Interactions of Borderline Personality Disorder and Mood Disorders Over 10 Years

John G. Gunderson, MD; Robert L. Stout, PhD; M. Tracie Shea, PhD; Carlos M. Grilo, PhD; John C. Markowitz, MD; Leslie C. Morey, PhD; Charles Sanislow, PhD; Shirley Yen, PhD; Mary C. Zanarini, EdD; Alex S. Keuroghlian, MD; Thomas H. McGlashan, MD; and Andrew E. Skodol, MD

ABSTRACT

Objective: To examine the relationship of borderline personality disorder (BPD) to mood disorders by using data from the Collaborative Longitudinal Personality Disorders Study on the reciprocal interactions of BPD with both depressive and bipolar disorders over the course of 10 years.

Method: The study included 223 BPD patients with *DSM-IV*–defined co-occurring major depressive disorder (MDD) (n = 161), bipolar I disorder (n = 34), and bipolar II disorder (n = 28) who were reliably and prospectively assessed over a period of 10 years between 1997 and 2009. Proportional hazards regression analyses were used to assess the effects of improvement or worsening of BPD and mood disorders on each disorder's time to remission and time to relapse.

Results: Borderline personality disorder and MDD had strong and statistically significant reciprocal effects, delaying each disorder's time to remission (BPD's effect on MDD, $P = .0004$; MDD's effect on BPD, $P = .0002$) and accelerating time to relapse (BPD's effect on MDD, $P = .0410$; MDD's effect on BPD, $P = .0011$), whereas BPD and the bipolar disorders were largely independent disorders except that bipolar II lengthened BPD's time to remission ($P = .0085$).

Conclusions: Borderline personality disorder and MDD interactions suggest overlap in their psychopathologies and argue for prioritizing the treatment of BPD. Borderline personality disorder and bipolar disorders appear to be independent disorders, underscoring the need to provide appropriate treatment for each.

J Clin Psychiatry 2014;75(8):829–834

Submitted: *December 30, 2013; accepted April 23, 2014.*
Online ahead of print: *June 10, 2014 (doi:10.4088/JCP.13m08972).*
Corresponding author: *John G. Gunderson, MD, McLean Hospital, 115 Mill St, Belmont, MA 02478 (jgunderson@mclean.harvard.edu).*

The long-standing controversy about the relationship of borderline personality disorder (BPD) to mood disorders[1,2] has already been informed by a large body of research,[3–5] but questions persist as to whether BPD should be considered an atypical form—or spectrum variant—of mood disorders.[6,7] The search for common underlying causes for these disorders has been encouraged by the Siever and Davis[8] concept of a psychobiological disposition called *affective instability*, cutting across traditional Axis I and personality disorders. The high prevalence, levels of health care utilization, and severe and persistent disability of these disorders all give major clinical and public health significance to the questions about their relationship.

The initial controversy arose around whether BPD was a variant of major depressive disorder (MDD). This controversy was fueled by the very high rates of co-occurrence between these disorders (about 50%).[9,10] Further suggesting an overlap were initial reports of family coaggregation[1,11] and the response of BPD to monoamine oxidase inhibitors.[12,13] While subsequent research has in many ways failed to confirm a strong overlap,[4,14,15] antidepressant medications have persistently been prescribed at very high rates to patients with BPD[16,17] despite their limited value.[18–21] The question about BPD's relation to bipolar disorder has subsequently superseded the question about BPD's relation to MDD. This question rests less on the rate of BPD and bipolar disorder co-occurrence (about 15%)[3] than it does on the phenotypic overlaps of emotionality and impulsivity. Moreover, several early studies reported high levels of familial coaggregation[1,2] and even that BPD evolved into bipolar disorder.[2] Despite the lack of replication,[3,4] clinicians continue to frequently misdiagnose patients with BPD with bipolar disorder.[3,22]

Since the 1980s, when studies on the interface of BPD and mood disorders began, research has shown that the diagnoses of personality disorders in general and BPD in particular are less stable than was originally believed.[4] Indeed, this research provides a rationale for why personality disorders have now been removed from a separate Axis II in the *DSM-5*.[4] With this new knowledge, concepts of remission and relapse have been applied to personality disorders, and, as a consequence, the opportunity has arrived to explore how such shifts in BPD's course interact with similar events in the course of mood disorders. This article uses the final 10-year follow-up data from the Collaborative Longitudinal Personality Disorders Study (CLPS)[23,24] to examine the effects that BPD and mood disorders have on each other's course over time.

Four prior reports from the naturalistic follow-along CLPS data have addressed the topic of longitudinal interactions between BPD and mood disorders. A report using 2-year follow-up data showed that improvement in either BPD or MDD significantly predicted remission in the other disorder, although the hazard ratios suggested a somewhat larger effect for BPD on MDD remission than vice versa.[25] Three-year data indicated more unidirectional effects: changes in BPD significantly predicted improvement in MDD but not vice versa.[26] Analyses using 6-year follow-up data of

Clinical Points

- Borderline personality disorder (BPD) and major depressive disorder (MDD) appear to have overlapping psychopathologies that negatively affect each other's prognosis.
- When BPD and MDD co-occur, psychosocial interventions for BPD are likely to have greater effectiveness than medications, especially antidepressants.
- Bipolar I disorder and BPD appear to be independent disorders for which mood stabilizers should be used in conjunction with BPD's psychosocial interventions.

co-occurring MDD and BPD examined the rates of relapse of MDD in BPD compared to MDD co-occurring with other personality disorders. Findings showed that MDD relapsed more frequently in BPD than when co-occurring with other personality disorders.[27] Together, these studies seemed to indicate that BPD steered the course of co-occurring MDD and prompted more relapses.

The only CLPS article examining co-occurring bipolar disorder used 4-year follow-up data.[28] That report showed that co-occurring BPD effected a modest increase in new onsets of bipolar I and II disorders and in length of manic episodes in patients compared to those with other types of personality disorder who also had co-occurring bipolar disorder. However, neither bipolar I nor II had much effect on BPD's course. These findings strongly disconfirm that BPD is a *forme fruste*, or prodromal variant, of bipolar disorder. All 4 reports have indicated that mood disorders have modest effects on BPD's course, but that BPD has strong negative effects on the course of MDD with relatively modest negative effects on the course of bipolar disorders.

This article extends the prior CLPS reports of BPD's interaction with mood disorders in 3 significant ways: (1) MDD and bipolar disorders are studied concurrently, (2) the final (10-year follow-up) data are utilized, and (3) both time to remission and time to relapse/onset are used to examine the effects of BPD and mood disorders on each other. The clinical implications from this report's findings will be discussed with respect to prognosis, prioritizing treatments, and for the persisting questions about whether BPD shares an underlying psychopathology with MDD or bipolar disorder.

METHOD

Detailed descriptions of the CLPS aims, background, methods, and sample characteristics have been reported.[9,23] Briefly, the CLPS is a multisite, prospective, naturalistic longitudinal study of a clinical population. Recruitment sought a diverse, clinically and demographically representative sample from inpatient and outpatient programs affiliated with 4 recruitment sites (Brown, Columbia, Harvard, and Yale universities). The institutional review boards at each site approved the project, and all patients gave written informed consent. The CLPS enrolled 668 participants aged 18 to 45 years with at least 1 of 4 specific personality disorders (schizotypal, borderline, avoidant, and obsessive-compulsive) or with current MDD without any personality disorder. The 4 personality disorder types were selected because of their prevalence and research base in clinical samples and to span the 3 *DSM-IV* clusters. Exclusion criteria included conditions that precluded a valid interview (eg, active psychosis, acute substance intoxication or withdrawal) or a history of schizophrenia or schizoaffective disorder. Methods specifically relevant to this report are detailed below.

Sample

Baseline demographics and comorbidities for the full CLPS sample have been reported previously.[9] The sample for this report is comprised of the 223 individuals who at baseline met criteria for the diagnosis of BPD, who also met criteria (at baseline and/or at some later point during the follow-up period) for MDD (n = 161), bipolar I disorder (n = 34), or bipolar II disorder (n = 28). Of the 223 persons, 73% were female, mean age (at intake) was 32.1 years (SD = 8.2), 13% were black, 18% had a Hispanic background, and 2% were Asian. Fifty-six percent were single, 24% were married or cohabiting, and 20% were separated, divorced, or widowed. The patients were prospectively assessed between 1997 and 2009.

Measures

Criteria for all disorders were based on the *DSM-IV*.[29] All subjects were evaluated at baseline with the Diagnostic Interview for *DSM-IV* Personality Disorders[30] and the Structured Clinical Interview for *DSM-IV* Axis I Disorders[31] by clinically experienced interviewers trained to pay particular attention to distinguishing Axis I mental states from Axis II personality traits. These interviews were repeated at 2 years and then at 4, 6, 8, and 10 years. The interrater and test-retest κ values for BPD were 0.68 and 0.69, respectively. For MDD, the interrater κ was 0.80, and the test-retest κ was 0.64. For bipolar disorder, interrater reliability had a κ across rater pairs of 0.74.[32]

Borderline personality disorder was also assessed yearly with the Diagnostic Interview for *DSM-IV* Personality Disorders–Follow Along Version,[33] which recorded monthly variations in criteria. Retrospective reliability was good (κ = 0.70), and rater drift was minimal.[34] Mood disorders were assessed yearly with psychiatric status ratings from the Longitudinal Interval Follow-up Evaluation (LIFE),[35] which records weekly variations in depressive, manic, and hypomanic *DSM-IV* criteria. The LIFE has been the seminal measure of course for mood disorders since its use in the Collaborative Depression Study.[36] The use of these measures to examine short-interval changes in BPD and mood disorder criteria allows exploration of their interactions.

Remission from BPD was operationally defined as a minimum of 2 consecutive months with 2 or fewer criteria. Relapse events were defined as 2 consecutive months at 5 or more criteria (the *DSM-IV* threshold) following remission. Of note, in some CLPS reports,[33,37] we used a definition of BPD

Table 1. Effect of Borderline Personality Disorder on Time to Remission and Time to Relapse/Onset of Mood Disorders (N = 223)

Variable	n[a]	No. of Events	Hazard Ratio	95% CI	χ^2	*P*
Time to remission						
MDD	161	77	0.787	0.69–0.90	12.978	.0004
Bipolar I	34	26	0.698	0.44–1.11	0.291	.1302
Bipolar II	28	23	0.759	0.45–1.29	1.039	NS
Time to relapse/onset						
MDD	87	70	1.107	1.00–1.22	4.174	.0410
Bipolar I	29	28	0.918	0.76–1.11	0.7589	.3873
Bipolar II	24	23	1.070	0.87–1.32	0.3967	.5288

[a]Number of subjects with borderline personality disorder with each mood disorder at baseline or that had new onsets during follow-up.
Abbreviations: MDD = major depressive disorder, NS = not significant.

Table 2. Effect of Mood Disorders on Time to Remission and Time to Relapse of Borderline Personality Disorder (N = 223)

Variable	n[a]	No. of Events	Hazard Ratio	95% CI	χ^2	*P*
Time to remission						
MDD	161	139	0.847	0.78–0.93	13.640	.0002
Bipolar I	34	25	0.757	0.52–1.10	2.182	.1396
Bipolar II	28	21	0.461	0.26–0.82	6.918	.0085
Time to relapse						
MDD	91	20	1.519	1.18–1.96	10.571	.0011
Bipolar I	19	7	0.876	0.37–2.07	0.0091	.7610
Bipolar II	19	4	2.095	0.62–7.08	1.415	.2342

[a]Number of subjects with mood disorders at baseline or that had new onsets during follow-up who also had borderline personality disorder.
Abbreviation: MDD = major depressive disorder.

remission and relapse requiring 12 months' duration because it has greater clinical significance. In this report, as in prior reports in which we examined BPD's interactions with mood disorders,[25–28] we used the shorter-term 2-month definition. Making the duration of remission for BPD equivalent with the definition used for mood disorders[38,39] facilitated equating the effects that mood disorder remissions or relapses have on BPD to the effects that BPD remissions or relapses have on mood disorders and improved our statistical power by increasing the number of remission/relapse events.

Statistical Analysis

Proportional hazards regression analyses were used to assess the effects of BPD status on time to remission and time to relapse/onset. To increase power, we combined new onsets with time to relapse for the mood disorders. Proportional hazards regression analysis was also used to measure how the status of mood disorders affects time to remission and time to relapse for BPD. We chose proportional hazards regression because the key analyses involve within-subject change, ie, the extent to which changes in one disorder are temporally coupled to changes in another disorder. When time-varying variables are used to predict survival outcomes, proportional hazards regression analysis is a well-established methodology.[40,41]

Missing data and changing subsets of subjects having remitted or relapsed meant that the samples used for analyses (see Tables 1 and 2) varied from the sample sizes of the baseline diagnostic groups. Remission or relapse times were censored (partially missing data due to loss to follow-up or nonoccurrence of remission or relapse) after the last nonmissing observation for each participant. Overall, of this study's 223 participants, we obtained data throughout the 10 years of follow-up for 67%. That we found only a weak correlation ($r < 0.12$) of subjects' age, gender, education, and cell assignment with their length of follow-up suggested that attrition did not bias the sampling in any obvious way.

RESULTS

Table 1 shows that BPD had a highly significant negative effect in delaying MDD's time to remission ($P = .0004$) and a modestly significant effect in accelerating MDD's time to relapse ($P = .0410$). Borderline personality disorder did not significantly influence time to remission or time to relapse of bipolar I or bipolar II episodes, although the confidence intervals for the hazard ratios (effect sizes) are quite broad and overlap considerably for MDD and the 2 bipolar samples. Table 2 shows that MDD had highly significant effects by delaying BPD's time to remission ($P = .0002$) and by accelerating BPD's time to relapse ($P = .0011$). Neither bipolar I nor bipolar II had statistically significant interactions with BPD, except that bipolar II delayed BPD's time to remission ($P = .0085$); however, because of the low sample size of the bipolar cells relative to MDD, the confidence intervals for the hazard ratios (effect sizes), again, overlap considerably for MDD and the bipolar samples.

DISCUSSION

The findings are notable for documenting reciprocal negative effects of BPD and co-occurring MDD on one another's time to remission and time to relapse/onset. Our finding that BPD affects MDD's course in this report extends and modifies the conclusions from our 3 earlier CLPS reports[25–27] and is consistent with findings from a large general population sample in which the co-occurrence of BPD accounted for 57% of the variance in persistently depressed people.[42] Finding a clearly significant, though weak, effect of change in MDD on BPD's course (hazard ratio = 0.847) confirms the report from 2-year data (hazard ratio = 0.77).[24] That this effect was not evident in our 3-year data, wherein changes in BPD predicted change in MDD but not vice versa,[26] may be a result of having used cross-lagged panel analyses in the 3-year report (examining fine-tune changes in criteria) as opposed to the proportional hazards regression analyses used at 2 years and in this report (examining "big" remission/relapse events). Still, the difference in results raises the question as to whether patients with more persistent BPD are a subgroup whose MDD is more integral to the psychopathology and more strongly determines its course.

Examination of the interaction of BPD with bipolar disorders extends and generally confirms the findings from our earlier CLPS report.[28] In that report, as noted, 4-year follow-up data showed that BPD had weak effects in worsening the course of co-occurring bipolar I disorder

but that bipolar disorders had little effect on BPD's course. This lack of interaction could be due to sample size, insofar as these analyses yielded effect sizes similar to those in the analyses with much larger MDD samples. In the current 10-year follow-up report, BPD failed to demonstrate negative effects on bipolar I or II's time to remission or relapse, and, similarly, bipolar I disorder failed to exert effects on BPD's course. The only statistically significant interaction from this set of analyses was that bipolar II lengthened BPD's time to remission. That bipolar II had this effect, whereas the presumably more severe bipolar I seemingly had a lesser effect, is counterintuitive. A possible explanation is that *DSM-IV*–diagnosed bipolar II may be a heterogeneous syndrome in which a subset has a variation of BPD.[3] This possibility is suggested by *DSM-IV*–diagnosed bipolar II's relatively weak familial relationship to bipolar I[14] and its weak and inconsistent response to mood stabilizers.[43] This possibility is also suggested by bipolar II's high prevalence of typical BPD characteristics such as rejection sensitivity,[44] childhood trauma,[22] and repeated suicide attempts.[45] Thus, some patients whose bipolar II disorder co-occurs with BPD might have a "characterological" variant that is less tied to bipolar I than are "purer" variants of bipolar II. Akiskal[46] once advanced this argument for dysthymia. Whatever the explanation for this particular finding, it should be seen as the exception to the overall conclusion from these analyses: namely, in almost all respects, BPD and the bipolar disorders emerge as independent.

The longitudinal interactions between BPD and MDD found in this study suggest overlapping psychopathologies, perhaps, as suggested earlier, especially in individuals with more persistent BPD. Such reciprocal effects do not, however, rule out the possibility that other factors that this study did not assess account for the changes in both disorders. The possibility of overlapping but distinct forms of psychopathology is consistent with the data showing high levels of BPD/MDD comorbidity,[4] with their having neurobiological similarities and differences,[5,15,47] and with prior family history studies that have also shown a likely, though not very strong, relationship between BPD and MDD.[4] Though BPD's effect on MDD is clearer and stronger than the reverse, the results are consistent with a model that both disorders frequently share an underlying disposition.

The evidence for interaction between BPD and MDD has useful clinical implications. Clinicians should inform patients that the co-occurrence of BPD and MDD has a negative effect on their prognosis and that their MDD is only weakly and inconsistently responsive to antidepressants or other pharmacotherapies.[18–21] In keeping with results from the Sequenced Treatment Alternatives to Relieve Depression study,[48] antidepressant use should be restricted to more severe MDD and should be prescribed with appropriate cautions about expectable benefits. On the other hand, clinicians should also inform these patients that treatments for BPD, primarily psychosocial, appear to be unaffected by co-occurring MDD.[49] As shown here and in prior reports,[25–27] BPD improvement will typically presage improvement in MDD, and, hence, treatment for BPD should be given priority or at least not be postponed.

This study's results offer only weak evidence for interactions between BPD and bipolar disorder. Supporting the conclusion that these disorders are independent—with the possible exception of some variants of bipolar II—are their relatively low levels of comorbidity and the research showing little familial coaggregation.[4,14] This evidence for the independence, ie, true comorbidity, of these disorders may seem surprising given their phenomenological overlaps (emotionality, impulsivity). Clinicians who treat such patients should convey this independence even while initiating trials of mood stabilizers. The still limited research on mood stabilizers in patients with BPD has shown broad albeit rarely dramatic effectiveness.[19,20] Moreover, resolution of mania or hypomania with mood stabilizers (or with other psychotropic medications) will, in our experience, often facilitate use of psychosocial treatments of BPD. Problems develop when patients with comorbid BPD and bipolar disorder receive only mood stabilizers. Under these circumstances, BPD response to these medications is typically modest, while the need for informed psychosocial treatments is neglected. Research has demonstrated frequent overdiagnosis of bipolar disorders in BPD patients[22] and underdiagnosis of BPD in those with bipolar disorder.[50] The misdiagnosis of bipolar disorder in BPD patients can have destructive consequences by encouraging exaggerated hopes for pharmacologic efficacy, while robbing patients of effective treatments that target and strengthen a sense of agency, ie, help patients learn how to control their feelings and impulses. In this regard, psychiatrists should note that an empirically validated treatment for BPD, General Psychiatric Management, has demonstrated that experienced psychiatrists who combine good case management strategies with informed pharmacotherapy can be very effective—especially for borderline patients with more comorbidity.[51,52]

Three studies of the genetic relationship of BPD to its phenotypes have shown that while the affective/emotional phenotype contributes significantly to BPD, neither it nor any other component phenotype (ie, interpersonal, behavioral, cognitive) is more heritable than the disorder itself.[53–55] These results argue for a model of BPD psychopathology in which some latent integrative and unifying factor is present that exceeds the contribution of the affective/emotional—or any other—component phenotype. The current study's results support the idea that this affective/emotional phenotype might be reflected by the covariation of BPD with MDD, but that it is not operative when BPD co-occurs with bipolar disorder. The latent factor that unites BPD with MDD, but not with bipolar II disorder, might be reflected in the personologic construct of neuroticism (anxious negativity), more than in the psychobiological construct of affective instability.

Strengths of this study are its good-size sample of patients with BPD and MDD, reliable assessments, and the unique quality of the CLPS short-interval ratings that permit longitudinal interaction analyses. In addition, this report has

the strength of 10 years of follow-up. Despite these strengths, the CLPS is a naturalistic follow-along study. Medications and psychosocial treatments were not controlled, thereby obscuring how they affected course or the interactions between disorders. A second regrettable limitation is the modest sample size of bipolar I and II patients, with a correspondingly low number of remission/relapse events. The size of our bipolar samples limited our statistical power. Replication with larger samples is needed to strengthen the generalizability of our findings.

This study demonstrates the significant interaction that co-occurring BPD and MDD have on one another over a 10-year course, suggesting an overlap in their psychopathology and having significant implications about prognosis and treatment. This study demonstrates the independence (ie, comorbidity) of BPD and bipolar I disorder, thereby strengthening a conclusion evident in other bodies of research and underscoring the need to treat both disorders. This study also raises the question as to whether *DSM-IV*–defined bipolar II disorder might include some patients with a variant of BPD.

Author affiliations: Department of Psychiatry, Harvard Medical School, Boston, Massachusetts (Drs Gunderson, Keuroghlian, and Zanarini); Pacific Institute for Research and Evaluation, Providence Rhode Island (Dr Stout); Department of Veterans Affairs, Veterans Affairs Medical Center, Providence, Rhode Island (Dr Shea); Department of Psychiatry and Human Behavior, Alpert Medical School, Brown University, Providence, Rhode Island (Drs Shea and Yen); Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut (Drs Grilo and McGlashan); Department of Psychiatry, New York State Psychiatric Institute and Columbia University, New York, New York (Drs Markowitz and Skodol); Department of Psychology, Wesleyan University, Middletown, Connecticut (Dr Sanislow); Department of Psychiatry, University of Arizona, Tucson (Dr Skodol); and Department of Psychology, Texas A & M, College Station (Dr Morey).
Potential conflicts of interest: None reported.
Funding/support: This research was supported by National Institute of Mental Health grants R01 50838, R01 50839, R01 50840, R01 50850, K23 073708, and K23 080221. This research is the result of work supported in part with resources from and the use of facilities at the Veterans Affairs Medical Center, Providence, Rhode Island.
Role of the sponsor: The sponsor had no role in the execution of the study, data analysis, or manuscript preparation.
Disclaimer: The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government.

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