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Interactions of Borderline Personality Disorder and Anxiety Disorders Over 10 Years

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ABSTRACT

Objective: This report examines the relationship of *DSM-IV* borderline personality disorder (BPD) to anxiety disorders using data on the reciprocal effects of improvement or worsening of BPD and anxiety disorders over the course of 10 years.

Method: We reliably and prospectively assessed borderline patients ($n = 164$) with *DSM-IV*-defined co-occurring generalized anxiety disorder (GAD; $n = 42$), panic disorder with agoraphobia ($n = 39$), panic disorder without agoraphobia ($n = 36$), social phobia ($n = 48$), obsessive-compulsive disorder (OCD; $n = 36$), and posttraumatic stress disorder (PTSD; $n = 88$) annually over a period of 10 years between 1997 and 2009. We used proportional hazards regression analyses to assess the effects of monthly improvement or worsening of BPD and anxiety disorders on each other's remission and relapse the following month.

Results: BPD improvement significantly predicted remission of GAD (hazard ratio [HR] = 0.65, $P < .05$) and PTSD (HR = 0.57, $P < .05$), whereas BPD worsening significantly predicted social phobia relapse (HR = 1.87, $P < .05$). The course of anxiety disorders did not predict BPD remission or relapse, except that worsening PTSD significantly predicted BPD relapse (HR = 1.90, $P < .05$).

Conclusions: BPD negatively affects the course of GAD, social phobia, and PTSD. In contrast, the anxiety disorders, aside from PTSD, had little effect on BPD course. For GAD and social phobia, whose course BPD unidirectionally influences, we suggest prioritizing treatment for BPD, whereas BPD should be treated concurrently with panic disorders, OCD, or PTSD. We discuss state/trait issues in the context of our findings.

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Patients diagnosed with borderline personality disorder (BPD) carry a high risk of comorbid *DSM-IV* anxiety disorders.^{1–4} Cross-sectional rates of anxiety disorders in patients with BPD range from 14%–22% for generalized anxiety disorder (GAD), 2%–48% for panic disorder with or without agoraphobia, 19%–46% for social phobia, 16%–20% for obsessive-compulsive disorder (OCD), and 25%–56% for posttraumatic stress disorder (PTSD).^{1,3,5,6} Our data address *DSM-IV* anxiety disorders; in 2013, *DSM-5* removed OCD and PTSD from its anxiety disorder section.

Research since the 1990s has shown less stability for personality disorders generally and BPD specifically than had been believed.^{7,8} Indeed, the instability of personality disorders offered a rationale for dissolving Axis II and listing personality disorders among other major mental disorders in *DSM-5*. Increasing evidence that personality disorders can have mutable courses has focused research on predictors of personality disorder remission and relapse. Such research provides an opportunity to explore how the remitting and relapsing course of personality disorders may affect fluctuations of other diagnoses such as anxiety disorders. This study uses the final 10-year follow-up data from the Collaborative Longitudinal Personality Disorders Study (CLPS)^{9,10} to examine how BPD and anxiety disorders influence each other's longitudinal course.

Confounding understanding of the comorbidity of Axis I and II disorders has been the confusion of state and trait: whether anxiety disorders exaggerate or magnify subthreshold personality traits to the level of personality disorder and, conversely, whether BPD features bleed into anxiety disorders criteria. We hoped these analyses might help to discriminate whether one seemingly comorbid disorder constituted an epiphenomenon of the other.

Three previous studies^{11–14} have examined longitudinal interactions of BPD and *DSM-IV* anxiety disorders. The McLean Study of Adult Development (MSAD) assessed whether PTSD or an aggregate of other anxiety disorders (panic, agoraphobia, social phobia, simple phobia, OCD, and GAD) affected BPD time to remission.¹¹ Anxiety comorbidity lengthened BPD time to remission in both cases, particularly with PTSD.

The CLPS 2-year follow-up showed that time-varying changes in symptomatic severity of neither anxiety disorders nor BPD predicted the other's remission, with one exception: BPD improvement predicted PTSD remission.¹² The 7-year CLPS follow-up assessed whether baseline BPD predicted anxiety disorder remissions or relapses. Baseline BPD status did not predict remission of any anxiety disorder (including OCD or PTSD) but did predict increased risk of OCD relapse.¹³

Recently, the National Epidemiologic Study of Alcohol and Related Conditions found that after 3 years, baseline BPD predicted longer time to remission of 4 *DSM-IV* anxiety disorders: GAD, social phobia, specific phobia, and panic disorder.¹⁴

The current study seeks to enhance understanding of reciprocal interactions between BPD and *DSM-IV* anxiety disorders in 4 ways: (1) examining monthly, time-varying interactions (as opposed to predictions

from baseline disorder status alone); (2) assessing effects on both remission and relapse; (3) examining a 10-year follow-up period (the definitive CLPS follow-up data); and (4) assessing for the first time the influence of anxiety disorders' courses on BPD relapse. We used the methodology from our recent report¹⁵ of 10-year interactions of BPD and mood disorders. On the basis of previous studies,¹¹⁻¹⁵ we hypothesized that BPD would more negatively affect the course of anxiety disorders than vice versa and that BPD would have a particularly strong and reciprocal relationship with PTSD.

METHOD

Detailed CLPS aims, background, methods, and sample characteristics have been reported.^{9,10} This multisite, prospective, naturalistic, and longitudinal study enrolled a diverse, clinically and demographically representative sample from inpatient and outpatient clinical programs affiliated with 4 recruitment sites (Brown, Columbia, Harvard, and Yale), whose institutional review boards all approved the project. Participants received a complete study description and gave written informed consent. The CLPS enrolled 733 participants aged 18 to 45 years with at least 1 of 4 personality disorders (schizotypal, borderline, avoidant, and obsessive-compulsive) or with current MDD but no personality disorder. To the original CLPS sample of 668 participants, 65 participants were subsequently added to enhance the proportion of minorities. The 4 personality disorders were selected because of their prevalence, their research base in clinical samples,⁹ and their presence in each of the 3 *DSM-IV* clusters. Exclusion criteria included conditions precluding valid interview (eg, active psychosis, acute substance intoxication or withdrawal) or history of schizophrenia or schizoaffective disorder.

The current study sample (Table 1) comprises the 164 individuals having ≥ 12 successive months of follow-up data and who at baseline met *DSM-IV* diagnostic criteria for BPD and ≥ 1 of 6 *DSM-IV* anxiety disorders: GAD ($n=42$), OCD ($n=36$), panic disorder with agoraphobia ($n=39$), panic disorder without agoraphobia ($n=36$), social phobia ($n=48$), and PTSD ($n=88$). Of the 164 participants, 75% were women and mean age at intake was 31.8 years ($SD=7.9$). Sixty-eight percent were white; 12%, black; and 10%, Hispanic. Fifty-eight percent were single, 22% were married or cohabiting, and 20% were separated, divorced, or widowed.

The CLPS recruited 243 participants with baseline BPD. No significant demographic or diagnostic differences emerged between BPD participants with ($n=222$) and without ($n=21$) 12 months of follow-up data. The 12-month follow-up sample included over 90% of participants recruited with baseline BPD. Twenty-nine of the 222 BPD participants with 12 months of follow-up lacked a baseline diagnosis of *any DSM-IV* Axis I disorder and were therefore excluded from the current study sample. Of the remaining 193 BPD participants with at least 12 months of follow-up data and at least 1 co-occurring *DSM-IV* Axis I disorder, 29 participants

- The relapsing and remitting longitudinal courses of borderline personality disorder (BPD) and anxiety disorders influence each other in complex ways.
- Clinicians should prioritize treatment of BPD in the presence of co-occurring generalized anxiety disorder or social phobia.
- Clinicians should treat BPD concurrently with panic disorders, obsessive-compulsive disorder, or posttraumatic stress disorder when these co-occur.

Clinical Points

were excluded for not meeting baseline criteria for any of the 6 *DSM-IV* anxiety disorders studied, leaving $n=164$.

Although no significant demographic differences emerged between the study sample ($n=164$) and participants excluded for lacking baseline comorbid *DSM-IV* anxiety disorders ($n=29$), excluded participants had significantly lower rates of comorbid avoidant personality disorder (40% vs 63%, $\chi^2=6.3$, $P<.01$) and obsessive-compulsive personality disorder (OCPD; 17% vs 37%, $\chi^2=4.4$, $P<.05$) and higher rates of alcohol use disorders (52% vs 16%, $\chi^2=18.0$, $P<.0001$) and drug use disorders (62% vs 16%, $\chi^2=29.9$, $P<.0001$). The lower avoidant personality disorder and OCPD rates among participants without baseline anxiety disorders inversely complement evidence of elevated rates of comorbid anxiety disorders among individuals having these 2 personality disorders.¹⁶

All subjects were evaluated at baseline with the Diagnostic Interview for *DSM-IV* Personality Disorders (DIPD-IV)¹⁷ and Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID-I)¹⁸ by clinically experienced interviewers trained particularly to distinguish Axis I psychopathology from Axis II personality traits. Participants were reinterviewed at 6 months, 12 months, and 1-year intervals thereafter for 10 years. The study was conducted between 1997 and 2009. Interrater and test-retest κ values for BPD ranged from fair to good, 0.68 and 0.69, respectively.¹⁹ For anxiety disorders, interrater reliability and test-retest reliability were 0.63 and 0.44 for GAD, 0.57 and 0.60 for OCD, 0.65 and 0.65 for panic disorder, 0.63 and 0.59 for social phobia, and 0.88 and 0.78 for PTSD.¹⁹ These κ values were fair to good for GAD, OCD, panic disorder, and social phobia and were excellent for PTSD.

Borderline personality disorder was assessed yearly with the Diagnostic Interview for *DSM-IV* Personality Disorders-Follow Along Version,²⁰ which recorded monthly variations in criteria. Reliability was good ($\kappa=0.70$) and rater drift minimal.⁷ Anxiety disorders were assessed with psychiatric status ratings (PSRs) from the Longitudinal Interval Follow-up Evaluation,²¹ which records weekly variations in *DSM-IV* criteria for these Axis I disorders. The CLPS designed and implemented these measures to examine short-interval changes in BPD and anxiety disorder criteria and to explore their interactions. We used a 3-point scale consistent with prior CLPS studies of anxiety disorders¹³: PSR = 1, no symptoms/full remission from diagnosis; PSR = 2, moderate symptoms not meeting full diagnostic criteria; and PSR = 3, symptoms meeting full diagnostic criteria.

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For current analyses, participants followed for anxiety disorders were considered remitted if they reported ≥ 8 successive weeks with PSRs < 2 , ie, minimal or no symptoms. For BPD, we used a parallel definition for remission (≥ 2 months with ≤ 2 of the 9 *DSM-IV* criteria, well below the *DSM-IV* diagnostic threshold of 5 criteria). Some earlier CLPS reports^{7,22} defined BPD remission and relapse based on 12 months' duration, consistent with the historical assumption that personality disorders are less susceptible to change. Here, as in previous reports examining BPD interactions with anxiety¹³ or mood disorders,¹⁵ the shorter-term, 2-month definition of BPD remission provides an indicator of change parallel to anxiety disorder remission, recognizing that personality disorders may remit.

Participants who remitted from an anxiety disorder were considered relapsed if they met full *DSM-IV* diagnostic criteria for at least 4 successive weeks following a remission, a measure consistent with previous CLPS report.¹³ Borderline personality disorder relapse was defined as ≥ 2 successive months endorsing ≥ 5 BPD criteria (*DSM-IV* threshold) following remission, again consistent with prior CLPS¹³ and other research.^{21,23} These remission and relapse definitions have wide usage in longitudinal investigations of Axis I and II disorders.^{12,23} Analyses considered only the first remission and first relapse among participants reporting multiple events.

Statistical analyses used SAS version 9.2.²⁴ Cox proportional hazards regression analysis²⁵ with time-varying covariates examined whether changes in the courses of clinical disorders in diagnostic pairs were correlated or independent, ie, whether improvement or worsening in both disorders occurred around the same time. We used proportional hazards regression because the key analyses involve within-subject change: the extent of temporal coupling between changes in one disorder and changes in another disorder. Using time-varying variables to predict survival outcomes is considered an optimal use of proportional hazards regression methodology.^{26,27} Analyses were conducted for all BPD-anxiety disorder pairings (cases with both BPD and anxiety disorder at baseline) comprising ≥ 20 participants. Analyses excluded agoraphobia without panic disorder, which only 1 BPD subject had. For each BPD-anxiety disorder pair, 4 Cox regressions evaluated effects of changes in the anxiety disorder on BPD event (remission, relapse) and effects of changes in BPD criteria on anxiety disorder event (remission, relapse) within a 1-month timeframe. The time-varying predictor for BPD events was the anxiety disorder PSR for the last week of the month preceding the BPD event. In predicting anxiety disorder events, the time-varying predictor was BPD symptom severity (full criteria; partial criteria [> 2 but less than full criteria]; minimal criteria [0–2]) for the month preceding the anxiety disorder event. The size of the association was estimated by the hazard ratio (HR) value, with an HR of 1.5–2.0 considered a medium effect and an HR ≥ 2.0 , a large effect.²⁸ When using Cox regressions to determine (1) impact of *DSM-IV* anxiety disorder symptomatology

Table 1. Baseline Characteristics of Study Sample

Characteristic	Sample (n = 164)
Gender, n (%)	
Female	123 (75)
Male	41 (25)
Race, n (%)	
White	111 (68)
Black	20 (12)
Hispanic	17 (10)
Other	16 (10)
Age, mean (SD), y	31.82 (7.92)
Hollingshead-Redlich score, mean (SD)	3.48 (1.03)
Education, n (%)	
< High school	24 (15)
High school diploma	37 (23)
Some college	66 (40)
College graduate	9 (5)
Postgraduate education	28 (17)
Marital status, n (%)	
Single	95 (58)
Married	25 (15)
Living together	12 (7)
Separated	13 (8)
Divorced	16 (10)
Widowed	3 (2)
Axis II disorder, n (%)	
Borderline	164 (100)
Avoidant	103 (63)
Obsessive-compulsive	61 (37)
Schizotypal	26 (16)
Anxiety disorder, n (%)	
Generalized anxiety disorder	42 (26)
Panic with agoraphobia	39 (20)
Panic without agoraphobia	36 (19)
Social phobia	48 (29)
Obsessive-compulsive disorder	36 (22)
Posttraumatic stress disorder	88 (54)
Any non-posttraumatic stress disorder anxiety disorder	119 (72)
No. of anxiety disorders, n (%)	
1	81 (49)
2	52 (32)
3	20 (12)
≥ 4	11 (7)

on BPD course and (2) impact of BPD symptomatology on anxiety disorder course, we set the family-wise error rate for the 2 sets of outcomes at 0.05 (2-tailed). Missing data and different overlaps due to subsets having remitted or relapsed account for sample variations in the reported results from baseline diagnostic groups (Tables 2 and 3).

RESULTS

Table 1 shows baseline rates of comorbid *DSM-IV* anxiety disorders among the borderline patient sample. Posttraumatic stress disorder was the most prevalent baseline comorbidity (54%). Few borderline patients (19%) had more than 2 comorbid baseline anxiety disorders.

Course of BPD and Anxiety Disorders

We first examined the 10-year courses of BPD and comorbid anxiety disorders independently. Of the 164 participants, 138 (84%) experienced BPD remission by year 10. Of these 138, 14% subsequently experienced BPD relapse. Remission among co-occurring disorders was highest for panic disorder with agoraphobia (100%), followed by panic

Table 2. Course of Borderline Personality Disorder Influencing Anxiety Disorder Remission and Relapse

Anxiety Disorder	n	No. of Events	Hazard Ratio	95% CI	χ^2	P
Remission						
Generalized anxiety disorder	42	33	0.65	0.44–0.96	4.60	.032
Panic disorder with agoraphobia	39	39	0.99	0.64–1.60	0.02	.987
Panic disorder without agoraphobia	36	32	0.92	0.55–1.56	0.09	.770
Social phobia	48	36	0.73	0.51–1.07	2.55	.110
Obsessive-compulsive disorder	36	25	0.66	0.43–1.03	3.20	.074
Posttraumatic stress disorder	88	73	0.57	0.44–0.75	16.36	<.000
Relapse						
Generalized anxiety disorder	33	25	1.16	0.75–1.79	0.46	.501
Panic disorder with agoraphobia	39	20	1.42	0.84–2.39	1.68	.196
Panic disorder without agoraphobia	32	18	0.99	0.60–1.68	0.01	.992
Social phobia	36	12	1.87	1.01–3.64	3.73	.043
Obsessive-compulsive disorder	25	12	1.62	0.82–3.21	1.97	.160
Posttraumatic stress disorder	73	28	0.81	0.51–1.27	0.87	.352

Table 3. Course of Anxiety Disorder Influencing Borderline Personality Disorder Remission and Relapse

Anxiety Disorder	n	No. of Events	Hazard Ratio	95% CI	χ^2	P
Remission						
Generalized anxiety disorder	42	37	1.02	0.71–1.48	0.02	.902
Panic disorder with agoraphobia	39	33	0.79	0.23–2.70	0.15	.698
Panic disorder without agoraphobia	36	29	0.85	0.56–1.29	0.60	.439
Social phobia	48	37	0.77	0.52–1.15	1.62	.204
Obsessive-compulsive disorder	36	31	0.74	0.48–1.14	1.82	.178
Posttraumatic stress disorder	88	74	0.97	0.73–1.28	0.06	.810
Relapse						
Generalized anxiety disorder	37	6	0.46	0.15–1.48	2.19	.139
Panic disorder with agoraphobia	33	2	1.08	0.62–3.89	0.08	.775
Panic disorder without agoraphobia	29	4	1.18	0.37–3.73	0.43	.782
Social phobia	37	7	0.60	0.24–1.52	1.17	.287
Obsessive-compulsive disorder	31	3	1.52	0.40–5.77	0.37	.544
Posttraumatic stress disorder	74	15	1.90	1.01–3.90	4.43	.044

disorder without agoraphobia (92%), PTSD (87%), GAD (82%), OCD (77%), and social phobia (76%). Relapse (after prospectively observed remission) was highest for GAD (78%), then panic disorder without agoraphobia (58%), panic disorder with agoraphobia (53%), OCD (50%), PTSD (40%), and social phobia (35%).

Next, we examined reciprocal interactions of the symptomatic courses of BPD and anxiety disorders. As Table 2 illustrates, BPD worsening significantly decreased likelihood of remission from GAD (HR = 0.65, $P < .05$), PTSD (HR = 0.57, $P < .001$), and, at trend level, OCD (HR = 0.66, $P = .07$). Worsening of BPD also significantly increased likelihood of social phobia relapse (HR = 1.87, $P < .05$). Monthly fluctuations in symptoms of co-occurring disorders did not significantly influence BPD course, with 1 exception. Worsening of PTSD significantly increased likelihood of BPD relapse by a factor of almost 2 (HR = 1.90, $P < .05$) (Table 3).

To explore the apparent difference between these findings and the MSAD results, Cox regressions were refitted to adopt model specifications used in MSAD's 6-year report.¹¹ Baseline covariates selected in the 6-year MSAD report were controlled for, including participant age, gender, race, socioeconomic status, global functioning, and prior treatment. Paralleling this MSAD report, analyses considered effects of (1) presence/absence of PTSD or (2) presence/

absence of other anxiety disorders in aggregate on BPD remission at 2-year intervals. Thus modified, the absence of PTSD significantly increased likelihood of BPD remission (HR = 1.48, $P < .05$). Unlike the MSAD report, however, presence of anxiety disorders in aggregate did not affect BPD remission (HR = 0.91, $P = .43$).

DISCUSSION

This study found that BPD negatively affects the course of some anxiety disorders but not others, and that most anxiety disorders, excepting PTSD, minimally affect BPD. We discuss these interactions, then review implications for treatment and nosology.

Influence of BPD on Anxiety Disorder Remission

The lack of influence of BPD improvement on remission for most anxiety disorders generally confirms and extends findings from earlier clinical follow-ups.^{11–13} That monthly BPD improvement predicted PTSD remission the following month corroborates our 2-year results¹² and MSAD 6-year results.¹¹ The CLPS 7-year finding that baseline presence of BPD did not diminish likelihood of PTSD remission complements our current findings showing monthly interactions between BPD and PTSD.¹³

Improvement in BPD predicted GAD remission in the following month, a finding consistent with GAD occurring as an epiphenomenon of BPD. This extends 2-year CLPS results wherein a similar trend was nonsignificant.¹² Significance resulted from our greater statistical power (2-year report: 15 remission events from 33 patients; 10-year report: 33 remission events from 42 patients).

Influence of BPD on Anxiety Disorder Relapse

Over 10 years, worsening BPD pathology significantly predicted next-month social phobia relapse. Monthly changes in BPD course did not influence relapse of other anxiety disorders studied. Interestingly, the 7-year CLPS follow-up found BPD baseline presence significantly increased likelihood of OCD relapse.¹³ Borderline patients who self-mutilate have more obsessive-compulsive symptoms,²⁹ and self-injury is more severe early in BPD course.³⁰ More self-mutilation and OCD behaviors earlier in BPD course may reflect impaired impulse control that characterizes early stage BPD.⁷ Subsequent improvement in impulsivity may contribute to the rapid remission of self-mutilation³¹ in parallel with improvement in OCD, which remits in 60% of borderline patients by 2-year follow-up and 77% by 10-year follow-up.⁵ Monthly variation in BPD criterion count over 10 years, during which underlying impulsivity has largely remitted, predicts OCD relapse less than did baseline BPD presence at 7 years.

Influence of Anxiety Disorders on BPD Remission

Fluctuations in anxiety disorders' courses did not influence BPD remission over 10 years, corroborating our 2-year follow-up.¹² When we reanalyzed our data using the strategy from the 6-year MSAD report,¹¹ absence of PTSD increased likelihood of BPD remission, whereas anxiety disorders in aggregate had no effect.

Influence of Anxiety Disorders on BPD Relapse

Among the anxiety disorders, only PTSD had a course predicting BPD relapse. Prior reports have similarly found that PTSD adversely affects BPD course.^{11,32} We previously found that stressful life events, particularly interpersonal stressful events, precede declines in psychosocial functioning among borderline patients.³³ Stressful interpersonal events may have triggered the synchronized relapses we observed over 10 years in BPD and PTSD.

As neither GAD nor social phobia course predicted BPD course, the unidirectional influence of BPD on these 2 disorders suggests that GAD and social phobia arise as secondary state expressions extending from more fundamental borderline traits. Perceived social threats may trigger generalized fearfulness among borderline patients. That worsening BPD course predicts social phobia relapse is consistent with borderline patients' fears of separation and abandonment, increasing their propensity for social fears and withdrawal.

Obsessive-compulsive and panic disorders had no longitudinal interactions with BPD over a decade. For panic

disorder, absence of significant interaction with BPD may suggest that most panic attacks in borderline patients are better accounted for by other *DSM-IV* disorders, such as substance use, social phobia ("eg, occurring on exposure to feared social situations"), and PTSD ("eg, in response to stimuli associated with a severe stressor"), which *DSM-IV* lists as exclusion criteria for panic disorder. Alternatively, panic attacks constituting an independent syndrome, unrelated to posttraumatic stress or to interpersonal triggers,³⁴ may simply co-occur with BPD over time.

Clinical Implications

Clinicians planning treatment for patients with BPD and co-occurring OCD or panic disorders should treat these as independent conditions, as they might BPD and bipolar disorder.¹⁵ In contrast, our findings that BPD improvement predicts GAD and PTSD remission and BPD worsening predicts social phobia relapse mean that BPD's co-occurrence may help explain persistent variants of these 3 disorders, just as it demonstrably affects major depressive disorder.^{15,35,36} Generalized anxiety disorder and social phobia symptoms may occur as epiphenomena of BPD; alternatively, BPD may amplify subthreshold symptoms of these disorders. Thus, borderline patients not achieving sustained GAD or social phobia remission most likely suffer principally from BPD, which clinicians should assess and target as the clinical priority during treatment planning to optimize the prognosis of these co-occurring disorders.¹⁴ The uniquely strong and reciprocal interactions of BPD and PTSD suggest that neither of these disorders should be treated independently. Therapies expediting BPD remission, or sustainably reducing its symptoms, would logically expedite GAD and PTSD remission and delay social phobia relapse.

That BPD worsens GAD, social phobia, and PTSD course may be understood according to emerging dimensional models in which anxiousness is a primary BPD phenotype, and dysfunctions of internal threat management systems cause emotional dysregulation when interpersonal challenges arise.^{37,38} Dimensional models extend our understanding of these diagnostic interactions, as *DSM-IV* symptom changes do not fully overlap with shifts in dimensional anxiety measures.³⁹

Strengths of this study include its large sample size, reliable assessments, 10-year prospective follow-up, unprecedented analysis of anxiety disorder effects on BPD relapse, and the quality of our CLPS data set involving short-interval ratings that permit novel time-varying interaction analyses. One study limitation is that limited, nonrandom treatment data in a naturalistic follow-along study cannot explain course fluctuations or interactions between disorders. For instance, we cannot know if treatment with selective serotonin reuptake inhibitors promoted synchronous improvements in BPD and anxiety disorders.

This naturalistic study invites future hypothesis-driven clinical treatment trials. Our results suggest future investigations should assess whether BPD-focused

treatments promote GAD and PTSD remission and prevent social phobia relapse and whether treatments targeting PTSD prolong BPD remission. Research should assess differences in duration of remission and relapse for the disorders we studied and the relationship of stressful life events to relapse, particularly for BPD and PTSD. Studies

should examine the influence of other comorbid personality disorders on the time-varying course of anxiety disorders. Our results suggest BPD generally exerts greater effect on the course of some anxiety disorders than vice versa. The exception is the reciprocal interaction found between BPD and PTSD.

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REFERENCES

- McGlashan TH, Grilo CM, Skodol AE, et al. The Collaborative Longitudinal Personality Disorders Study: baseline Axis I/II and II/II diagnostic co-occurrence. *Acta Psychiatr Scand.* 2000;102(4):256–264.
- Yen S, Shea MT, Battle CL, et al. Traumatic exposure and posttraumatic stress disorder in borderline, schizotypal, avoidant, and obsessive-compulsive personality disorders: findings from the collaborative longitudinal personality disorders study. *J Nerv Ment Dis.* 2002;190(8):510–518.
- Zimmerman M, Mattia JI. Axis I diagnostic comorbidity and borderline personality disorder. *Compr Psychiatry.* 1999;40(4):245–252.
- Zanarini MC, Frankenburg FR, Dubo ED, et al. Axis I comorbidity of borderline personality disorder. *Am J Psychiatry.* 1998;155(12):1733–1739.
- Silverman MH, Frankenburg FR, Reich DB, et al. The course of anxiety disorders other than PTSD in patients with borderline personality disorder and Axis II comparison subjects: a 10-year follow-up study. *J Pers Disord.* 2012;26(5):804–814.
- Zanarini MC, Hörz S, Frankenburg FR, et al. The 10-year course of PTSD in borderline patients and axis II comparison subjects. *Acta Psychiatr Scand.* 2011;124(5):349–356.
- Gunderson JG, Stout RL, McGlashan TH, et al. Ten-year course of borderline personality disorder: psychopathology and function from the Collaborative Longitudinal Personality Disorders study. *Arch Gen Psychiatry.* 2011;68(8):827–837.
- Zanarini MC, Frankenburg FR, Reich DB, et al. Attainment and stability of sustained symptomatic remission and recovery among patients with borderline personality disorder and axis II comparison subjects: a 16-year prospective follow-up study. *Am J Psychiatry.* 2012;169(5):476–483.
- Gunderson JG, Shea MT, Skodol AE, et al. The Collaborative Longitudinal Personality Disorders Study: development, aims, design, and sample characteristics. *J Pers Disord.* 2000;14(4):300–315.
- Skodol AE, Gunderson JG, Shea MT, et al. The Collaborative Longitudinal Personality Disorders Study (CLPS): overview and implications. *J Pers Disord.* 2005;19(5):487–504.
- Zanarini MC, Frankenburg FR, Hennen J, et al. Axis I comorbidity in patients with borderline personality disorder: 6-year follow-up and prediction of time to remission. *Am J Psychiatry.* 2004;161(11):2108–2114.
- Shea MT, Stout RL, Yen S, et al. Associations in the course of personality disorders and Axis I disorders over time. *J Abnorm Psychol.* 2004;113(4):499–508.
- Ansell EB, Pinto A, Edelen MO, et al. The association of personality disorders with the prospective 7-year course of anxiety disorders. *Psychol Med.* 2011;41(5):1019–1028.
- Skodol AE, Geier T, Grant BF, et al. Personality disorders and the persistence of anxiety disorders in a nationally representative sample. *Depress Anxiety.* 2014;31(9):721–728.
- Gunderson JG, Stout RL, Shea MT, et al. Interactions of borderline personality disorder and mood disorders over 10 years. *J Clin Psychiatry.* 2014;75(8):829–834.
- Grant BF, Hasin DS, Blanco C, et al. The epidemiology of social anxiety disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *J Clin Psychiatry.* 2005;66(11):1351–1361.
- Zanarini MC, Frankenburg FR, Sickel AE, et al. *The Diagnostic Interview for DSM-IV Personality Disorders (DIPD-IV).* Belmont, MA: McLean Hospital; 1996.
- First MB, Gibbon M, Spitzer RL, et al. *Structured Clinical Interview for DSM-IV Axis I Disorders—Patient Edition (SCID-I/P).* New York, NY: Biometrics Research Dept, New York State Psychiatric Institute; 1996.
- Zanarini MC, Skodol AE, Bender D, et al. The Collaborative Longitudinal Personality Disorders Study: reliability of axis I and II diagnoses. *J Pers Disord.* 2000;14(4):291–299.
- Zanarini MC, Shea MT. *The Diagnostic Interview for DSM-IV Personality Disorders—Follow-Along Version (DIPD-FAV).* Belmont, MA: McLean Hospital; 1996.
- Keller MB, Lavori PW, Friedman B, et al. The Longitudinal Interval Follow-up Evaluation: a comprehensive method for assessing outcome in prospective longitudinal studies. *Arch Gen Psychiatry.* 1987;44(6):540–548.
- Grilo CM, Sanislow CA, Gunderson JG, et al. Two-year stability and change of schizotypal, borderline, avoidant, and obsessive-compulsive personality disorders. *J Consult Clin Psychol.* 2004;72(5):767–775.
- Bruce SE, Yonkers KA, Otto MW, et al. Influence of psychiatric comorbidity on recovery and recurrence in generalized anxiety disorder, social phobia, and panic disorder: a 12-year prospective study. *Am J Psychiatry.* 2005;162(6):1179–1187.
- SAS software, Version 9.2 [computer program]. Cary, North Carolina: SAS Institute, Inc; 2008.
- Cox DR. Regression models and life-tables. *J R Stat Soc, B.* 1972;34(2):187–220.
- Kalbfleisch JD, Prentice RL. *The Statistical Analysis of Failure of Time Data.* New York, NY: John Wiley & Sons; 2002.
- Singer JD, Willett JB. *Applied Longitudinal Data Analysis: Modeling Change and Event Occurrence.* New York, NY: Oxford University Press; 2003.
- Schoenfeld DA. Sample-size formula for the proportional-hazards regression model. *Biometrics.* 1983;39(2):499–503.
- McKay D, Kulchick S, Danyko S. Borderline personality and obsessive-compulsive symptoms. *J Pers Disord.* 2000;14(1):57–63.
- Zanarini MC, Frankenburg FR, Reich DB, et al. The 10-year course of physically self-destructive acts reported by borderline patients and axis II comparison subjects. *Acta Psychiatr Scand.* 2008;117(3):177–184.
- Zanarini MC, Frankenburg FR, Reich DB, et al. The subsyndromal phenomenology of borderline personality disorder: a 10-year follow-up study. *Am J Psychiatry.* 2007;164(6):929–935.
- Gunderson JG, Daversa MT, Grilo CM, et al. Predictors of 2-year outcome for patients with borderline personality disorder. *Am J Psychiatry.* 2006;163(5):822–826.
- Pagano ME, Skodol AE, Stout RL, et al. Stressful life events as predictors of functioning: findings from the collaborative longitudinal personality disorders study. *Acta Psychiatr Scand.* 2004;110(6):421–429.
- Gunderson JG, Links PS. *Handbook of Good Psychiatric Management for Borderline Personality Disorder.* Washington, DC: American Psychiatric Publishing; 2014.
- Gunderson JG, Morey LC, Stout RL, et al. Major depressive disorder and borderline personality disorder revisited: longitudinal interactions. *J Clin Psychiatry.* 2004;65(8):1049–1056.
- Skodol AE, Grilo CM, Keyes KM, et al. Relationship of personality disorders to the course of major depressive disorder in a nationally representative sample. *Am J Psychiatry.* 2011;168(3):257–264.
- Livesley WJ. A framework for integrating dimensional and categorical classifications of personality disorder. *J Pers Disord.* 2007;21(2):199–224.
- Livesley J. Toward a genetically-informed model of borderline personality disorder. *J Pers Disord.* 2008;22(1):42–71.
- Brown TA, Barlow DH. A proposal for a dimensional classification system based on the shared features of the DSM-IV anxiety and mood disorders: implications for assessment and treatment. *Psychol Assess.* 2009;21(3):256–271.