Delta R^2=0.02$, $p<0.05$) although no individual predictors within this model were significant (ps>0.05). Model 3 was also significant, ($F(1,417)=5.16$, $\Delta R^2=0.01$, $p<0.05$) indicating that diagnosis of a BPSD spectrum disorder predicted increased P-BIS scores above and beyond mood symptoms ($\beta=0.18$, $p<0.05$). In sum, neither A-BIS nor P-BIS was predicted by mood symptoms but P-BIS was significantly predicted by a BPSD diagnosis.

Hypothesis 3 Results: Comparing Self- and Parent-Reports of BIS/BAS

In order to compare the efficiency of parent- and self-reported BIS-BAS in predicting concurrent depression and

Table 4 Hierarchical multiple regression analyses using from current symptoms and diagnostic status to predict BIS-BAS scores (N=425)

Predictor	BAS-Reward				BAS-Drive				BAS-Fun				BIS			
	Adolescent (A-Reward) ΔR^2	β	Parent (P-Reward) ΔR^2	β	Adolescent (A-Drive) ΔR^2	β	Parent (P-Drive) ΔR^2	β	Adolescent (A-Fun) ΔR^2	β	Parent (P-Fun) ΔR^2	β	Adolescent (A-BIS) ΔR^2	β	Parent (P-BIS) ΔR^2	β
Step 1 (Demographics)	0.00		0.02*		0.02		0.03*		0.01		0.02		0.03*		0.01	
Age		−0.01		−0.15*		0.12*		−0.00		0.08		−0.08		−0.01		−0.01
Female		0.06		0.06		−0.01		0.02		−0.03		−0.04		0.17*		0.05
Caucasian		0.01		0.01		0.05		0.07		−0.02		0.03		−0.05		−0.05
Site		−0.03		−0.34		−0.13		0.10		0.01		0.08		0.05		0.03
Step 2 (Symptoms)	0.03*		0.03*		0.01		0.05*		0.01		0.04*		0.00		0.02*	
KDRS		−0.20*		−0.17*		−0.13*		−0.07		−0.08		−0.13*		0.07		0.07
KMRS		0.13*		0.18*		0.10		0.26*		0.09		0.23*		−0.01		0.11
Step 3 (Diagnosis)	0.00		0.00		0.00		0.00		0.00		0.00		0.00		0.01*	
BPSD[a]		−0.05		0.00		−0.04		0.02		−0.05		−0.01		0.04		0.18*

KDRS KSADS depression rating scale; *KMRS* KSADS mania rating scale; *BAS* behavioral activation system; *BIS* behavioral inhibition system

[a] Diagnosis of bipolar spectrum disorder (i.e., combination of BD I, BD II, cyclothymia, BD NOS diagnoses) as compared with all other groups

*p<0.05

mania symptoms, we compared the correlation coefficients between A-BIS/BAS scores and P-BIS/BAS scores with mood symptoms using Steiger's *t*-test for dependent correlations (See Table 3). With respect to mania symptoms, results suggested that P-BAS-Drive and P-BAS-Fun were stronger predictors of manic symptoms as compared to A-BAS-Drive and A-BAS-Fun. No differences emerged for BAS-Reward. For symptoms of depression, there were no significant differences between parent- and adolescent-reports. Thus, parent report appears to be slightly more sensitive to detecting associations between mania and BAS, but no significant differences emerged for depression symptoms with BIS/BAS scores.

Areas Under the Curve (AUCs) from receiver operating characteristic analyses quantified the extent to which BIS-BAS scores discriminated a BPSD diagnosis from all other cases. For parent-report, P-BAS-Drive showed the greatest discriminating power, with an AUC=0.65, $p<0.001$ (CI: 0.59, 0.72). Although better than chance, this is substantially lower than the AUCs for various symptom measures and diagnostic aids. P-BAS-Fun (AUC=0.59, $p<0.01$; CI: 0.53, 0.66, $p<0.05$) and P-BIS (AUC=0.55, $p<0.05$; CI: 0.56, 0.70) both discriminated BPSD diagnosis at modest but better than chance levels. P-BAS-Reward did not significantly contribute to discriminating a BPSD diagnosis (AUC=0.56, $p=0.11$) and did not significantly contribute to discriminating a BPSD diagnosis. For adolescent self-report, none of the BIS-BAS scales achieved statistical significance in ROC analyses ($ps>0.05$).

Logistic regression analyses found that P-BAS-Drive was the best predictor of BPSD diagnosis (Wald statistic: 9.39), and both P-BAS-Drive and P-BIS (Wald statistic: 6.01) made significant incremental contributions to BPSD diagnosis ($ps<0.05$). Notably, adolescent self-report BIS-BAS subscales were not significant either entering first or after controlling for parent reported BIS-BAS subscales.

Discussion

Although research on BPSD in adolescence has increased in the last decade, there remains a dearth of work identifying potential endophenotypic markers associated with illness onset and course. The present study examined whether reward dysregulation—as measured by both self- and parent-reported BIS/BAS activity—represents an endophenotypic marker that contributes to BPSD diagnosis and mood symptom severity in an adolescent sample.

The first aim examined associations between BAS with a diagnosis of BPSD and concurrent mood symptoms. Results supported the hypothesis that BAS scores are a state (and not trait) like marker of mood symptom severity independent of diagnostic status. In general, we found that symptoms of mania predicted increased parent-reported BAS, and symptoms of depression predicted decreased parent- and adolescent-reported BAS. With respect to manic symptoms, these findings are consistent with work in adults suggesting that increased reward sensitivity is concurrently associated with increased manic symptoms (Alloy and Abramson 2010; Johnson 2005; Meyer et al. 2001; Urosevic et al. 2008) and prospectively predicts increases in manic symptoms over a 4-month period (Alloy et al. 2008; Lozano and Johnson 2001). Such findings also converge with literature suggesting that those with a history of mania exhibit increased drive towards pursuing rewards even after success is attained (Fulford et al. 2010). This suggests that manic symptoms may be a more proximal measure of reward dysregulation as compared to a lifetime BPSD diagnosis. Our findings are in contrast with one study conducted in an adolescent BPSD sample reporting associations between BAS and decreased manic symptoms (Biuckians et al. 2007), though this study included only youth reports which may be less accurate measures of mania, a point to which we return to below.

With respect to depression and decreased BAS (notably the Reward subscale), these findings in adolescents are consistent with work in adults revealing associations between depressive symptoms and decreased reward responsiveness (e.g., Bogdan and Pizzagalli 2006; Meyer et al. 1999) as well as theoretical models associating lower BAS levels with depressive symptoms (Carver and Scheier 1998). In sum, these findings extend prior work by replicating associations between BAS-Reward and mood symptoms in an adolescent sample. These results, furthermore, suggest a potentially transdiagnostic (Harvey et al. 2004) association between reward dysregulation and mood symptoms in adolescence above and beyond a BPSD diagnosis.

The second aim examined whether associations between depression and increased behavioral inhibition (or BIS) in adults extended to adolescents (e.g., Davidson et al. 2002; Dillon and Pizzagalli 2010). Results did not support the hypothesis that BIS scores were a state marker of depression mood symptom severity across both parent and adolescent self-reports. However, findings somewhat supported the hypothesis that BIS scores are a trait marker of BPSD. Specifically we found that parent (but not adolescent) reported BIS scores were significantly predicted by a BPSD diagnosis. In sum, findings for the second aim suggest that BIS may be a trait-like marker of BPSD diagnosis, while BAS may reflect a more state-like marker of mood symptom severity in adolescence.

The third and final aim compared the efficiency of parent- and self-reported BIS-BAS in predicting concurrent mood symptoms and a DSM-IV-TR diagnosis of BPSD in adolescents. With respect to symptom severity, parent-reported BIS-BAS scores were stronger predictors for manic symptoms compared to adolescent-reports. There were no

differences between parent and adolescent-reported BIS-BAS for depression symptoms. For BPSD diagnosis, results suggested that parent-reported BIS-BAS scores in general were better at discriminating a BPSD diagnosis compared to adolescent self-reports; which appeared to be most strongly driven by BAS-Drive and BIS subscales. These findings are consistent with prior work revealing that parent reports of manic symptoms are a more robust and valid measure of symptom severity as compared with youth self-reports (e.g., Geller and Luby 1997; Youngstrom et al. 2004; 2005). This is consistent with a long tradition of cross-informant assessment techniques in child and adolescent populations in which parent reports are frequently used a robust indices of child behavior (Achenbach et al. 1987; Conners et al. 1998; Hawley and Weisz 2003). This suggests that parent reports may have greater validity for manic symptoms (and hence, accurate BPSD diagnoses) which may be difficult for adolescents to accurately self-report given associations between poor insight into illness and mania severity (Ghaemi and Rosenquist 2004).

The results of the present study need to be interpreted within the confines of several limitations. First, the results of the present study were assessed exclusively with self-report questionnaire indices of reward regulation. While self-report studies are a worthwhile first step, future studies should utilize experimental inductions of reward dysregulation (e.g., behavioral and neuroimaging paradigms) measuring concurrent physiological and behavioral indices of reward sensitivity. Although reliability estimates of these self-report measures were low in the current sample such reliability estimates are consistent with prior research using the BIS/BAS in adolescent BPSD samples (Biuckians et al. 2007). Second, the sample was comprised of a demographically diverse sample that contained a high percentage of African-American and low-income adolescent families. Although this represents a strength of the present research by representing underserved and understudied minority groups, it may make comparisons with earlier work more difficult. Third, the present study did not contain a non-psychiatric control group, which likely attenuated size of effects presented in the present study that were modest. Fourth, given evidence suggesting differences in reward processing associated with puberty (e.g., Steinberg 2010), the present study would have benefited by assessing the effects of pubertal status on BIS/BAS and symptom relationship. Fifth, the current design was concurrent and as such a longitudinal prospective high-risk sample design is warranted to more clearly disentangle the state versus trait association between diagnosis and symptoms with BAS scores. Finally, the BPSD group designation included a broad spectrum of participants and thus added heterogeneity to group-based analyses. We note, however, that when we focused more narrowly on BD I diagnosed participants parallel results emerged as for BPSD group comparisons.

Despite these limitations, the present study adds to the small, but growing, literature examining associations between reward dysregulation and mood symptom severity, extending this work in a demographically diverse adolescent sample. Critical next steps include identifying pathophysiological processes associated with subgroups of adolescents characterized by reward dysregulation that will inform new treatment development (Insel et al. 2010). Furthermore, it is important to show that such processes contribute to the etiology or maintenance mood symptoms developmentally from the transition of adolescence to adulthood. If prospective and experimental studies establish that reward dysregulation plays such a causal role, it is possible that treatment may be improved by developing preventative treatment modules to target reward dysregulation.

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