Major Depressive Disorder and Borderline Personality Disorder Revisited: Longitudinal Interactions

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Background: This report investigates the longitudinal association of changes in major depressive disorder (MDD) and borderline personality disorder.

Method: A DSM-IV–diagnosed sample of 161 patients with borderline personality disorder who have been followed with repeated measures at 6, 12, 24, and 36 months are investigated to see whether those with co-occurring MDD differ at baseline and in their course. Proportional hazard regression and cross-lagged panel analyses are used to demonstrate whether changes in the course of either disorder have predictable effects on the course of the other.

Results: The rate of remissions of borderline personality disorder was not affected by whether patients had co-occurring MDD. The rate of MDD remissions was significantly reduced by co-occurring borderline personality disorder. Both regression analyses and panel analyses indicated that improvements in borderline personality disorder were often followed by improvements in MDD but that improvements in MDD were not followed by improvements in borderline personality disorder. Five of the 9 borderline criteria, including those that most relate to affects, were particularly apt to remit prior to MDD remissions.

Conclusions: When borderline personality disorder and MDD co-occur, they can sometimes have independent courses, but more often improvements in MDD are predicted by prior improvements in borderline personality disorder. Clinicians should not ignore borderline personality disorder in hopes that treatment of MDD will be followed by improvement of borderline personality disorder.

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Since the inception of the borderline personality disorder diagnosis, the nature of its interface with depressive disorders has been debated.[1–3] One viewpoint is that borderline personality disorder is a more fundamental and dominant form of psychopathology that accounts for co-occurring depressions, i.e., that the depressive experiences found in patients with borderline personality disorder should be understood as epiphenomena intimately connected to the abnormal sensitivity and to the failed interpersonal relationships inherent in this personality structure. This viewpoint is supported by qualitative differences of the borderline patients' depressive experiences compared to those of major depressive disorder (MDD) patients,[4–6] by the series of follow-up studies that—in contrast to what had once been predicted by Stone[7] and Akiskal[1]—failed to show that borderline psychopathology evolves into more typical depressive disorders over time,[8] and by the comparatively modest response of borderline patients to antidepressants.[3,9] An-

other viewpoint holds that borderline personality disorder is a subordinate and atypical expression of a primary depressive disorder; i.e., that borderline personality disorder is best classified as an atypical presentation of an underlying biogenetically based depressive disorder. This view has been supported by the ubiquitous—and often very severe—depressive experiences described by borderline patients,[10–12] by evidence of neurobiological overlap,[3] and by evidence suggesting a heightened risk of depressive disorders among first-degree relatives.[13,14] A third, and less directly competitive, model is that the 2 disorders are independent of each other. A fourth model posits overlapping etiologic factors, wherein persons having either borderline personality disorder or MDD are predisposed to the development of the other disorder. Koenigsberg et al.[3] extended this overlapping model by proposing that the psychosocial sequelae (e.g., alienation, unemployment) of having either disorder further predisposes to the development of the other. We hypothesized that this fourth model would be confirmed in the present report.

This report examines the longitudinal association of borderline personality disorder to MDD, using data from the Collaborative Longitudinal Personality Disorders Study (CLPS).[15] This database allows us to examine the interface of depressive disorders and borderline personality disorder using a much improved design (prospective, substantial sample size) and methodology (reliable, short interval repeated-measures assessments). A report based on the CLPS 2-year data examined whether changes in any of the study's 4 personality disorders (schizotypal, borderline, avoidant, and obsessive-compulsive) were associated with changes in any Axis I disorder and vice versa.[16] Those analyses showed that the predictive power of remissions of borderline personality disorder on the course of MDD ($p = .001$, RR = .57) was much stronger than the predictive power of remissions of MDD on the course of borderline personality disorder ($p = .16$, RR = .77). This result did not offer strong support for the mutually interactive model we expected.

This article extends that report's examination of the relationship between borderline personality disorder and MDD in 5 ways. First, we utilize a longer, i.e., 3-year follow-up period. Second, we use 2 different methods of sampling; i.e., for most analyses, we use the borderline personality disorder sample as defined by cell assignment, a narrower, more clinically rigorous means of establishing the diagnosis, and for other analyses we examine all patients with any borderline personality disorder criteria. Third, we use additional data analytic methods, i.e., cross-lagged panel analysis, that make use of the full CLPS sample including subjects with MDD without a personality disorder. Fourth, we look at the more severe subtypes from each disorder to test our hypothesis that these types are most apt to determine the subsequent course of the other disorder. Fifth, in this report we examine whether changes in the various criteria for either borderline personality disorder or MDD differ in their degree of association with subsequent fluctuations of course for the other disorder.

METHOD

Detailed descriptions of the CLPS aims, background, methods, and sample characteristics have been reported separately.[15,17] Relevant methods for this substudy are elaborated here.

Sample

The sample for this report derives from 570 subjects (85.3% of the original sample) on whom complete 6-, 12-, 24-, and 36-month follow-up data were collected. All patients signed informed consent before entering the study. For most analyses, the 161 (from the original 175) cell-assigned borderline subjects on whom we have 36-month follow-up data were used. From these, the subsample of 67 patients with coexisting MDD were of particular importance. There were no demographic differences between the 36-month borderline study sample and the 14 borderline subjects on whom follow-up data were absent or incomplete.

Assessments

All subjects were evaluated at baseline with the Diagnostic Interview for DSM-IV Personality Disorders (DIPD-IV)[18] and the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)[19] by clinically experienced interviewers trained to pay particular attention to distinguishing Axis I mental state conditions from Axis II personality trait phenomena. For a subject to be assigned to the borderline diagnostic cell, the DIPD-IV–generated diagnosis required corroborating evidence, reflecting our effort to determine a "primary" personality disorder diagnosis.[15] The interrater and test-retest kappa values for borderline personality disorder were 0.68 and 0.69, respectively. For MDD, the interrater kappa was 0.80, and the test-retest kappa was 0.61.[20] The subjects were evaluated again at 6, 12, 24, and 36 months by a follow-along version of the DIPD that records monthly variations in borderline criteria and by the Longitudinal Interval Follow-Up Evaluation (LIFE)[21,22] that records weekly variations in depressive criteria. Follow-along reliability for the diagnosis of borderline personality disorder had a kappa of 0.70, for individual borderline criteria ranged from 68% to 85% agreement, and for the number of borderline criteria met had a Pearson r of 0.66. To examine stability, *remissions* were operationally defined as 2 consecutive months with 2 or fewer criteria for both borderline personality disorder and MDD. This definition, as used in other CLPS reports,[23–25] is a widely used precedent in studies of MDD and other Axis I disorders.[26,27] This definition of

remission is arbitrary with respect to personality disorders, but it is used here to assure that most aspects of borderline psychopathology were absent—rather than merely having subthreshold or very temporary lulls in criteria. Developmental adversities were assessed with the Revised Childhood Experiences Questionnaire (CEQ-R).[28]

Analyses

To examine the relationship of MDD to borderline personality disorder, we divided the borderline sample (N = 161) into subgroups based on types of course. The 94 borderline personality disorder without MDD subjects were divided into those who remitted (N = 50) and did not remit (N = 44). From the 67 borderline personality disorder with MDD subjects, subgroups were identified in which borderline personality disorder remitted before MDD remitted (N = 12) and in which MDD remitted before borderline personality disorder remitted (N = 27).

The various samples (or subsamples) were compared on demographic variables (age, gender, minority status, employment status, marital status), on baseline co-occurrence of other personality disorders and of Axis I disorders, on types of depression (age at onset, number of prior episodes, and whether ever melancholic), and on childhood adversity (severity, and whether abusive or neglectful). Due to the number of comparisons (N = 31) between subsamples, a Bonferroni correction was used for χ^2 analyses that meant statistical significance was attained at p = .0016. The comparative rates of remission for the various samples were analyzed using Kaplan-Meier survival methods.

We first compared the 94 borderline subjects without MDD to our target sample of the 67 borderline subjects with co-occurring MDD at baseline (χ^2 or ANOVA). We next compared subsamples within those 67 patients with borderline personality disorder and MDD to all the others within the borderline personality disorder and MDD sample. First, we looked at the subsample of 12 subjects in which the remission of borderline personality disorder preceded remission of MDD. We hypothesized that this subgroup would be distinguished by more childhood abuse and neglect because such histories distinguish borderline personality disorder from MDD[29] and are associated with a worse prognosis (reference 30 and J.G.G., M.T.D., T.H.M., et al. Unpublished data, 2003). Second, we looked at the subsample of 27 subjects in which the remission of MDD preceded remission of borderline personality disorder. We hypothesized that these patients had a type of MDD characterized by being melancholic (i.e., somatic) and more episodic.[26]

Proportional hazards regression analyses (Cox regression) were used to look at how remission of MDD affects the course of borderline personality disorder, and vice versa. In these analyses, the goal is to see how variation in the predictor variable, i.e., the severity of either MDD or borderline personality disorder, is related to the odds of remission for the other disorder (the dependent variable). In the prediction of MDD remission, the time-varying predictor was the 9-point scale of number of borderline criteria for the month preceding the timepoint being analyzed. In the prediction of remission of borderline personality disorder, the time-varying predictor was the 6-point psychiatric status rating (PSR) for MDD in the last week of the month preceding the timepoint being analyzed. Hazard ratios and p values for a 2-tailed test that the risk ratio is different from 1.0 were determined. Risk ratios less than 1 indicate that improvement (lower value) in the predictor variable is associated with a higher likelihood of remission for the dependent variable. Risk ratios of 0.50 to 0.67, and 1.5 to 2.0, are roughly equivalent to medium effect sizes. Risk ratios below 0.50 and > 2.0 would be considered large effect sizes. An alpha level of less than .05 was considered statistically significant. From these assessments, we can determine whether improvement in either condition is significantly associated with a subsequent remission in the other disorder.

Because the Cox regression analyses are anchored by remission events, they do not capture the full range of interaction of less dramatic changes in either disorder upon the other. As noted,[16] Cox regression analyses also have the limitation of depending upon a subject's ability to retrospectively remember accurately changes on a month-by-month basis during time intervals of from 6 months' to 1 year's duration. To address these limitations, we also conducted the analysis with cross-lagged panel analyses.[31] These analyses rely on the subjects' account of their mental state at the time that the 6-, 12-, 24-, and 36-month assessments were conducted, thereby diminishing the likelihood of retrospective distortions. For these analyses, we used scores on MDD severity (PSR scale of 1–6) and on borderline criteria (DIPD scale of 1–9) for the entire CLPS sample on whom 3-year data were available (N = 570). Use of this sample expanded the range of scores on both borderline and depressive psychopathology and thereby heightened the power available for analyses as well as the ability to see less dramatic interactions.

RESULTS

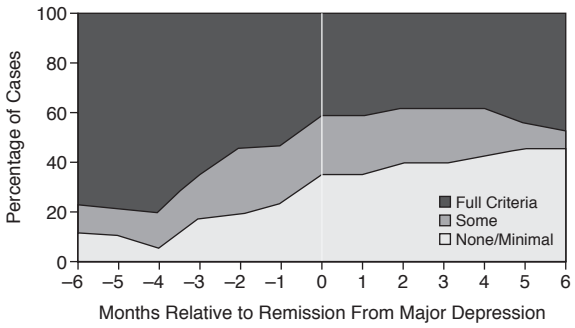
Samples, Subsamples, and Types of Course

In comparison with the 94 borderline subjects without baseline MDD, the 67 with baseline MDD were significantly more apt to ever have been married (54% vs. 22%, $\chi^2 = 16.9$, df = 1, p = .0001) and to have posttraumatic stress disorder (49% vs. 33%, $\chi^2 = 4.32$, df = 1, p = .038) and had a higher mean age (33.9 vs. 30.5 years, ANOVA F value = 7.42, p = .0072). Significant differences were not found on other Axis I disorders, on other Axis II disorders, or on the demographic variables of gender, race, and work status.

In the 67 cases with MDD plus borderline personality disorder, the MDD underwent remission in 43 (64.2%), and the borderline personality disorder underwent remission in 26 (38.8%)—a statistically higher rate for MDD ($\chi^2 = 9.87$, df = 1, p = .0017). The 38.8% rate of borderline remissions in the borderline personality disorder plus MDD sample is not significantly less than the 53.2% rate (i.e., 50 of 94) in the 94 borderline subjects without MDD at baseline ($\chi^2 = 0.16$, df = 1, p = 0.69). The 64.2% fraction of borderline personality disorder subjects whose co-occurring MDD underwent remission is significantly lower ($\chi^2 = 16.3$, df = 1, p = .0001) than the 89% rate (i.e., 81 of 91) of MDD remissions found in the CLPS control sample of patients with MDD without comorbid personality disorder.

We next compared the subgroup of 12 subjects in which a remission of borderline personality disorder occurred before the remission of MDD to the other 55 borderline subjects on the following baseline variables: demographics, comorbidity, childhood abuse/neglect, whether MDD was melancholic, and the number of previous MDD episodes. A number of characteristics distinguish the subgroup in which borderline personality disorder remitted first at the $p < .05$ level, i.e., less impulsivity (57% vs. 88%, $\chi^2 = 4.80$, df = 1, p = .0284), less unstable relationships (43% vs. 56%, $\chi^2 = 5.43$, df = 1, p = .0198), less sexual abuse (14% vs. 56%, $\chi^2 = 4.25$, df = 1, p = .0393), and a later age at onset of MDD (mean age = 23 vs. 14 years, ANOVA F value = 8.64, p = .0046), but when Bonferroni corrected, these finding are trends. All of these trends reflect less severe borderline psychopathology. The comparison of the 27 subjects whose MDD remitted before borderline personality disorder to the other 40 borderline subjects with baseline MDD on the same baseline variables revealed no significant differences.

Figure 1. Criteria for Borderline Personality Disorder in the Months Before and After Remission From Major Depressive Disorder (N = 67)[a]



[a]0 = month remission occurred.

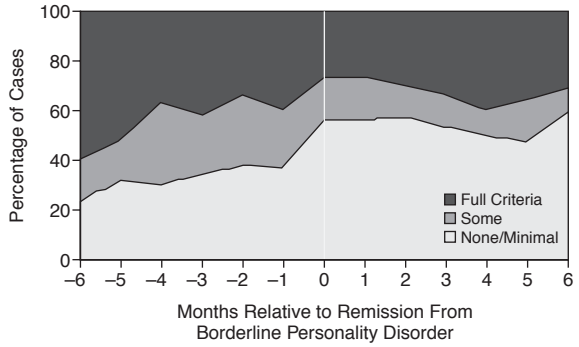
Interaction-Over-Time Analyses

Proportional hazards regression analyses with time-varying covariates revealed that MDD was not a significant predictor of remission of borderline personality disorder (risk ratio = 0.93; $\chi^2 = 0.07$, df = 3, p = .7909). Conversely, when we used borderline personality disorder as the predictor and MDD as the dependent variable, borderline personality disorder proved to be a significant predictor of remission for MDD (risk ratio = 0.75; CI = 0.65 to 0.87; $\chi^2 = 15.89$, df = 3, p = .0012). These analyses were both done controlling for baseline medication status and for 1-year treatment intensity (a composite measure of the days spent in hospitals or partial hospitals and the number of hours spent in professionally led therapies of all kinds). Neither of these treatment variables was a significant predictor of either MDD or borderline remission. These analyses indicate that borderline patients who had a high number of borderline criteria initially had a relatively low chance of their MDD remitting. Moreover, regardless of the baseline severity of the borderline personality disorder, improvement in borderline psychopathology significantly increased the likelihood of MDD remitting.

The time-varying association between borderline personality disorder and MDD is also shown graphically (Figures 1 and 2). For purposes of clarity, we reduced both the 6-point MDD scale and 9-point borderline scale to equivalent 3-point scales reflecting severe ("full"), moderate ("some"), and low ("none/minimal") levels of severity. Thus, for borderline personality disorder, 3 = 5 or more criteria, 2 = 3 or 4 criteria, 1 = 2 or fewer criteria from DIPD-Follow Along–based ratings.[32] For MDD, 3 = PSR scores of 5 or 6; 2 = PSR scores of 3 or 4; 1 = PSR scores of 0, 1, or 2. These figures display changes in the MDD/borderline diagnostic scores at each level (full, some, or none/minimal criteria) in the 6 months leading up to a remission as well as in the 6 months after remission among those subjects who remitted. The month the remission occurred is designated on the x-axis as month 0. The figures are restricted to the 6 months before and after the remission because the amount of data available on subjects outside that time interval rapidly declines.

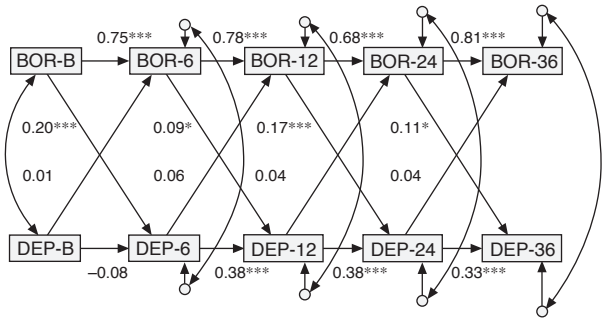
Figure 1 illustrates the process in which borderline criteria change before and after the remissions of co-occurring MDD. There is clearly diminished severity of borderline personality disorder prior to remissions of MDD (indicated by the increased proportion of the borderline subjects who scored 0 or 1). At month 0 (the month of the MDD remission), about 30% of the patients had a remission in their borderline psychopathology and approximately another 20% were subthreshold. Though continued improvement in borderline personality disorder was observed after the remissions of the depressions (i.e., 6 months after the MDD remissions, another 10% of the borderline patients remitted), the rate of improvement was clearly less than that before the remission. This figure

Figure 2. Criteria for Major Depressive Disorder in the Months Before and After Remission From Borderline Personality Disorder (N = 67)[a]



[a]0 = month remission occurred.

Figure 3. Cross-Lagged Panel Analysis Relating Borderline and Depressive Psychopathology Over 3 Years (N = 570)[a]



This cross-lagged path analysis model has been rerun, with the 4-year data, using dimensional symptom counts for borderline personality disorder and somewhat dimensionalized scores (none, minimal, moderate, severe). There are 5 time periods, with baseline, 6-month, and 1-, 2-, and 3-year timepoints represented (DEP-B being baseline, DEP-6 being 6 months, etc.). As a true lagged effect, attention must be paid to the last 3 sets of diagonals; these represent the effects of a change at one point upon the other diagnosis at the next point. In 2 of the 3 lagged instances, the lagged effect of borderline personality disorder upon depression was significant, while the lagged effect of depression upon borderline personality disorder was not, with one exception at the final timepoint. The "horizontal" values, which tend to be larger, represent stability effect estimates for the 2 diagnoses. These indicate that both diagnoses have some stability, with borderline personality disorder being considerably more stable than MDD.

	Lagged partial correlation estimates	
Timepoint	MDD → BPD	BPD → MDD
Baseline to 6 mo	0.019	0.039
6 mo to 12 mo	0.010	0.150***
12 mo to 24 mo	0.024	0.016
24 mo to 36 mo	0.051*	0.115***

[a]BPD = borderline features, assessed at baseline (B) and 6-, 12-, 24-, and 36-month follow-ups; DEP = depression diagnostic status assessed at the same intervals.
*p < .05, ***p < .001.
Overall fit of the model: normed goodness-of-fit index = 0.927, comparative fit index = 0.935, root-mean-square error of approximation = 0.107 (adequate fit).

also shows that in a significant fraction of the cases, i.e., about 30% to 40%, the severity of borderline personality disorder does not change when MDD remits.

Figure 2 illustrates the process in which MDD criteria change in the 6 months before and after remissions of borderline personality disorder. Though the number of people with more severe depressions (i.e., scores 4–6) diminished from about 60% to 40% during the 6-month interval before the remissions of borderline personality disorder, the rate of diminution was somewhat less than in Figure 1 and was quite unremarkable following the borderline remissions. This figure also shows that there are more than 30% of cases whose MDD severity does not change when borderline personality disorder remits.

Figure 3 illustrates the results of the cross-lagged panel analysis. The model presented in the figure, i.e., showing that the variables correlate in a sequential way, is largely confirmed by adequacy-of-fit indices. The overall normed goodness-of-fit index equals 0.927, the comparative fit index (CFI) equals 0.935, and the root-mean-square error of approximation equals 0.107 (adequate fit). The results show considerable stability in the borderline personality disorder psychopathology across the assessments (correlations of 0.68 to 0.81). The MDD also shows reasonable stability (correlations of 0.33 to 0.38), except for the time interval from baseline to 6 months. Here, the correlation (–0.08) indicates that the level of MDD at baseline had very little predictive relationship to MDD scores at 6 months.

When the relationship between the disorders is examined, the lag effect of MDD on subsequent borderline scores was insignificant, except for the interval from 24 months to 36 months (correlation of 0.051, $p < .05$). This probably reflects the effects of having weeded out most of those patients with episodic depressions that had remitted. The depressions that had not already remitted were likely to be those belonging to subjects with borderline personality disorder; i.e., those patients who did not show much change in depression status were more likely to be borderline in subsequent assessments. The lag effect of borderline personality disorder on MDD was significant for 2 time intervals; i.e., correlation of 0.150, $p < .001$, for the 6-month to 12-month time interval, and correlation of 0.115, $p < .001$, for the interval from 24 months to 36 months.

Criteria Analyses of Borderline Personality Disorder

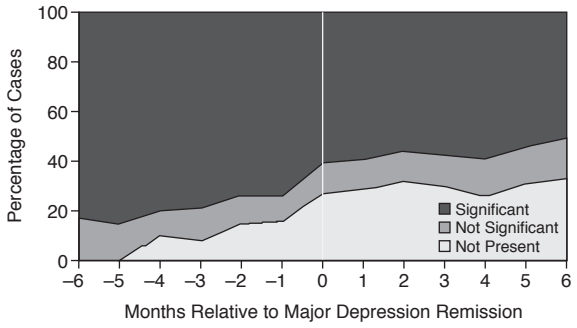
Returning to the sample of 67 subjects with borderline personality disorder and MDD at baseline, Table 1 portrays the relationship between individual borderline criteria and MDD remissions. These data reveal that all of the borderline criteria were well represented in our sample at baseline, and, with a Bonferroni correction, 5 were predictive of MDD remissions. In other words, their presence meant that the remission of MDD was less likely and their absence increased the likelihood that the concurrent

Table 1. Relationship of BPD Criteria to MDD Remission Over 3 Years (N = 67)

Criterion	% With Criteria at Baseline	Risk Ratio	95% CI	Wald χ^2	p
Unstable relationships	77.6	0.67	0.46 to 0.96	4.86	.0274
Impulsivity	85.1	0.79	0.56 to 1.10	1.97	.1605
Avoids abandonment	64.2	0.70	0.49 to 0.99	3.98	.0461
Identity disturbance	58.2	0.65	0.46 to 0.92	5.80	.0160
Emptiness	76.1	0.45	0.32 to 0.63	22.16	< .0001
Brief psychotic experiences	65.7	0.55	0.40 to 0.77	12.38	.0004
Affective instability	95.5	0.47	0.34 to 0.66	18.95	< .0001
Anger	91.0	0.59	0.41 to 0.84	8.54	.0035
Self-injurious behavior	65.7	0.48	0.32 to 0.74	11.16	.0008

Abbreviations: BPD = borderline personality disorder, MDD = major depressive disorder.

Figure 4. Borderline Personality Disorder Criterion 2[32] (Affective Instability) Before and After Remission of Major Depression[a]



[a]0 = month remission occurred.

MDD would remit. Notably, the stronger predictors were the more symptomatic criteria, i.e., emptiness, affective instability, anger, brief psychotic experiences, and self-injurious behaviors.

All criteria diminished during the 6 months before remission of MDD, with the reduction in frequency ranging from 2% (impulsivity) to 26%. In the 6 months after the MDD remission, most criteria became modestly less frequent, but no criterion was reduced by more than 10%. The patterns in which the 9 borderline criteria change in the 6 months before and after the MDD remissions are illustrated by looking at the affective instability criterion in Figure 4.

DISCUSSION

The conflicting models and clinical approaches to patients with borderline personality disorder and MDD, as well as the high prevalence of this form of comorbidity in clinical settings, frame the background for this report. The 42% rate of concurrent MDD found in the borderline sample used in this study is comparable to the rates found in the entire borderline sample at baseline (i.e., 77 of 175: 44%) and is comparable to the rates of co-occurrence observed in previous studies (reviewed elsewhere).[3,12,33] The differences found between the 67 borderline patients who had MDD at baseline compared to the 94 borderline patients who did not were that the baseline MDD patients were more apt to have been married, to have co-occurring posttraumatic stress disorder, and to be somewhat older. Of note, we failed to confirm[34] finding of greater childhood abuse in borderline subjects with comorbid mood disorder.

When we looked for baseline characteristics that might discriminate the subsamples in which one or the other disorder remitted first, we found no features that predicted when MDD would remit first. Because our results failed to demonstrate an effect whereby a "primary" type of MDD predicted changes in borderline personality disorder (i.e., model 2), our negative result has unclear clinical significance. We did find trends indicating that subjects whose borderline personality disorder remitted before their MDD might be distinguished by less severe borderline psychopathology as measured by different variables. We had not hypothesized these trends, and in view of the relatively small samples involved, these results need replication.

The results from our analyses that involve comparative rates of remission are clinically valuable. The rate of remission of borderline personality disorder was not significantly reduced when MDD co-occurred. In contrast, the rate of remission of MDD was reduced when it co-occurred with borderline personality disorder. These findings are consistent with the results from our interaction-over-time analyses. The proportional hazards regression analyses showed that improvements in symptoms of borderline personality disorder are often associated with subsequent remission of MDD, but that improvements of MDD failed to be significantly predictive of remissions of borderline personality disorder, though there was evidence of some association. The cross-lagged panel analysis further buttressed the conclusion that borderline personality disorder affects MDD, but not vice versa. The relatively weak ability of changes in MDD to predict change of borderline personality disorder was contrary to our expectations. It is consistent, however, with a report[35] that used cross-lagged analyses on dysthymic patients and found that borderline features influenced depressive symptoms but not vice versa. Our results are also consis-

tent with a report[36] that severity of borderline psychopathology is a stronger predictor of subsequent MDD episodes than is a history of prior episodes of depression, and with the less intensive examination of our 2-year data.[16]

The third set of analyses involved the course of improvement after a remission had occurred. The finding that borderline psychopathology continued to diminish after the MDD remitted suggests that the MDD remissions are part of an ongoing process of improvement in the borderline psychopathology. This is consistent with a model (i.e., model 4) of overlapping psychopathology and with the idea that remission of concurrent MDD could provide added impetus to the resolution of borderline psychopathology. However, and inconsistent with this model, the remissions of borderline personality disorder were not associated with continued improvement in MDD.

Our study suggests that there are 3 overall types of course: (1) those whose depression and borderline personality disorder generally got better, with the borderline personality disorder usually getting better first, (2) those whose borderline personality disorder improved but not their depression, and (3) those whose depression got better but not their borderline personality disorder. The first pattern occurred in 60% to 70% of the patients. This supports the first model described in the introduction of this article. Patients with the latter 2 types of course constitute a significant proportion—an estimated 30% to 40%—of patients with borderline personality disorder and MDD. For example, in Figure 1, while the proportion of cases at full criteria for borderline personality disorder declines dramatically from over 75% at the beginning, close to 40% remain at full criteria for borderline personality disorder after depression has remitted. This indicates that for a substantial number of patients the 2 disorders behave independently, i.e., the third model.

The specific criteria that were most reduced prior to the MDD remissions involved the affect-related symptoms of anger, affect instability, and emptiness as well as self-injurious behaviors and brief psychotic experiences. Conceivably, these aspects of borderline psychopathology had a causal role in sustaining MDD. This possibility is consistent with the idea that these criteria reflect an underlying affective instability phenotype[37,38] that predisposes borderline patients to exacerbations in depressive symptoms.

Some limitations of the study need mention. As noted, the limitations of retrospective recall could affect the Cox regression analyses. It should also be noted that difference in the scales on which borderline personality disorder (1 to 9 criteria) and depression (a 6-point PSR scale) were measured may have affected to some degree which disorder appeared to improve first. However, when we talk about remission, we are talking about very substantial clinical changes, which make the scales' particularities somewhat less important. The subgroups hypothesized to be the more severe variants of MDD and of borderline personality disorder had relatively small Ns, which placed some limitations on the analyses that were possible. On the flip side, this is the largest prospectively gathered borderline sample with short interval change scores and had a high follow-up rate over an extended period. The fact that we used 2 very different analytical methods (Cox regression and cross-lagged panel analysis) that point to the same result substantially buttresses the main conclusion. Still, in the future, we will be able to do analyses looking at relapse to depression or borderline personality disorder. Those analyses may provide even sharper tests of the different models of how depression and borderline personality disorder are related.

The findings from this study are provocative. They suggest that the major depressive episodes experienced by borderline patients are sometimes independent, i.e., truly *comorbid* disorders, but more often their course can be predicted by what occurs with co-occurring borderline personality disorder. The findings surprisingly fail to verify that the course of borderline psychopathology is very much dependent upon, i.e., can be predicted by, having comorbid MDD. While these conclusions require replication, the immediate clinical implication is that the depressions found in borderline patients should not be expected to respond to the same treatments as do depressions in other patients. Here, when we controlled for baseline medication status and 1-year treatment intensity, we continued to find that borderline personality disorder could predict MDD remission but MDD did not predict remission of borderline personality disorder. This means that it is unwise to overlook or postpone providing treatment for the borderline psychopathology while first undertaking treatment for co-occurring depression. This conclusion is consistent with results reported from treatment studies[3,9,39,40] that indicate medications have weakened effects on MDD in the presence of borderline personality disorder. When these 2 disorders co-occur, our results suggest it is wise to treat the borderline personality disorder, since improvement in borderline personality disorder often leads to subsequent resolution of MDD.

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