Published in final edited form as:

Acta Psychiatr Scand. 2015 October ; 132(4): 270–280. doi:10.1111/acps.12415.

Borderline Personality Disorder in Transition Age Youth with Bipolar Disorder

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Abstract

Objectives—To determine the longitudinal impact of Borderline Personality Disorder (BPD) on the course and outcome of Bipolar Disorder (BP) in a pediatric BP sample.

Method—Participants (N=271) and parents from the Course and Outcome of Bipolar Youth (COBY) study were administered structured clinical interviews and self-reports on average every 8.7 months over a mean of 93 months starting at age 13.0 +/- 3.1 years. The Structured Interview for DSM-IV Personality Disorders (SIDP-IV) was administered at the first follow-up after age 18 to assess for symptoms of BPD. BPD operationalized at the disorder, factor, and symptom level, was examined as a predictor of poor clinical course of BP using all years of follow-up data.

Results—The number of BPD symptoms was significantly associated with poor clinical course of BP, above and beyond BP characteristics. Affective dysregulation was most strongly associated with poor course at the factor level; the individual symptoms most strongly associated with poor course were dissociation/stress-related paranoid ideation, impulsivity, and affective instability.

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Declaration of Interests: Doctors Yen, Frazier, Weinstock, Topor, Ryan, Heather Hower, and Mary Kay Gill report no declarations of interest.

Conclusions—BPD severity adds significantly to the burden of BP illness and is significantly associated with a more chronic and severe course and outcome beyond what can be attributable to BP characteristics.

Keywords

bipolar disorder; borderline personality disorder; comorbidity; longitudinal

Introduction

Bipolar disorder (BP) and borderline personality disorder (BPD) are moderately comorbid conditions characterized by affective instability, impulsivity, and increased risk for deleterious outcomes including suicidal behaviors. It is estimated that approximately 11% (1) of adults with BP meet criteria for BPD, though depending on the methodology of the study, rates vary widely (2). Nonetheless, it is significantly higher than the 4.6% observed in the general population (3). Conversely, in patients with BPD, rates of BP-I range between 5.6%-16.1%, and BP-II between 8%-19% (2). There is general consensus that BPD is associated with worse clinical course of BP as well as worse treatment outcomes. Studies of adults with BP show those with comorbid BPD fare worse with regard to poorer medication adherence (4), more days hospitalized (5), lower rates of recovery (6), more severe mood symptoms and lower levels of functioning (7), increased incidence of substance use disorders (SUD) (8), absence of social supports (9), and increased likelihood of suicidal ideation (10) and suicide attempts (11). However, these studies that are mostly cross-sectional, cannot speak to the longitudinal impact of BPD on BP course.

The phenotypic overlap between BPD and BP, specifically mood lability and impulsivity, and moderate rates of comorbidity have generated controversial positions. While some advocate that BPD should be part of the BP spectrum (12-16), others strongly disagree, citing differences in phenomenology and in medication response (2, 17) or suggest BPD is under-diagnosed in this population (18). Recent reviews synthesizing empirical studies using classic diagnostic validators defined by Robins and Guze (19) suggest that BPD and BP are different, can be distinguished, and can be truly comorbid (20, 21). The specificity of BP and BPD domains has been addressed in recent studies which indicate that, even within areas of shared symptomology, there are significant differences in the phenomenology of BPD as compared to BP (18, 22). For example, while both BPD and BP patients experience affective lability, the severity and direction of affective shifts differ between groups (23, 24). Findings reported by Gunderson et al (25) from the Collaborative Longitudinal Personality Disorders Study (CLPS) have shown that clinical course, one of the hallmarks of validity for psychiatric disorders, clearly varies for BP and BPD. A review by Bayes et al. (26) found that key differentiating parameters between the disorders included family history, onset pattern, clinical course, phenomenological profile of depressive and elevated mood states, and symptoms of emotional dysregulation.

Furthermore, whereby there is consensus that medication is the first line of treatment (with psychotherapy suggested as an adjunct treatment) in BP (27), there is a similarly strong consensus that psychotherapy is central to the treatment of BPD (28) with medications

showing modest, if any, incremental benefits (29). Given the different treatment guidelines for BP and BPD (27, 30), recognition of comorbidity where it exists and understanding the incremental and long term impact of comorbid BPD on BP is essential.

While many cross-sectional studies report incremental burden associated with BPD, it remains unclear whether this is attributable to an overall (non-specific) increase in psychopathology, whether this is due to shared characteristics with BP, or whether a specific aspect(s) within the heterogeneous BPD syndrome is especially problematic. Studies of BPD have empirically derived three homogenous factors (affective dysregulation, behavioral dysregulation, and disturbed relatedness) to better describe the diverse constellation of BPD symptoms (31-36). Affective dysregulation in particular has been postulated to be central to BPD development (37). Examining the impact of BPD in BP by these BPD factors could improve conceptual clarity and enhance clinical relevance by targeting the most deleterious factor of this pernicious disorder.

Aims of the study

The aim of this study is to examine whether BPD attributes, operationalized at the disorder, factor, and symptom level, predict a more pernicious course of BP into adulthood. We hypothesize that number of BPD symptoms, and the affective dysregulation factor in particular, significantly adds to the burden of BP beyond BP characteristics such as age of mood disorder onset, BP subtype, and baseline depression and mania severity ratings.

Material and methods

Participants

Children and adolescents aged 7 to 17 years 11 months (mean±SD age, 13.0±3.1 years) whose primary diagnoses were *DSM-IV* BP-I (n=244) or BP-II (n=28) or an operationalized definition of BPNOS (n=141) were enrolled in the Course and Outcome of Bipolar Youth (COBY) study. Because the *DSM-IV* definition of BP-NOS is vague, BP-NOS was defined as the presence of clinically relevant BP symptoms that did not fulfill the *DSM-IV* criteria for BP-I or BP-II. In addition, participants were required to have a minimum of elated mood plus 2 associated *DSM-IV* symptoms or irritable mood plus 3 *DSM-IV* associated symptoms, along with a change in the level of functioning, duration of a minimum of 4 hours within a 24-hour period, and at least 4 cumulative lifetime days meeting the criteria (38). Diagnostic conversion to BP-I/II occurred in 63 participants (45%), 32 (23%) to BP-I (9 of whom had initially converted to BP-II) and 31 to only BP-II (22%) (39). Participants with current or lifetime diagnoses of schizophrenia, mental retardation, autism, and mood disorders secondary to substance abuse, medical conditions, or use of medications were excluded. Participants were recruited from consecutive admissions to outpatient clinics (65%), inpatient units (16%), advertisement (11%), and referrals from other physicians (8%) and were enrolled independent of current BP state or treatment status. Participants were enrolled at 3 academic medical centers: Brown University (n=144), University of California at Los Angeles (n=90), and University of Pittsburgh Medical Center (n=204). Informed consent was obtained before initiation of the assessment from the participant's parent or guardian and from participants 14 years or older. The study procedures were explained in age-

appropriate language to younger participants, and verbal assent was obtained before the assessment. The institutional review boards at the 3 centers reviewed and approved the study protocol before enrollment of any participant.

As the Structured Interview for DSM-IV Personality Disorders (SIDP-IV) was administered at the first follow-up after age 18, to date 271 participants (66% of the COBY sample with any follow-up data) had analyzable Structured Interview for DSM Personality Disorders (SIDP-IV), Borderline Personality Disorder Module (40) data. This subset of COBY participants reflects those who were older at intake compared to those not included in these analyses. Examination of additional potential baseline differences, controlling for shared variance with age, reveals no other demographic, diagnostic, or clinical differences between these groups; hence, data suggests that these 271 are representative of the entire COBY sample.

Procedures

At baseline, youth and parents were directly interviewed for psychiatric disorders using the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (K-SADS-PL) (41). Lifetime histories of suicidal ideation, suicide attempts, self-injurious behaviors, number and duration of psychiatric hospitalizations (weeks), duration of illness (years), physical and sexual abuse, and whether the participant lived with a biological parent were also recorded on the KSADS-PL. Mood symptom severity was recorded on the Kiddie Mania Rating Scale (KSADS-MRS) (42) and Depression Rating Scale (K-DEP). Week-by-week longitudinal change in psychiatric symptoms was assessed using the Longitudinal Interval Follow-up Evaluation (LIFE) and quantified using the instrument's Psychiatric Status Rating (PSR) scale (43). The PSR uses numeric values linked to DSM-IV criteria and participant's functioning. For mood disorders, PSR scores 2 indicate euthymia, 3-4 subsyndromal symptoms, and 5 syndromal symptomatology. Analyses used consensus scores obtained after interviewing parents and their children. At the first follow-up after age 18, the SIDP-IV (40) was administered to the young adults.

Assessments were conducted by research staff trained to reliably administer the interviews. The intraclass correlation coefficients for the K-SADS-MRS and -DEP were 0.75. With regard to the SIDP-IV, cases rated as meeting full threshold for any BPD criterion were cased and reviewed with either a psychiatrist or clinical psychologist.

Socioeconomic status (SES) was ascertained using the Hollingshead scale (44). The Children's Global Assessment Scale (CGAS) was used to establish global level of functioning (45). Symptoms of comorbid internalizing and externalizing disorders plus ratings of family functioning were recorded by participants and their parents on self-reports, including the Screen for Child Anxiety Related Emotional Disorders (SCARED) (46), Child Behavior Checklist (CBCL) (47), Youth Self Report (YSR) (48), Family Adaptability and Cohesion Evaluation Scales-II (FACES-II) (49), and Conflict Behavior Questionnaire (CBQ) (50).

Statistical Analysis

Analyses used Statistical Package for Social Sciences (SPSS) version 22 (IBM Corp, Armonk, NY, USA). All p values are based on two-tailed tests with an alpha level set at 0.05.

Variables assessed at baseline were examined using chi-square analyses for categorical variables and t-test analyses for continuous variables to determine whether baseline demographic, diagnostic, clinical, and family characteristics differed in those diagnosed as BPD+ vs. BPD- at the first SIDP-IV assessment. Fisher's exact test was used when cell sizes were smaller than ten; Mann Whitney U-test was applied to continuous variables with non-normal distributions as determined by the Shapiro Wilk test for normality. As per the DSM-IV criteria (51) participants who endorsed ≥ 5 criteria at threshold level on the SIDP-IV BPD module were considered BPD+ (n=33, 12.2%); those who endorsed < 5 were considered BPD- (n=238, 87.8%).

To determine the longitudinal impact of BPD on course of BP illness, we examined a number of BPD attributes as the predictor variable. At the disorder level, in addition to dichotomous BPD+ vs. BPD-, BPD was operationalized continuously by threshold criterion count (range 0-9). At the factor level, affective dysregulation was represented by the inappropriate anger, affective instability, and fear of abandonment criteria, behavioral dysregulation was represented by the impulsivity and self-injurious behaviors criteria, and disturbed relatedness was represented by the identity disturbance, dissociative stress/paranoid ideation, emptiness, and unstable relationships criteria. Factor scores were mean number of criteria endorsed. At the symptom level, each criterion of BPD was examined. All BPD variables were standardized to facilitate comparison across variables and correct for uneven distributions.

The outcome of interest (poor BP course over follow-up) was derived from a recent latent class growth analyses (LCGA) of the COBY sample of participants who had a minimum of four years of follow-up (average total follow-up = 7.75 years) (52). Four classes were identified based on percentage of time euthymic (PSR ≥ 2). Number of classes was determined by selecting the model with a minimum value of Bayesian Information Criterion (BIC), a minimum of 20 participants per class, and clinical interpretability of the classes. The present model, which has been validated against other clinical indicators in the COBY study, yielded four class solutions: Class 1 ("predominantly well" class [n=67, 25.7%]) in which participants were mostly euthymic throughout follow-up; Class 2 ("moderately well" class [n=97, 37.2%]) in which participants had a stable course of moderate euthymia throughout follow-up; Class 3 ("ill with improving course" class [n=43, 16.5%]) in which participants showed an initial poorer course and then improvement over time; and Class 4 ("predominantly ill" class [n=54, 20.7%]) in which participants were mostly symptomatic throughout follow-up and only euthymic for 11.5% of the 7.75 years. This class represents the worst clinical trajectory of the four class solutions, and is the outcome (class) of interest to the present investigation. These analyses utilized PSR data from intake through follow-up and thus encompass time before and after the SIDP-IV administration.

Logistic regression analyses were conducted to determine whether BPD attributes predicted membership in the predominantly ill class (vs. all other classes combined). A prior paper from COBY (52) reported this class was significantly associated with younger age of mood onset, depression severity at baseline, history of suicide attempts, childhood sexual abuse, and family history of BP and SUD. These variables were thus individually analyzed as covariates along with each BPD attribute, to ascertain the incremental predictive validity of BPD. Similarly, baseline characteristics of BP such as age of mood disorder onset, age of BP onset, BP subtype, depression severity ratings, and mania severity ratings, were examined individually as covariates with each BPD attribute to examine the incremental predictive validity of BPD beyond the BP characteristics. Any variable identified as a significant predictor of comorbid BPD was also examined as a covariate in the analyses predicting the predominantly ill group. All covariates were initially examined individually due to concerns of multicollinearity. Covariates that remained significant with the BPD attribute in the model were subjected to simultaneous multivariate logistic regression analyses.

Results

Of those 271 participants who were assessed for BPD during their first follow-up interview after age 18 (mean age 20.65), 33 (12.2%) met criteria for BPD. As seen in Table 1, there were no significant differences between the BPD+ and BPD- groups on demographic or diagnostic variables including sex, race, ethnicity, SES, anxiety, attention deficit hyperactivity, oppositional defiant, conduct, and SUD. There were also no differences regarding BP subtype (BP-I, BP-II, or BP-NOS), age of BP onset, and lifetime family history of BP or SUD.

Results of clinical characteristic analyses revealed several significant differences between BPD groups (Table 1). Rates of lifetime suicide attempts as well as self-injurious behaviors were significantly higher in the BPD+ group compared to the BPD- group, with a majority of BPD+ participants endorsing these behaviors. In addition, the BPD+ group had significantly higher baseline depression severity (DEP-P), self-reported anxiety symptoms (SCARED), and self-reported internalizing symptoms (YSR). There were no other significant clinical differences between BPD groups. Family functioning variables did not significantly differ across BPD groups.

The dichotomous representation of BPD (BPD+ vs. BPD-) was not statistically significantly associated with membership in the predominantly ill class, possibly due to insufficient power. Though not statistically significant, 32.4% of those with BPD+ were in the predominantly ill class compared to 19.4% of the BPD- subgroup. Furthermore, 19.3% of those in the predominantly ill class met criteria for BPD compared to only 2.9% of those who were in the predominantly well class.

Number of BPD symptoms was examined as a predictor of poor BP course (predominantly ill vs. all other classes) using logistic regression analyses (Table 2). Covariates based on a prior report (52) that identified predictors of predominantly ill course (i.e., age of mood onset, family history of BP, family history of SUD, history of childhood sexual abuse,

history of suicide attempts, and depression severity rating at baseline) were examined in separate logistic regression analyses models with number of BPD symptoms. Number of BPD symptoms was significantly associated with predominantly ill class membership in each of the models containing an a priori identified covariate. Furthermore, only three a priori identified covariates remained significant after accounting for BPD symptoms (age of mood onset, family history of BP, and family history of SUD), and were thus examined in a multivariate model. Of the baseline variables that were significantly different between BPD + and BPD-, only child-reported anxiety severity (SCARED) significantly predicted predominant illness course and was thus also included in the multivariate model. In a multivariate logistic regression analysis with all four significant covariates, number of BPD symptoms remained significantly associated with predominantly ill class (Table 2).

Each BPD factor was also significantly associated with poor BP course (predominantly ill class vs. all others) in univariate analyses (Table 3). Affective dysregulation remained significant in both individual covariate analyses, as well as the multivariate model with covariates age of mood onset, family history of BP, family history of SUD, and anxiety severity. Behavioral dysregulation and disturbed relatedness were not significant in multivariate models, though behavioral dysregulation trended towards significance.

With regard to individual BPD criteria, only four criteria, impulsivity, affective instability, anger, and stress/paranoid ideation, were significantly associated with poor BP course/predominantly ill class in univariate analyses (Table 3). Stress/paranoid ideation had the strongest effect in univariate analyses, which was reduced to a trend approaching significance in the multivariate model with other significant covariate predictors. Similarly, affective instability was significant in univariate analysis and trended towards significance in the multivariate model. Impulsivity was significantly associated with poor BP course/predominantly ill class in both univariate and multivariate models.

Discussion

This is the first study to our knowledge that examined the longitudinal impact of BPD symptoms in youth diagnosed with BP. As expected, elevated rates of BPD (compared to the general population) were observed in our BP sample. The 12.2% prevalence rate observed in our BP sample is comparable to the 11% reported in adult BP studies (1); and higher than the 4.6% observed in the general population (3). As our data are based on assessments made in the earliest years of adulthood, it is likely there are additional emergent cases not yet identified.

Based on available data in COBY, it appears that there are few differences between BP young adults with and without BPD on a number of baseline demographic, diagnostic, and family characteristics. While the lack of significant differences with regard to family environment was particularly surprising given prevailing etiological models of BPD, this may be more a reflection of the familial impairment associated with BP. Observed differences between BPD+ and BPD- groups were mostly with regard to clinical characteristics such as history of suicide attempts and self-injurious behaviors, severity of depression and anxiety, and dimensional measures of internalizing problems. Arguably, the

observed differences suggest those with comorbid BPD occupy the more symptomatic and clinically severe spectrum of BP illness. However, the lack of significant associations between BPD and BP characteristics (i.e., BP subtype, age of onset, mania ratings, family history of BP) suggests a more complicated and independent relationship between these disorders. Contrary to several theories, BPD comorbidity was no more likely among those occupying the severe end of BP manifested as BP-I (18). Nor was it more likely among those with BP-II or BP-NOS (53), as suggested by some who attribute the stronger link of these disorders to diagnostic error (18).

Our results indicate that number of BPD symptoms was significantly associated with a predominantly worse BP illness course, as nearly a third of those diagnosed with comorbid BPD were classified as predominantly ill and symptomatic throughout the majority of the 7.75 years of follow-up. Furthermore, we found that BPD adds substantially to the burden of BP beyond BP characteristics such as BP subtype, age of onset, and other previously identified individual risk factors including history of suicide attempts and self-injurious behaviors, history of childhood sexual abuse, depression and anxiety severity at baseline, and family characteristics such as family history of BP and SUD. Our results are consistent with those from the National Epidemiological Survey on Alcoholism and Related Conditions which found that BPD robustly predicted persistence of mood symptoms, even after controlling for demographic variables, and other psychiatric comorbidities including SUD, family history, and depression characteristics (54). Furthermore, longitudinal studies of BP and BPD in adults suggest each disorder has a modest effect on the other, but with BPD having a stronger effect on depression than mania, as well as a stronger effect on mood episodes than vice versa (55-57). As COBY had no comparison group of BPD participants without BP, it is difficult to quantify the additive effect of BPD beyond additional psychopathology. In a study of 3,465 outpatients, Zimmerman and colleagues (58) compared three conditions of comorbid BPD and BP, BP without BPD, and BPD without BP, and reported that the co-occurrence of these disorders conferred additive risk for suicide attempts, with BPD conferring a greater risk. Collectively, these studies highlight the importance of recognizing comorbid BPD and the concomitant additive risk.

The examination of the BPD factors suggests that, while each factor was associated with persistent illness, affective dysregulation was most robust. This factor is comprised of inappropriate anger, affective instability, and fears of abandonment. Affective instability appears to be a transdiagnostic feature present both in BP and BPD (23, 59), has been demonstrated to be linked to neural mechanisms (i.e., hyper-reactive amygdala activity) (60), and may serve as an innovative treatment target based on dimensional psychopathology rather than traditional categorical DSM constructs. Traditionally, the affective instability in BPD has been considered to be reactive, typically triggered by a perceived attack or a stressful situation, whereas the affective instability in BP has been conceived as more endogenous (23, 61). However, it may be that differences in affective instability may be accounted for by differences in the sensitivity of the limbic systems in addition to environmental triggers (60). Future research to examine the neural substrates underpinning affective stability and how it is similar or different in BP and BPD can potentially elucidate these complexities.

Our finding that, of the three BPD factors, affective dysregulation is most strongly associated with poor outcome in these participants with early stage BPD warrants consideration as to whether affective dysregulation is a transdiagnostic marker mechanism underlying multiple disorders as they are currently classified in DSM, varying degrees of which may influence clinical presentation. Notwithstanding the nosological controversies surrounding BPD and BD, even within BPD research there is widespread disagreement on what constitutes core BPD. Many would argue that affective instability represents “classic” BPD (62-65), while others have argued that it is interpersonal sensitivity that is the central feature of BPD (66-69). Furthermore, many associate self-injurious with prototypical BPD; however, recent empirical studies suggest that the prevalence of these behaviors do not differ between those with and without BPD, spurring support for the provisional diagnosis of Nonsuicidal Self-injury (NSSI) as a category distinct from BPD (70-73). Thus conceptualizing affective stability and dysregulation as a transdiagnostic marker that – in confluence with environmental triggers – may result in varying clinical presentations, may be a pathway to synthesizing the heterogeneous presentation of BPD.

Even though research shows the affective instability of patients with BP vs. BPD can be differentiated with respect to frequency and intensity (74), their respective presentations are difficult to distinguish in spite of these presumed differences. There is the potential for affective instability to be conflated in our data, though we believe that this possibility is lessened due to our protocol of discussing all threshold BPD ratings. It is the remaining affective features (i.e. inappropriate anger, fear of abandonment) that more reliably distinguish BPD from BP. Nevertheless, the most salient distinction between BPD and BP is that BPD criteria span multiple domains (affect, behavior, interpersonal); our data suggest that dysfunction across these multiple domains contribute meaningfully to BP prognosis.

On an individual criterion level, the two criteria that potentially overlap in both BP and BPD (affective instability and impulsivity) were both significant in univariate analyses; only impulsivity remained significant in the multivariate analyses with covariates. Somewhat more surprising was that stress/paranoid ideation was significantly associated with predominant illness. Dissociative stress is more commonly observed in those who have experienced traumatic events (75) and thus may reflect the possible influence of response to trauma. Although we examined childhood sexual abuse as a covariate, differences in trauma characteristics (e.g., frequency, severity, duration, proximity of abuser) as well as individual differences (e.g., resiliency) may yield different responses to trauma. Nonetheless, no single BPD criteria was more robustly associated with predominant illness than the sum of BPD symptoms, suggesting that there is value to assessing the entire BPD construct, as opposed to its core factor components (e.g. affective dysregulation) or individual symptoms.

Our study is limited in that it is based on retrospective reports, which is subject to recall bias. In addition, our assessment of BPD was not always corroborated by parental report. As study participants were at least age 18 at the time of BPD assessment, they were given the choice of having either their parent or a significant other to provide collateral information; in some cases study participants declined to have an informant participate in the study. While it would have been preferable to assess for BPD at an earlier age, due to the wide age range of study participants it was determined to keep the age of the first assessment uniform after age

18 to mitigate developmental confounds. Nevertheless, in recent years there has been a growing literature to substantiate the validity of diagnosing personality disorders in youth, indicating that BPD features in adolescents are comparable in frequency and symptoms to those of adults (76-80), internal consistency of BPD in adolescent samples is comparable with adult samples, and assessments of BPD in adolescents yield good convergent and concurrent validity (53, 81). Recent findings from other large scale longitudinal studies suggest the longitudinal course of personality disorders is more likely to be fluctuating rather than one of persistent illness (25). Given this, the observed cases of BPD in COBY may or may not be stable even if BPD is associated with a predominant illness trajectory as operationalized by mood symptoms; additional years of follow-up will elucidate the long-term trajectory of BPD illness in BP, and the effect of BPD on BP trajectory. Furthermore, all study participants met criteria for BP, and were recruited from clinical settings, thus limiting generalizability and the inferences that can be made regarding the diagnostic interrelationship between BP and BPD. Finally, the diagnosis of BP applied to children and adolescents, as well as the diagnostic independence between BP and BPD is historically controversial due to overlapping phenotype; thus alternative interpretations of our results are possible.

In summary, this study utilizes a large sample of youth with BP, carefully evaluated with detailed structured diagnostic interviews, along with prospective assessments of mood and functioning ratings. We found that 12.2% of the sample met criteria for BPD, but there were few differences between those with and without comorbid BPD. BP and BPD are independently each associated with higher rates of suicidal behavior and increased risk of death by suicide. Our results demonstrate that comorbid BPD in a BP sample is significantly associated with poor illness course over years of follow-up. The additional risk and burden that exists in those presenting with both disorders suggests the need for combined or adjunctive treatments (e.g. psychotherapy and pharmacotherapy), particularly those that target the reduction of high risk behaviors. One possibility is dialectical behavior therapy (DBT), which incorporates a multimodal approach and has been empirically examined and supported for patients with BPD (37) as well as adolescents with BP (82). Finally, our results show that while individual criterion and BPD factors are significantly associated with poor BP course, none are as robust as using the entire BPD construct.

Acknowledgments

We thank the families for their participation, the COBY research staff, and Shelli Avenevoli Ph.D. from the National Institutes of Mental Health for their support. This paper was supported by NIMH grants MH59691 (to Doctors Keller/Yen), MH059929 (to Doctor Birmaher), and MH59977 (to Doctor Strober). Doctor Hunt is a senior editor of *Brown Child and Adolescent psychopharmacology* update, and receives honoraria from Wiley Publishers. Doctor T. Goldstein receives royalties from Guilford Press. Doctor B. Goldstein is a consultant for BMS, has received research support from Pfizer, and has received speaker's honoraria from Purdue Pharma. Doctor Strober receives support from the Resnick Endowed Chair in Eating Disorders. Doctor Birmaher has received research support from the National Institute of Mental Health. He receives royalties from Random House, Inc., and Lippincott Williams & Wilkins. Doctor Keller receives research support from Pfizer, and has received honoraria from Medtronic.

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Significant Outcomes

- In the present study 12.2% of the BP sample met criteria for BPD, a rate comparable to other studies; there were few baseline differences between those that did and did not meet criteria for BPD after age 18.
- BPD severity adds significantly to the burden of BP illness and is significantly associated with a more chronic and severe course and outcome of BP, beyond BP characteristics. Among the BPD factors, affective dysregulation (comprised of affective instability, fear of abandonment, and anger) was most robustly associated with BP chronicity and severity.
- The additional symptom burden that exists in those presenting with both BPD and BP suggests the need to recognize, treat, and manage both disorders.

Limitations

- Our study is limited in that it is based on retrospective interview and self-report data, which is subject to recall bias.
- While it would have been preferable to assess for BPD at an earlier age, due to the wide age range of study participants it was determined to keep the age of the first assessment uniform after age 18 to mitigate developmental confounds.
- The DSM-IV diagnostic constructs of bipolar disorder and borderline personality disorder are overlapping and controversial, particularly as applied to a youth population, and are thus subject to alternative interpretations of the data.

Baseline demographic, clinical and family environment characteristics by borderline personality disorder group status

Table 1

	Borderline personality disorder+ N= 33 (12.2%)	Borderline personality disorder-N = 238 (87.8%)	Test Statistic	P
Demographic variables				
Sex (Female, n/%) ^a	20 (60.6%)	113 (47.5%)	1.58	0.21
Race (White, n/%) ^b	27 (81.8%)	186 (78.2%)	--	1.00
Non-Hispanic ethnicity (n/%) ^b	31 (93.9%)	214 (89.9%)	--	1.00
Socio-economic status ^c	3.15 (1.15)	3.48 (1.18)	-1.59	0.11
Psychiatric disorders at intake				
Anxiety disorder ^a	13 (39.4%)	85 (35.7%)	0.17	0.68
ADHD ^a	19 (57.6%)	131 (55.0%)	0.75	0.78
Oppositional defiant disorder ^a	12 (36.4%)	91 (38.2%)	0.04	0.84
Conduct disorder ^b	4 (12.1%)	31 (93.9%)	--	1.00
Substance use disorder ^b	6 (18.2%)	21 (8.8%)	--	0.12
Bipolar diagnoses:				
Bipolar disorder-I ^b	24 (75.0%)	122 (59.8%)	--	0.119
Bipolar disorder-II ^b	3 (9.4%)	17 (8.3%)	--	0.740
Bipolar disorder-not otherwise specified ^b	5 (15.6%)	65 (31.9%)	--	0.064
Age of bipolar disorder onset ^c	11.05 (3.32)	10.17 (3.90)	1.25	0.22
Family history bipolar disorder ^a	20 (60.6%)	135 (56.7%)	0.18	0.67
Family history substance use disorder ^b	27 (81.8%)	163 (68.5%)	--	0.16
Clinical characteristics				
Suicidal ideation history ^b	28 (84.8%)	178 (74.8%)	--	0.28
Suicide attempt history ^a	19 (57.6%)	65 (27.3%)	12.41	0.001
Self-injurious behavior history ^a	18 (54.5%)	82 (34.5%)	5.03	0.03
Psychiatric admissions (total) ^c	2.59 (2.63)	2.24 (2.31)	- 0.55	0.58

	Borderline personality disorder+ N=33 (12.2%)	Borderline personality disorder-N = 238 (87.8%)	Test Statistic	P
Psychiatric admissions (wks) ^c	4.32 (4.25)	5.21 (9.23)	-1.17	0.24
Duration of illness (years) ^c	5.06 (3.71)	4.43 (2.96)	-0.63	0.53
Depression rating (DEP-P) ^d	22.18 (12.40)	14.17 (9.96)	17.58	<0.001
Mania ratings (MRS) ^d	21.45 (12.53)	22.70 (12.21)	0.30	0.58
SCARED Total – Child ^c	30.40 (19.01)	23.09 (16.97)	-1.99	0.05
SCARED Total – Parent ^d	27.48 (17.27)	23.44 (15.57)	1.67	0.20
CBCL internalizing problems ^c	62.77 (14.04)	56.06 (11.75)	-1.33	0.18
CBCL externalizing problems ^c	60.27 (9.60)	57.93 (11.05)	-1.26	0.21
CBCL total problems ^c	62.77 (12.60)	57.68 (11.09)	-1.35	0.18
YSR internalizing problems ^d	62.77 (14.04)	56.06 (11.75)	5.84	0.02
YSR externalizing problems ^d	60.27 (9.60)	57.93 (11.05)	0.88	0.35
YSR total problems ^d	62.77 (12.60)	57.68 (11.09)	3.85	0.05
C-GAS ^d	53.19 (9.76)	55.23 (12.68)	0.75	0.39
Family environment				
Physical abuse ^b	8 (24.2%)	30 (12.6%)	--	0.10
Sexual abuse ^b	6 (18.2%)	26 (10.9%)	--	0.25
Living with both bio parents ^a	13 (39.4%)	101 (42.4%)	0.11	0.74
FACES total cohesion-child ^c	53.97 (11.17)	54.42 (13.53)	-0.45	0.66
FACES total adaptability-child ^d	43.76 (9.05)	43.37 (9.59)	0.04	0.84
FACES total cohesion-parent ^c	55.86 (10.70)	58.26 (11.41)	-1.21	0.23
FACES total adaptability-parent ^c	46.71 (8.32)	45.56 (7.52)	-0.87	0.38
CBQ total parent about child ^c	11.20 (5.01)	11.08 (5.91)	-0.01	0.99
CBQ total child about mother ^c	3.90 (3.93)	5.67 (5.60)	-1.18	0.24
CBQ total child about father ^c	6.64 (5.66)	6.13 (6.11)	-0.64	0.53

ADHD: Attention Deficit Hyperactivity Disorder; SCARED: Screen for Child Anxiety Related Emotional Disorders, CBCL: Child Behavior Checklist, YSR: Youth Self Report, C-GAS: Children's Global Assessment Scale, FACES: Family Adaptability and Cohesion Evaluation Scale-II, CBQ: Conflict Behavior Questionnaire;

d^1 t-test.

c Mann Whitney U test;

b Fisher's exact test;

d Chi-Square test;

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Table 2
Multivariate logistic regression analyses: Number of BPD symptoms predicting predominantly ill class, controlling for baseline covariates

	B (SE)	Wald X ²	OR	95% CI	p
Anxiety severity	0.03 (.01)	6.55	1.03	1.01–1.05	0.01
Age of mood onset	-0.14 (.05)	9.27	0.87	0.79–0.95	0.002
Family history of BP	0.60 (.39)	2.42	1.82	0.86–3.89	0.12
Family history of SUD	-1.11 (.49)	5.15	3.04	1.16–7.94	0.02
Number BPD symptoms	0.36 (.16)	5.25	1.43	1.05–1.95	0.02

BP = Bipolar Disorder; SUD = Substance Use Disorder; BPD = Borderline Personality Disorder

Table 3
Logistic regression models of borderline personality disorder attributes predicting predominantly ill class

	Univariate Model			Multivariate Model with Covariates ^d		
	Wald X ²	OR	95% CI	Wald X ²	OR	95% CI
Affective dysregulation	7.83**	1.49	1.13-1.98	4.39*	1.40	1.02-1.93
Behavioral dysregulation	6.28*	1.42	1.07-1.86	3.74 ^f	1.36	1.00-1.87
Disturbed relatedness	5.74*	1.38	1.06-1.79	3.02	1.29	0.97-1.73
Inappropriate anger	5.04*	1.39	1.04-1.85	3.25	1.34	0.97-1.86
Affective instability	5.81*	1.41	1.07-1.86	3.36 ^f	1.34	0.98-1.84
Abandonment	2.10	1.20	0.94-1.53	0.45	1.09	0.84-1.43
Self-injurious behaviors	3.22	1.28	0.98-1.66	0.20	1.07	0.79-1.46
Impulsivity	4.48*	1.35	1.02-1.77	6.01*	1.50	1.09-2.08
Unstable relationships	2.23	1.23	0.94-1.60	1.34	1.19	0.89-1.59
Dissociation/Paranoid	7.23**	1.41	1.10-1.80	3.42 ^f	1.30	0.98-1.73
Emptiness	1.36	1.17	0.90-1.54	0.27	1.08	0.81-1.46
Identity disturbance	2.01	1.20	0.93-1.56	2.02	1.24	0.92-1.66

^a Covariates include anxiety severity, age of onset of mood disorder, family history of bipolar disorder, family history of substance use disorder

^f p .06;

* p<.05;

** p<.01