

REVIEW

The Case for Shifting Borderline Personality Disorder to Axis I

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Through reviewing what is known about the nature, course, and heritability of borderline personality disorder (BPD), we argue for a reconceptualization of this disorder that would lead to its placement on Axis I. Borderline personality disorder is a prevalent and disabling condition, and yet the empirical research into its nature and treatment has not been commensurate with the seriousness of the illness. We not only review empirical evidence about the etiology, phenomenology, and course of the disorder in BPD but we also address fundamental misconceptions about BPD that we believe have contributed to misunderstanding and stigmatization of the disease. Finally, we suggest future directions for research that might permit the identification of core features of this disorder, with a focus on the importance of naturalistic assessments and of assessments through the course of development.

Key Words: Axis I, Axis II, borderline personality disorder, nosology, specificity, validity

Borderline personality disorder (BPD) is a disabling condition with high morbidity and mortality, yet the empirical research into its nature and treatment has not been commensurate with the seriousness of the illness. Despite recent advances in the treatment of BPD, it remains notoriously difficult to treat effectively, with many patients responding poorly even to the most widely accepted treatment strategies (1). In addition, because the disorder has as cardinal symptoms anger and interpersonal disruptiveness, it is often difficult to form a therapeutic alliance with afflicted patients. These features draw attention away from evidence that BPD is a serious mental disorder that deserves much more investigative scrutiny than it has received. A logical consequence of taking this disorder seriously is to consider reclassifying the disorder into Axis I. This reclassification would, we believe, provide a stimulus to new research into the nature and treatment of this severe illness.

Evidence for the Validity of BPD

The validity of the BPD diagnosis remains a question in the minds of many clinicians, and some doubt its existence altogether (2). A widely accepted approach to validating the boundaries of psychiatric disorders is the set of guidelines established by Robins and Guze (1970) (3), which considers accrual of information from five lines of evidence important for establishing the validity of a mental disorder. These criteria include: 1) a careful delineation of symptoms; 2) information about the course of illness; 3) evidence of familial clustering; 4) predictable treatment response, especially to somatic treatments; and 5) biological markers (3,4). We review each of these criteria as it relates to BPD.

Core Symptoms of BPD

A Single Diagnostic Construct? The current DSM criteria were developed from observations by experienced clinicians, and it remains a question as to whether these criteria cluster into one syndrome or into independent symptom dimensions. A

factor analysis of symptoms in a large sample of BPD patients ($n = 141$) revealed three factors: disturbed relatedness (unstable relationships, identity disturbance, and chronic emptiness), behavioral dysregulation (impulsivity and suicidality/self-mutilatory behavior), and affective dysregulation (affective instability, inappropriate anger, and efforts to avoid abandonment) (5). These factors were replicated in the CLPS (Collaborative Longitudinal Personality Disorders Study)—a prospective descriptive study of a large sample ($n = 668$) of patients with personality disorders, including schizotypal, borderline, avoidant, and obsessive-compulsive personality disorders and major depressive disorder (MDD) with no personality disorder (6).

Recent data, however, raise questions about the 3-factor model and instead suggest a single underlying core that leads to the diverse symptoms of BPD. Although Sanislow found that the 3-factor model yielded a better fit with their data than a single-factor model, the factors identified (disturbed relatedness, behavioral dysregulation, and affective dysregulation) were highly intercorrelated ($r = .90, .94, \text{ and } .99$, respectively), lending support to a single overarching BPD construct. A subsequent factor analysis identified three similar factors but also concluded that the factors were too highly intercorrelated to be considered separate factors (7). Providing even further evidence for BPD as a unified syndrome, a recent large study explored several 1-, 3-, and 4-factor models of DSM-IV BPD criteria and concluded that the BPD criteria describe a single construct rather than multiple co-occurring syndromes (8). Finally, a confirmatory factor analysis of DSM-III-R BPD criteria in a large clinical and non-clinical sample showed that a single factor fit the data best (9). This study also showed that “frantic efforts to avoid abandonment” was the criterion with the highest specificity and positive predictive power. Affective instability was also highly informative as to BPD diagnosis, whereas identity disturbance and feelings of emptiness were less informative. Even though factor analyses lend support to the presence of a unitary latent diagnostic construct, heterogeneity is observed in the clinical presentation of BPD. This might arise out of the fact that different aspects of the disorder might be present at different times, making the disorder appear quite heterogeneous when observed cross-sectionally. This highlights the importance of a developmental approach to characterizing the core features of BPD.

Specificity of BPD. The high rate of comorbidity with other disorders has also led to skepticism about the validity of the BPD diagnosis. Data from CLPS showed that the Axis I comorbidities most commonly seen with BPD were posttraumatic stress disorder (PTSD) and substance abuse. Although BPD subjects showed a high rate of MDD (79% lifetime), this was not higher than the

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prevalence of MDD across personality disorders (66%–82%). The most common Axis II comorbidities of BPD were antisocial and dependent personality disorders (10). Two-year follow-up found a significant association between BPD and MDD as well as PTSD (11).

The high rate of comorbid mood disorders in BPD has led some to argue that BPD is a bipolar spectrum illness. Empirical support for this view comes from a study following BPD patients, which showed a 15% rate of onset of bipolar I or II disorder over 3 years, compared with no new cases in an other personality disorder (OPD) group (2). Other studies, however, have failed to show elevated rates of bipolar diagnoses in BPD (10,12–14). Longitudinal follow-up of the CLPS sample showed modestly increased rates of bipolar I and II disorders in the BPD compared with the OPD group over 4 years (15). Although evidence suggests a moderately increased risk for bipolar disorder in BPD patients, the risk is not nearly as high as for MDD or substance abuse. Furthermore, if BPD were a bipolar spectrum disorder, one would expect BPD to run in families with bipolar disorder, and evidence suggests that this is not the case (16,17). In addition, if BPD were a bipolar spectrum disorder, then treatment with antidepressant drugs should worsen mood instability, as in bipolar disorder, whereas antidepressant drugs stabilize mood in BPD (18). Taken together, these data support some increased risk for bipolar disorder in BPD but also a heightened risk for other disorders. From a clinical vantage point, BPD is not most fruitfully viewed as a bipolar variant, because the prognosis and treatment recommendations differ substantially. However, the substantial phenotypic resemblance as well as the common comorbidity raise the possibility that BPD might be viewed as an affective spectrum illness as has been previously suggested (4); however, it seems to fit squarely in neither the unipolar nor bipolar group (Supplement 1).

Course/Prognosis

Borderline personality disorder is present in approximately 2% of the general population, making it as prevalent as schizophrenia and bipolar I disorder (19,20). Borderline personality disorder is heavily represented in clinical populations (21), and patients with BPD require extensive mental health services (22–25). The completed suicide rate in BPD approaches 10%, and at least 75% of afflicted individuals attempt suicide at least once (26). Borderline personality disorder is strongly associated with elevated risk of medical emergency room visits (24) and generalized occupational and psychosocial dysfunction (27).

Although BPD is associated with severe symptoms and functional impairment, the prognosis is not as unfavorable as had been previously assumed. Large longitudinal studies have shown that many BPD patients experience improvement and even resolution of borderline features over time, although a subset of patients experience long-term disability (28,29). Specifically, 88% of a sample of patients with BPD achieved remission over 10 years, with approximately one-third of those achieving remission in the first 2 years. Of note, remission in this sample was defined as not meeting the threshold for a full BPD diagnosis (30), but subjects might have continued to be symptomatic. Symptoms of affective instability seem to be the most consistent over time, enduring in many cases over 27 years (28,31).

Heritability and Familiality

Although limited in number, family studies of BPD show that the first-degree relatives of BPD probands are 10 times more likely to have been treated for BPD and significantly more likely to have been treated for MDD than the first-degree relatives of

schizophrenia probands (32). Subsequent family studies of BPD showed that affective instability and impulsivity as well as BPD diagnosis itself were significantly more common in first-degree relatives of BPD patients than of OPD or schizophrenia patients (17,33). In addition, MDD appeared more often in the relatives of BPD than of OPD patients, regardless of whether the BPD proband had a history of MDD (17). To tease apart the transmission of BPD from that of MDD, a study examined BPD outpatients with no history of MDD and demonstrated an increased risk for depression in the first-degree relatives, suggesting a common etiologic factor linking the two disorders (34).

Family studies indirectly reflect genetic heritability; however, only twin studies provide definitive evidence for it. Limited twin study data are available for BPD. One such study examining 92 monozygotic twins and 129 dizygotic twins showed that BPD was substantially heritable, with 69% of the variance in BPD accounted for by genetic factors (35). A recent study of Chinese twins showed similar heritability rates for cluster B personality disorders of 65%; however, BPD was not independently assessed (36). In a study of twin pairs in childhood, parents assessed personality disorder features in their monozygotic and dizygotic twins and demonstrated that 76% of the variance in BPD features seems to be genetic (37). Although the number of studies showing heritability for BPD are few, all such studies undertaken show substantial heritability.

Predictability of Treatment Response

We have reviewed evidence for the validity of BPD that meets the first three criteria for diagnostic validity: a delineation of symptoms; information about the course of BPD; and evidence of familial clustering. A feature that does set BPD apart from other mental illnesses is the absence of a predictable, robust response to somatic treatments. This is problematic not only because it leaves patients without the benefit of highly effective pharmacotherapy but also because psychiatrists often use information from pharmacologic treatment response as an avenue of investigation into the neurobiology of mental illnesses. The fact that depression, for example, responds to antidepressant drugs gave rise to the monoamine hypothesis of depression. The fact that conventional antipsychotic drugs block D₂ receptors gave rise to the dopamine hypothesis of schizophrenia. Evidence for the importance of cellular signaling pathways in bipolar disease came out of exploration of the mechanism of action of lithium and other mood stabilizers. The contrasting reality that BPD patients seem to respond to medications in a circumscribed and often transient manner, combined with the fact that the agents that have proven somewhat helpful come from almost all known psychotropic drug classes, has meant that a unifying theory of the biological underpinnings of BPD has not yet emerged. Much more needs to be learned about the neurobiology of BPD to permit the development of treatments specific to this disorder.

Although the modest efficacy and wide diversity of medication classes used in BPD present clinical and theoretical challenges, we believe that a feature of the disorder itself, the fluctuating symptoms of BPD, also contributes to the difficulty in defining highly effective pharmacotherapy for BPD. It might be that the widely used techniques in medication trials to assess treatment response—brief cross-sectional assessments of an individual in a clinical research office—might not be optimal to detect response in BPD. Because the symptoms of BPD fluctuate dramatically and flare up especially in the context of close relationships, cross-sectional assessments might be inadequate to detect a response to treatment with any sensitivity or specificity.

To a greater degree than other psychiatric populations, BPD patients might seem asymptomatic or highly symptomatic at the particular moment, depending on an immediate antecedent interpersonal interaction or on the relationship developed with the specific staff member assessing them. A better approach would be to assess patients across multiple situations, such that both average levels of symptoms and variability in symptoms over time can be measured. Methods for ecological momentary assessment of symptoms are becoming more readily available, including event-contingent recording methods (38), in which patients report on their behavior and mood in relation to specific social interactions over time. This method allows for the documentation of the naturalistic contexts in which symptoms arise and might provide a more clinically relevant assessment of treatment response. A recent study using event-contingent recording in BPD patients proved its feasibility in this population (39).

Biological Markers

Although there are no clear neurobiological markers for BPD, the absence of such markers is a ubiquitous concern across all psychiatric diagnoses. In BPD, as in other psychiatric disorders, findings from brain imaging studies, neurochemical markers, and genetic studies do not point to a simple pathophysiology. The body of research on neurobiological abnormalities in BPD has been thoroughly reviewed elsewhere (40,41). Briefly, studies employing a variety of methods have found widely replicated decreases in serotonergic responsiveness in BPD (42–45). These findings have informed neuroimaging research in BPD, in which a predominance of studies have employed pharmacologic probes of serotonin (46–50) or positron emission tomography ligands targeting serotonin receptors (51,52). A limitation of these findings is that abnormalities have tended to relate less to the overarching diagnosis than to symptoms dimensions (53). Another limitation is that the scope of neurochemical systems studied is narrow, focusing almost exclusively on serotonin. An extremely limited number of studies have explored other neurotransmitter systems in BPD, including dopamine (54) and acetylcholine (55).

Brain imaging studies have provided evidence for disruption of the neural circuitry in BPD (reviewed elsewhere [56]). However, two relatively consistent findings from brain imaging studies emerge: 1) BPD patients seem to have decreased volume in anterior cingulate gyrus (ACG), especially of gray matter, compared with healthy control subjects (57–59); 2) positron emission tomography studies have shown that orbital frontal cortex (OFC) and ACG are less active in BPD than control subjects (46–49,60). Functional magnetic resonance imaging (fMRI) studies have shown this less consistently (61–63), although the orbital floor is evaluated less effectively with fMRI, because of susceptibility artifact. Thus, brain regions, such as OFC and ACG, that normally put the brakes on expressions of emotions, might fail to come “on line” in BPD when needed. Although brain imaging findings in BPD are suggestive, it is important to note that many of the circuits implicated in BPD are the same as those implicated in MDD and bipolar disorder (64,65). For example, decreased subgenual ACG has been shown in depression (66–68) and in some studies of bipolar disorder (69,70). In addition, functional imaging studies have shown decreased activation in areas of prefrontal cortex in MDD (71), bipolar disorder (72), and PTSD (73). Clearly, new approaches in brain imaging will be needed to develop specific neural circuitry models for each of these disorders.

To move forward in understanding BPD specifically, it will be necessary to target those symptoms that are specific to BPD. Although affective dysregulation is a core feature of BPD (27,53,74) and might be the most prevalent and enduring symptom (75), it is also seen in bipolar disorder and to some degree in MDD. Too little attention has been paid to the interpersonal disruptions that are central to BPD. A recent review has argued that the relational style characteristic of BPD is “intense and unstable, marked . . . by abandonment fears and by vacillating between idealization and devaluation (and that this style offers) the best discriminators for the diagnosis” of BPD (76). Evidence for this view stems from consistent observation of profound interpersonal impairment in BPD (9,27,77), with more impairment in interpersonal functioning in BPD than in MDD, obsessive-compulsive disorder or OPDs (78). Furthermore, suicide attempts in BPD are more often associated with interpersonal stressors than suicide attempts in MDD (79).

Notwithstanding the centrality of interpersonal disruptions in BPD, very little empirical work has been done on what underlies these symptoms. One domain that has received some empirical scrutiny is the recognition of facial emotional expression. Borderline personality disorder patients correctly identify emotional expressions even more sensitively than healthy control subjects; however, they tend to over-read anger in neutral faces (80–83). More research into emotional information processing in BPD would be very helpful, because these skills are essential for navigating interpersonal relationships. If BPD patients over-read and misread emotional cues, this might help to explain the puzzling symptom of exaggerated emotional responses in interpersonal interactions. If indeed BPD patients over-read emotional responses and this deficit is present from early childhood, this might play a role not only in the disrupted interpersonal relationships but also, possibly, in the development of emotion dysregulation. Infants and children learn how to modulate emotions through relationships with caregivers (84), and individuals who continuously misread emotional cues are robbed of this basic mechanism of learning how to modulate emotion. New research into this aspect of BPD will be enhanced by rapid developments in the neuroscience of social interaction.

Implications of Shifting BPD to Axis I

The distinction between Axis I and Axis II disorders in the DSM system has received little empirical investigation, and the lack of empirical grounding for many assumptions that underlie the distinction has been well-argued by Siever and Davis (85). Some of the most compelling of these arguments include the fact that the current DSM-IV-TR definition of a personality disorder as “an enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual’s culture, is pervasive and inflexible, has an onset in adolescence or early adulthood, is stable over time and leads to distress or impairment” could well apply to many Axis I disorders also. For example, schizophrenia confers pervasive and enduring patterns of behavior that are inflexible, typically with onset in adolescence that become chronic in nature. However, we do not view schizophrenia as a disorder of “character.” Clearly, if schizophrenia fits the DSM definition of a personality disorder, the definition is overly inclusive. Simply stating that a character disorder is not better accounted for by an Axis I disorder begs the question of how to set personality disorders apart from Axis I disorders. Major depressive disorder is perhaps the prototype of an episodic disorder, yet even MDD can be associated with chronic mood symptoms that interfere with functioning.

Another feature used to distinguish personality disorders from other psychiatric illnesses is that personality disorders have traditionally been conceptualized as resulting from environmental factors, whereas Axis I disorders have been viewed as having a “biological” or “organic” basis (85). As reviewed in the preceding text, however, twin studies suggest that BPD is quite heritable. Although environmental stresses might play a role in the development of BPD, this is the case with many Axis I disorders as well, including MDD, in which environmental stresses in conjunction with vulnerability genes can give rise to the disorder (86). Thus neither the presentation nor the etiology of BPD differentiates it clearly from disorders classified on Axis I.

Not only is the distinction between Axis I and Axis II disorders problematic but BPD in particular does not fit in with traditional conceptualizations of personality disorders. For example, personality disorders have been viewed as egosyntonic, whereas the symptoms of BPD are often quite egodystonic, leading patients to seek treatment for their symptoms (87).

The current revision of DSM recognizes the difficulty in distinguishing Axis I from Axis II and is considering the possibility of abolishing Axis II or the reclassification of some Axis II disorders to Axis I (L.J. Siever, personal communication, September 2007). The present review does not take on that debate but instead argues that in light of what is known about BPD, this disorder specifically reaches the threshold for reclassification.

Misconceptions about BPD

So where do doubts about the validity of BPD as a major mental disorder come from? Although some of the difficulty in taking BPD seriously might relate to the complexity and heterogeneity of the symptoms, the high level of comorbidity, and poor medication response, these features are not unique to BPD. We believe that the evidence for the Robins and Guze criteria strongly argue for the consideration of BPD as a serious mental illness, and as such, BPD ought to be classified on Axis I.

We believe two fundamental misconceptions have contributed to misunderstanding and have been impediments to serious investigative scrutiny of this illness. The first relates to the name “borderline personality disorder” itself, which implies that this disease lies on the “border” between two states, a view that has its origins in early psychoanalytic conceptualizations of the disorder that are no longer widely accepted. A second misconception is that BPD is the direct consequence of early life trauma rather than a phenotypic expression of a vulnerability to symp-

oms and behaviors that then emerge in the context of past and present-day stressful life events.

The misconception that BPD is the result exclusively of environmental influences and not also influenced by heredity is not well-grounded empirically. The view that the cause of BPD is childhood trauma has held so fast that some therapists have used “recovered memory therapies” in the treatment of BPD, encouraging patients to file lawsuits even with little evidence of childhood trauma and no spontaneous memory of trauma (88). The field has moved strongly to condemn this approach.

The finding of heritability brings into serious question the view that trauma is the sole etiology of BPD. It suggests, alternatively, the possibility of an innate hypersensitivity to stress. A traumatic etiology for BPD is also brought into question by the consideration that, because most childhood trauma is perpetrated by family members (89) and this disorder is heritable, the family members perpetrating abuse are more likely than the average population to have BPD themselves. If the caregivers of BPD patients have BPD, they are more likely to have poor frustration tolerance, excessive anger and aggression, and therefore to be at risk for engaging in abuse towards their children. A further source of doubt about the traumatic etiology of BPD is that much of the research done to assess childhood trauma is based on data obtained retrospectively from adults with BPD, which is subject to the “negative halo” recall bias inevitable with already-ill probands (90). This bias might be especially pronounced in BPD patients who, as a group, are highly prone to cast a negative emotional tone over memories of prior experiences (91).

Although skepticism about the traumatic etiology of BPD is warranted, studies have shown that adults with BPD are more likely than those without BPD to give histories of early physical and sexual abuse and of witnessing domestic violence (92). Data from CLPS suggest that BPD is more strongly correlated with childhood abuse and neglect than are MDD or OPDs (93). In a community sample, childhood physical and sexual abuse were not predictors for BPD (94). However, a recent study suggests that childhood physical and sexual abuse are among a number of independent predictors of BPD (95), and a meta-analysis of 21 studies, with over 2000 subjects, looking at BPD and child abuse yielded a pooled effect size of only $r = .28$ (96).

Although childhood sexual abuse specifically has been implicated in BPD, it is not an inevitable prerequisite for the illness's development (97). An estimated 20%–45% of BPD patients have no history of sexual abuse (97), whereas 80% of individuals with sexual abuse histories have no personality pathology (98).

Table 1. BPD and Trauma: Studies Supporting and Undercutting a Traumatic Etiology for BPD

Studies Supporting Trauma Etiology for BPD	Studies Undercutting Trauma Etiology for BPD
<ul style="list-style-type: none"> • Adults with BPD more likely than those without BPD to report early physical and sexual abuse and witnessing domestic violence (92) • Adult BPD predicted by sexual abuse and/or emotional denial by male caretakers and inconsistent treatment by female caretakers (100) • Childhood sexual abuse, separation from parents, and unfavorable parental rearing styles predicted adult BPD (95) • Association of BPD with childhood abuse and neglect more than MDD or schizotypal, avoidant, or obsessive-compulsive personality disorders (93) 	<ul style="list-style-type: none"> • 20%–45% of BPD patients have no history of sexual abuse (97) • 80% of those with sexual abuse histories have no personality pathology (98) • Longitudinal follow-up of children with documented abuse shows a high rate of resilience (99) • Meta-analysis of 21 studies yielded a small pooled effect size ($r = .28$) for BPD/child abuse association (96) • Community samples of personality disorders childhood physical and sexual abuse did not predict BPD (94) • Familial neurotic spectrum disorders, childhood sexual abuse, separation from parents, and unfavorable parental rearing styles independently predicted BPD (95)

BPD, borderline personality disorder; MDD, major depressive disorder.

Table 2. BPD and Genetic Factors: Studies Supporting a Familial/Heritable Role for BPD

Familiality	<ul style="list-style-type: none"> • First-degree relatives of BPD patients are 10× more likely to have BPD and more likely to have MDD than first-degree relatives of schizophrenic patients (32) • Affective instability and impulsivity are more common in first-degree relatives of BPD patients than other personality disorders or schizophrenia, and MDD is more common in the relatives of BPD (17) • In large family study, BPD was more common in relatives of BPD patients than Axis II comparisons (33) • In outpatients with BPD and no history of MDD, an increased risk for MDD was seen in first-degree relatives (34)
Heritability	<ul style="list-style-type: none"> • A twin study of BPD showed a heritability score of .69 (35) • A twin study of cluster B personality disorders showed heritability score of .65 (36) • A twin study of children showed heritability of .76 for BPD symptoms by parental report (37)

BPD, borderline personality disorder; MDD, major depressive disorder.

Longitudinal studies of children followed after a report of child abuse show that a substantial proportion with quite severe abuse remains functionally resilient, with little impairment across social, occupational, and interpersonal domains (99). Unfortunately, longitudinal studies of children with childhood trauma to date have not assessed for BPD (89,99).

Taken together, these results support a model of the etiology of BPD as multifactorial, with childhood abuse as a contributing factor (95) but in which other factors such as family psychiatric history also play an important role (Tables 1 and 2). To clarify more fully the role of childhood trauma in the development of BPD, it will be necessary to follow prospectively children at risk for BPD.

Summary

We have suggested BPD's inclusion among the mood disorders because of the centrality of affective dysregulation symptoms in BPD as well as the comorbidity and co-familiality with MDD. Viewing BPD in this context opens up new avenues for research. One fruitful path in BPD research might be to build upon new findings in depression research (64). This logically would include continued exploration of the circuits implicated in both mood disorder and BPD and to search for diagnostic specificity in these circuits. We have suggested that a fruitful area to pursue will be exploring deficits in social cognition, with particular emphasis on the developmental trajectories of affective symptoms and interpersonal dysfunction in BPD. It is clear, however, that a deeper understanding of the neurobiology of BPD has the potential to open avenues for novel treatments as well as to diminish the stigma that serves to worsen the clinical course and outcome of this already disabling and hard-to-treat illness.

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Supplementary material cited in this article is available online.

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