

# Chapter 10

## Borderline Personality Disorder and Mood Disorders: Longitudinal Course and Interactions

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### Introduction

Borderline personality disorder (BPD) is often misdiagnosed as a mood disorder, especially bipolar disorder [1, 2]. Many variants of bipolar disorder have been conceived, such as bipolar II [3], bipolar III [4], and bipolar IV [5] in order to account for atypical features, a more chronic course, and lack of or adverse responses to standard psychopharmacologic treatments of bipolar disorder. Similarly, major depressive disorder (MDD) may have a more chronic than episodic course with waxing and waning of symptoms or incomplete remission with subthreshold symptoms [6]. Mood disorder diagnostic variants that broaden the definitions of disorders often lead in clinical practice to the inappropriate use of medications in false-positive cases [7], to a proliferation of medication changes, and sometimes to extensive and harmful polypharmacy aimed at addressing clinical problems that may well be the result of BPD, occurring either alone or as a comorbid condition. Since BPD and mood disorders frequently co-occur [8], examining the longitudinal course of BPD and comorbid mood disorders and their interactions over time may shed light not only on the disorder of primary importance but also, as a result, on the need to recognize and treat BPD with psychotherapy [9–11] in order to achieve optimal outcomes in such cases.

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## Naturalistic Studies of Clinical Course in Personality Disorder

Selected results of four large-scale studies of the naturalistic course of personality disorders and mood disorders will be reviewed in this chapter. The studies are the Collaborative Longitudinal Personality Disorders Study (CLPS) [12, 13], the McLean Study of Adult Development (MSAD) [14], the National Epidemiologic Study of Alcohol and Related Conditions (NESARC) [15, 16], and the Children in the Community Study (CICS) [17]. These studies were conducted on patient (CLPS and MSAD) and community (NESARC and CICS) populations, leading to a greater degree of confidence in findings that converge.

### *Collaborative Longitudinal Personality Disorders Study (CLPS)*

The CLPS [12, 13] is a multisite, NIMH-funded longitudinal study of the natural course of personality disorders. Participating sites are at Brown, Columbia (now in collaboration with the University of Arizona), Harvard, Yale, and Texas A&M Universities. The aims of the CLPS have been to determine the stability of personality disorder diagnoses and criteria, personality traits, and functional impairment and to determine predictors of clinical course. The original CLPS sample recruited 668 treatment-seeking or recently treated patients who were diagnosed with one of four DSM-IV personality disorders—schizotypal (STPD), borderline (BPD), avoidant (AVPD), or obsessive-compulsive (OCPD)—or with major depressive disorder (MDD) and no personality disorder. Personality disorders were diagnosed at baseline with the semi-structured Diagnostic Interview for Personality Disorders-IV (DIPD-IV) [18] and confirmed by at least one other personality assessment method. Mood and other nonpersonality disorders were diagnosed with the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) [19]. This original sample was supplemented with the recruitment of 65 additional minority patients to ensure adequate power to test differences between Caucasian, African-American, and Hispanic patients with the four personality disorders on various outcomes. The original CLPS sample completed 10 years of annual follow-up.

To provide more detailed data on persistence vs. change in personality disorder criteria and diagnoses, the interview used to make intake personality disorder diagnoses, the DIPD-IV, was modified in the CLPS to provide monthly ratings of the presence or absence of individual criteria for each of the four disorders under study. This approach was based on the method used to track the course of Axis I disorders in the study, the Longitudinal Interval Follow-up Evaluation (LIFE) [20], resulting in similar ratings of the course of both personality disorders and Axis I disorders in terms of the timing of assessments and the levels of symptoms or criteria present. The monthly ratings of personality disorder criteria also allow determination of various definitions of improvement or remission, based on the number of criteria present and the length of time present or absent. The LIFE has been the central

measure of course used in the most comprehensive longitudinal study to date of mood disorders, the Collaborative Depression Study (CDS) [21]. The similarity of methods allows for a comparison of the stability and course of the four CLPS personality disorders with that of several mood disorders and for documenting interactions in the course of personality disorders and mood disorders over time. Primary questions for the CLPS have been whether personality disorders are more diagnostically stable than mood disorders and, when changes occur, which disorder appears to exert an effect on the other, as evidenced by the relative timing of changes in the expression of each type of disorder.

### ***The McLean Study of Adult Development (MSAD)***

The MSAD [14] was the first NIMH-funded prospective study of the course and outcome of borderline personality disorder. The MSAD sample consists of 290 patients with BPD, diagnosed by both the DIPD-IV [18] and the Revised Diagnostic Interview for Borderlines [22], who were inpatients at McLean Hospital in the early 1990s, and 72 other hospitalized patients who were diagnosed with other personality disorders (OPDs). This comparison group included approximately 4 % with cluster A personality disorders, 18 % with other non-borderline cluster B personality disorders, 33 % with cluster C personality disorders, and 53 % with personality disorder not otherwise specified (PDNOS). The sample has been followed every 2 years for more than 16 years. Remission has been defined as no longer meeting criteria for the index personality disorder for a period of at least 2 years.

### ***The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)***

Participants of interest were respondents in Waves 1 and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) [15, 16]. The target population was the civilian non-institutionalized population 18 years and older residing in households and group quarters (e.g., college quarters, group homes, boarding houses, and non-transient hotels) in the United States. Blacks, Hispanics, and adults ages 18–24 were over-sampled, with data adjusted for over-sampling, household- and person-level nonresponse. Of the 43,093 respondents interviewed at Wave 1, census-defined eligible respondents for Wave 2 reinterviews included those not deceased ( $N=1,403$ ); deported and mentally or physically impaired ( $N=781$ ); or on active military duty ( $N=950$ ). In Wave 2, 34,653 of 39,959 eligible respondents were reinterviewed, for a response rate of 86.7 %. Sample weights further adjusted for Wave 2 nonresponse [16]. Overall, most respondents were female, white, over the age of 40, married or cohabiting, and had at least a college education.

In-person interviews were conducted at both waves by experienced lay interviewers with extensive training and supervision. Interviewers administered the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV Version (AUDADIS-IV) [23], a fully structured diagnostic interview developed to assess substance use and other mental disorders in large-scale surveys. Computer algorithms produced diagnoses of DSM-IV Axis I disorders and all DSM-IV PDs. Major depressive disorder (MDD) was defined according to DSM-IV inclusion criteria, including all symptom, duration, and clinical significance (i.e., distress or impairment) criteria. Diagnoses additionally required that the disorders be “primary,” i.e., not substance induced or due to a general medical condition.

At Wave 1, criteria for MDD were assessed in two time frames: (1) current, i.e., during the last 12 months, and (2) prior to the last 12 months. At Wave 2, 3 years later, these criteria were again assessed in two time frames covering the time period between Waves 1 and 2. *Persistent* MDD was defined as meeting full criteria for current MDD at Wave 1 and full criteria for MDD throughout the entire 3-year follow-up. *Recurrent* MDD was defined as meeting full criteria at Wave 1 and again during the last 12 months at Wave 2, but not during the first 24 months after the Wave 1 interview. The impact of all DSM-IV personality disorders on the 3-year persistence and recurrence of MDD was examined.

### *The Children in the Community Study (CICS)*

The CICS [17] is a longitudinal study of a representative sample of approximately 800 children, who were originally recruited (with their mothers) in upstate New York in 1975, when they were between 1 and 10 years of age. They have been followed now periodically for 30 years. Originally, the study was designed to assess level of need for children’s services in the community. When first followed-up in 1983, the focus of the study shifted to predictors of Axis I disorders in early adolescence, but an interest in the development of personality disorders in this age group also existed. Using various methods, personality disorders have been assessed four times: in 1983, when the children were at mean age 14; between 1985 and 1986, when they were at mean age 16; between 1991 and 1993, at mean age 22; and between 2001 and 2004, at mean age 33. The relationships of Axis I disorders and personality disorders have been studied over the follow-up periods.

### **Course of BPD and Depressive Disorders**

Borderline personality disorder (BPD) was one of three personality disorders (the others being avoidant and dependent) that were found most often to co-occur with mood disorders, especially depressive disorders, in the CLPS [8]. The severity of depression, recurrence of depressive episodes, and comorbid dysthymic disorder

predicted co-occurrence of major depressive disorder (MDD) with BPD. These results are consistent with the view that a history of a depressive disorder with an insidious onset, recurrence, chronicity, and progression in severity is suggestive of the presence of BPD in young adults.

The 24-month natural course of remission from MDD as a function of personality disorder comorbidity was examined prospectively in the CLPS [24]. The overall remission rate for MDD was 73.5 %. Patients with MDD who had BPD (or STPD or AVPD) as their primary PD diagnosis had a significantly longer time to remission from MDD than did patients with MDD without a co-occurring personality disorder. These personality disorders were robust predictors of slowed remission from MDD even when controlling for other factors often believed to exert a negative prognostic effect on MDD, such as co-occurring dysthymia, other Axis I disorder comorbidity, early age at onset of MDD, and a pattern of MDD recurrence. The relationship of comorbid personality disorder to MDD remission was examined again after 6 years of follow-up [25]. Patients with personality disorders continued to have a significantly longer time to remission of MDD. Of the patients whose MDD remitted, 70 % relapsed. Patients with MDD and comorbid BPD (or OCPD) had significantly shorter times to relapse than patients with MDD and no personality disorder. Research criteria for depressive personality disorder also resulted in a lower likelihood of remission of baseline MDD at 2-year follow-up, while comorbid dysthymic disorder did not [26]. At 6 years, already recurrent MDD predicted shorter time to future relapse, but again dysthymic disorder did not.

In another examination of predictors of recurrences and new onsets of MDD over 6 years of follow-up [27], patients with BPD were more likely to have recurrences of MDD and about equally likely to have new onsets compared to patients with other personality disorders (OPDs). The total number of BPD criteria and the number of BPD affective criteria were predictive of new onsets. The total number of BPD criteria and the number of BPD affective, impulsive, and relational criteria each predicted recurrences. There was no evidence that the number or the subgroups of BPD criteria were more predictive in patients diagnosed with BPD than in patients diagnosed with OPDs, suggesting that these dimensions of borderline personality psychopathology have prognostic significance for MDD outcomes independent of the DSM-IV (now DSM-5 Section II, as well) personality disorder categorical diagnosis.

At the 10-year CLPS follow-up [28], BPD again had a clearly significant negative effect on time to remission of MDD (i.e., longer time to remission) and a mildly significant negative effect on time to relapse (i.e., shorter time to relapse). MDD also had a significant negative effect on time to remission and time to relapse of BPD, so the relationships between the two disorders were reciprocal.

Patients with BPD in the MSAD experienced declining rates of many Axis I disorders over 6 years [29]. Rates of both mood and anxiety disorders continued to remain high, however. Consistent with the MSAD findings on the beneficial effects of remission on functioning, patients with BPD who had a remission experienced declines in all comorbid Axis I disorders assessed, while those who did not remit reported stable rates. Substance use disorders, but not mood or other Axis I disorders, had a negative effect on remission from BPD.

Although prospective studies of patient samples such as CLPS and the MSAD provide important information, patient studies may be biased by numerous confounds and selection factors [30]. To better understand the course of MDD and its predictors, prospective epidemiological studies are needed. The effects of specific personality disorder comorbidity on the course of MDD in a nationally representative sample were evaluated in the National Epidemiologic Survey on Alcoholism and Related Conditions (NESARC) [31]. The 3-year follow-up interview of the large NESARC sample provided the opportunity to determine the rates of persistence and recurrence of MDD in the community and the specific effects of all DSM-IV personality disorders compared to each other on its course while also allowing for multivariate analyses to account for a number of other potential predictors of chronicity. These data presented a unique opportunity to confirm the hypothesis generated in the CLPS clinical populations [24, 25] that personality disorders exert a strong, independent negative impact on the course of MDD.

15.1 % of NESARC participants had persistent MDD and 7.3 % of those who remitted had a recurrence during the 3 years of follow-up [31]. Univariate analyses indicated that avoidant, borderline, histrionic, paranoid, schizoid, and schizotypal personality disorders all elevated the risk for persistence of MDD. With Axis I comorbidity controlled, all but histrionic personality disorder remained significant. With all other personality disorders controlled, borderline and schizotypal remained significant predictors. In final, multivariate analyses that controlled for age at onset of MDD, number of previous episodes, duration of current episode, family history, and treatment, BPD remained a robust predictor of MDD persistence. Neither personality disorders nor other clinical variables predicted recurrence. Thus, in this nationally representative sample of adults with MDD, BPD robustly predicted persistence, a finding that converges with clinical studies.

In the CICS, adolescent or young adult cluster A personality disorder symptoms increased risk of subsequent mood as well as eating, anxiety, and disruptive behavior disorders. Adolescent or young adult cluster B symptoms increased risk of subsequent mood, anxiety, eating, disruptive, *and* substance use disorders. Cluster C symptoms increased risk of subsequent mood, anxiety, and disruptive behavior, but not eating or substance use, disorders [32–35]. Significantly, childhood MDD in the CICS increased the risk of young adult personality disorders, specifically dependent, antisocial, passive-aggressive, and histrionic PDs, but not borderline PD [36, 37]. Childhood or adolescent depression (and other psychopathologies) may set in motion a chain of maladaptive behaviors and environmental responses that lead to personality psychopathology. Personality disorders, therefore, may represent alternative pathways of continuity for MDD across the transition from childhood to adulthood, reminiscent of the findings on depressive and personality disorder co-occurrence reported earlier from the CLPS [8]. The lack of convergence in the CICS on the specificity of the relationships of mood and particular personality disorders, especially BPD, found in other longitudinal studies raises some questions. Differences could be due to different methods for assessing psychopathology in the studies, or perhaps current categorical conceptualizations of depressive and personality disorders may not be the ideal units of analysis for studying their interrelationships.

## Course of BPD and Bipolar Disorders

Considerably less is known from prospective longitudinal studies about the relationships between BPD and bipolar disorders than between BPD and depressive disorders. In an examination of recurrences and new onsets of bipolar disorder over 4 years of follow-up, however, significantly more patients with BPD developed new onsets of bipolar I and II disorders (7.9 %), compared to patients with OPD (3.1 %) [38]. Within the OPD sample, those with co-occurring bipolar disorder were more apt to develop new onsets of BPD than were those without co-occurring bipolar disorder. This study also showed that in the BPD sample, co-occurrence of bipolar I or bipolar II disorders did not much affect the course of BPD in terms of remission, functional level, or treatment utilization. At 10 years, BPD did not have a significant effect on the course of bipolar I or bipolar II, although the confidence intervals for the hazard ratios overlapped considerably due to the limited numbers of cases [39]. Neither bipolar I nor bipolar II had a statistically significant interaction with BPD with the exception of bipolar II, which had a negative effect on time to remission of BPD; however, again because of the low n's relative to MDD, the confidence intervals for the hazard ratios again overlapped.

## Implications of Studies of Longitudinal Course

### *Research Implications*

It is increasingly recognized that, despite conceptual distinctions, there is overlap in some of the psychopathology embedded in the criteria for mood disorders and personality disorders. One relevant model published over 20 years ago proposed that four psychobiological dimensions may underlie both the Axis I disorders and personality disorders: abnormalities in cognition and perception, affect regulation, impulsivity, and anxiety and inhibition [40]. This approach recognizes enduring vulnerabilities or propensities to manifest particular symptoms or behavior, very similar to the notion of personality traits, underlying Axis I disorders. From the perspective of personality, several models describe affective traits [41]. The Five-Factor Model (FFM) [42], for example, includes the trait domain of *neuroticism*, which is the enduring propensity to experience negative affects such as anxiety, depression, and irritability. Clark and colleagues have described a model of *positive* and *negative affectivity*, defining each as "...a stable, heritable, and highly general trait dimension with a multiplicity of aspects ranging from mood to behavior" [43]. They further describe these temperamental dimensions as vulnerabilities for the development of anxiety and depression [43]. The Alternative Model for personality disorders in DSM-5 Section III includes the trait domain of *negative affectivity* (NA), defined as "frequent and intense experiences of high levels of a wide range of negative emotions (e.g., anxiety, depression, guilt/shame, worry, anger, etc.), and

their behavioral (e.g., self-harm) and interpersonal (e.g., dependency) manifestations” [44]. The trait facet of *depressivity* within the domain of NA is defined as “feelings of being down, miserable, and/or hopeless; difficulty recovering from such moods; pessimism about the future; pervasive shame and/or guilt; feelings of inferior self worth; thoughts of suicide and suicidal behavior” and is one of the “B” (pathological personality trait) criteria for BPD in the DSM-5 Alternative Model. These trait dimensions have been shown to be stable over a period of 6–7 years in a nonclinical sample recruited as college students, at least with regard to rank order stability, although the mean level of negative affectivity showed a significant decrease [45]. As noted by Widiger [41], fluctuations in intensity of the affects associated with temperamental dimensions “...can at times reach clinically significant levels of maladaptivity and warrant a diagnosis of a mental disorder” [41].

Dimensions of temperament may help explain the chronicity of mood disorders, as these are enduring propensities to experience negative affects including depression. There may be increases in the intensity of such affects for periods of time, captured in the mood disorders as “episodes.” In an examination of the timing of the improvements in the personality and Axis I disorders, significant reciprocal time-varying associations were found for BPD with MDD and for AVPD with social phobia [46]. The 10-year CLPS findings are notable for documenting strong reciprocal effects of BPD and co-occurring MDD upon each other’s time to remission and time to relapse/onsets [28]. These findings extend those in earlier reports over briefer follow-up periods from CLPS [46–48] and are consistent with recent findings from the NESARC epidemiological sample [31] that also showed the strong effect of BPD status on the course of MDD. Finding a significant effect of change in MDD on BPD’s course also supports the finding from the 2-year CLPS follow-up [46]. Furthermore, despite the relative instability of the personality disorder diagnoses in the CLPS sample, and significant decreases in the mean number of criteria present, the rank order of individuals on the number of criteria met for the disorders (i.e. the correlations over repeated assessments) was very high, indicating stability in terms of the kinds of criteria present [49]. Thus, it may be that both mood disorders and certain personality disorders, especially BPD, are characterized by enduring vulnerabilities, with periodic exacerbations that reach full diagnostic criteria for the various disorders at various times. Furthermore, personality disorders and mood disorders may share at least some of the same enduring vulnerabilities. A strong interaction of BPD and MDD, suggesting overlapping psychopathologies and etiologies, alongside weaker evidence for dependencies between BPD and bipolar disorder is consistent with data from family history studies that also show a possible, albeit uncertain, relationship between BPD and MDD, but much weaker evidence for a relationship between BPD and bipolar disorder [50, 51].

Examination of the effect that the bipolar disorders had on the course of BPD in the CLPS yielded mostly insignificant results, but with one exception: bipolar II significantly increased time to remission of BPD. That bipolar II had this effect, whereas the presumably more severe bipolar I had a lesser effect, is surprising. A possible explanation is that many patients diagnosed as bipolar II may actually have a variation of BPD. This possibility is suggested by bipolar II’s relatively weak



familial relationship to bipolar I [51, 52] and by its weak and inconsistent response to mood stabilizers [53]. It is also suggested by bipolar II's high prevalence of typical BPD characteristics such as rejection sensitivity [54], childhood trauma [2], and repeated suicide attempts [55, 56]. Thus, what is commonly identified as co-occurrence of bipolar II with BPD may really be an indication of a more severe form of BPD and it is this level of severity that accounts for the longer time to BPD remission. Examination of the effect of BPD on the time to remission of bipolar disorder or time to relapse/onsets revealed no significant effects. This finding supports the overall conclusion drawn from a prior CLPS report about the independence of these disorders [38]. Though the findings of independence are based on new evidence, this conclusion must be considered with caution because the analyses involving bipolar disorders had significantly smaller samples than for MDD.

The implications of this conceptualization for the DSM suggest certain directions. First is the recognition and further delineation of common personality trait dimensions that underlie both personality disorders and mood disorders. It may further be important to identify individuals who experience episodes of mood disorders, such as major depression, who do not share an ongoing propensity toward negative affectivity. It is possible that the etiology of such episodes is different from those that represent an exacerbation of a persistent temperamental trait. For the personality disorders, it will be important to more clearly define the multiple underlying trait dimensions, including those that are and are not shared with mood disorders. Much work in this direction has already been accomplished, and much has been written regarding the relevance of various dimensional schemes for conceptualizing the personality disorders. Currently, such dimensions are assessed by self-report measures, such as the NEO-Personality Inventory Revised (NEO-PI-R) for the Five-Factor Model of Personality [57], the Dimensional Assessment of Personality Pathology (DAPP) for dimensions of personality disorder [58], the Schedule for Nonadaptive and Adaptive Personality (SNAP) for dimensions of normal and abnormal personality [59], and the Personality Inventory for DSM-5 (PID-5) for the recently published DSM-5 Alternative Model for personality disorders [60]. The ability to assess such dimensions by clinical interview, with additional consideration of the range and examples of behaviors that may be manifestations of the dimensions, will be important to establish the clinical relevance of the dimensions underlying the maladaptive traits and behaviors of personality disorders. With clearer descriptions of the traits underlying the personality disorders, including definitions and assessments that consider the range of possible manifestations of such traits, it will also be important to clarify what is distinctive about personality disorders, to aid in their differential diagnosis from mood and other mental disorders. The DSM-5 Personality and Personality Disorders Work Group developed a model of personality functioning based on impairments in self-concept and incapacities in interpersonal relationships [44]. Impairments in self (identity, self-direction) and interpersonal (empathy, intimacy) functioning appear to be central to BPD, as conceptualized from many different theoretical perspectives [61], as well as to other DSM personality disorder types [62–64].

Finally, will the initial longitudinal relationships linking pathological traits, personality disorders, and other symptoms of psychopathology hold up over time? Such relationships point strongly toward shared endophenotypes, whose identification is critical for genetic studies, treatment development, and classification [65].

### *Clinical Implications*

Personality psychopathology, particularly BPD, should be assessed in all patients with MDD, considered in prognosis, and addressed in treatment. Furthermore, the clinical implications of the findings of the studies reviewed in this chapter include informing patients that the co-occurrence of BPD and MDD can have a negative effect on their prognoses. The response of MDD to antidepressants in the presence of BPD is weak and inconsistent [66, 67]. Thus, the use of antidepressant medications should be restricted to more severe MDD with appropriate cautions about expectable benefits. Treatment of BPD, primarily psychodynamic or cognitive psychotherapy [9–11], should uniformly be offered and given priority; improvement in BPD will be typically followed by improvement in MDD. With respect to co-occurring BPD and bipolar disorders, patients should be treated as if these were independent disorders. Clinical experience suggests that control of mania and hypomania with mood stabilizers or other psychotropic medications often facilitates the use of psychosocial treatments for patients with BPD.

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