BORDERLINE PERSONALITY DISORDER: INTERFACE WITH MOOD AND OTHER AXIS I DISORDERS

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ABSTRACT

The definition of borderline personality disorder has evolved since it was first described more than 60 years ago. It currently is recognized as a disorder within the mood disorder spectrum, rather than a forme fruste of subchizophrenia or other psychotic disorders. The disease affects 1% to 2% of the general population, and there is extensive comorbidity with Axis I disorders. Recent evidence suggests there is a strong genetic component to the disease, which is characterized by mood instability, impulsivity, and poor self-image. Psychotherapy is the main method of treatment, but pharmacologic intervention is being increasingly recognized as having an important role in controlling the symptoms. (Adv Stud Med. 2004;4(10F):S965-S969)

DEFINING BPD

Borderline personality disorder (BPD) is a serious mental illness characterized by impulsive self-injurious behavior, affective instability, cognitive perceptual symptoms, and impulsive aggression. Instability caused by BPD often disrupts family and work life, long-term planning, and the person’s sense of self-identity.

BPD has been an officially recognized diagnosis since its listing in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III) in 1980, although the term had been used to describe various patient groups for 40 years before that. Stern first used the term “borderline” in 1938 to describe patients manifesting symptoms between psychosis and neurosis.1 Knight used borderline as a diagnostic entity and as a description of severely ill patients who are not psychotic but who fall within the realm of psychosis without qualifying for a diagnosis of schizophrenia.2 Other efforts to characterize this population include the 1942 publication by Deutsch describing the “as if personality” in patients who adapt to a role in a specific situation, yet have little sense of themselves and are thought to be internally disorganized and probably psychotic.3 Several years later, Schmideberg characterized patients with a consistent clinical presentation of emotional lability or affective reactivity as having “stable instability,” representing the patient’s adaptation to the world.4

In the 1960s, the concept of borderline was broadened to include cognitive disturbance, impaired sense of self, and emotional lability. Kernberg defined “borderline personality organization” as impaired self-identity, primitive defense mechanisms, and impaired reality testing caused by impaired object relations.5 Grinker et al described the “borderline syndrome,” which includes 4 subgroups of persons—those bordering on psychosis, those bordering on neurosis, those whose personality disorder is similar to that of Deutsch’s “as if” group, and those who constitute the core borderline group, with elements of anger and loneliness, fragmented sense of self, and labile interpersonal relationships.6

By 1980, Gunderson and Singer defined 6 diagnostic criteria for BPD.7 The DSM-III included BPD as a formal diagnosis based on the work of Gunderson and Singer and also on a study by Spitzer et al differentiating...
BPD from schizotypal personality disorder. The latter includes the psychotic aspect, and the former includes the neurotic or emotional lability aspect. Thus, a conceptual shift was made of the borderline notion from a subschizophrenic disorder to a subaffective disorder.

**Epidemiology**

**Prevalence of BPD and Comorbid Bipolar Disorder**

The prevalence of BPD is approximately 1% to 2% in the general population. Moreover, there is a high frequency of comorbidity of BPD and Axis I disorders. In a chart review conducted by Fabrega et al, approximately two thirds (267/390) of the patients with a diagnosis of BPD received concurrent Axis I diagnoses. Zimmerman and Mattia reported that 58 of 59 patients with BPD had concurrent Axis I diagnoses and that 69.5% had 3 or more Axis I diagnoses.

Many studies reported a high frequency (35%-51.5%) of comorbidity between BPD and major mood disorders, such as bipolar disorder. Some publications suggested that approximately 15% to 29% of patients with bipolar disorder have diagnoses of comorbid BPD. Additionally, Skodol et al showed that of 240 patients with BPD, 13.3% also had diagnoses of bipolar disorder (9.2%, bipolar I; 4.1%, bipolar II).

The presence of BPD has important implications for the treatment of patients with many Axis I disorders. Patients with bipolar disorder and comorbid BPD experience earlier onset of disease, have less favorable outcomes, attempt suicide more often, and respond more poorly to treatment than those without BPD.

**Genetic and Environmental Association in BPD**

BPD appears to be governed by an interaction of genetic and environmental factors. One prominent environmental precursor to BPD is a history of abuse (often sexual or physical) or neglect. Many studies suggest that a high proportion of patients with BPD have experienced some form of abuse and trauma during their development.

Studies suggest that abuse may sensitize or alter the activity of the hypothalamic-pituitary-adrenal axis involved in stress responses and may have long-term effects on the monoamine systems. In addition, early abuse (before age 18) can lead to a variety of neurodevelopmental abnormalities with different behavioral sequelae. Trauma or early abuse also may cause structural changes in the brain. Using measurements derived from magnetic resonance images, Stein et al found markedly reduced hippocampal volume among 21 women with histories of prolonged sexual abuse before age 15 compared with 21 nonabused women.

Recent interest in genetic influences has led to a greater understanding of the nature of BPD and its treatment. Familial transmission of BPD is reported in several studies. Zanarini et al suggest that a strong genetic component is associated with BPD. Supporting this contention, Nigg and Goldsmith concluded from their study that the morbid risk for BPD in first-degree relatives is 11.5%, and Torgersen et al reported a Norwegian twin study of 92 monozygotic (MZ) and 129 dizygotic (DZ) twin pairs in which concordance for BPD was 35% in MZ pairs and 7% in DZ pairs.

Impulsive aggression also is heritable, as demonstrated by twin and adoption studies. Comorbidity (with Axis I disorders) itself is a genetic factor, and studies suggest that bipolar disorders and BPD can be cotransmitted in families.

Specific genes are beginning to be associated with traits seen in BPD. The tryptophan hydroxylase L allele and the serotonin transporter S allele have been associated with impulsivity and neuroticism, whereas the 5-hydroxytryptamine 1B receptor gene has been associated with suicidality.

**Symptoms of BPD**

The essential features of BPD as defined by the DSM-IV are pervasive patterns of unstable interpersonal relationships, self-image, and affects, along with marked impulsivity (exemplified by suicidality and substance abuse). A person with BPD also may have cognitive/perceptual dysfunction involving impaired reality testing and other psychotic-like symptoms (eg, paranoia).

At least 5 of 9 DSM-IV criteria must be met for a diagnosis of BPD. This polythetic criteria set for BPD results in 151 different possible combinations. Some combinations of diagnostic criteria are more likely than others, but it is evident that substantial diversity exists among persons given the BPD diagnosis.

**Symptom Overlap Between Bipolar Disorder and BPD**

Considerable overlap occurs between BPD and other personality disorders; nearly 95% of patients meeting criteria for BPD meet criteria for at least 1 other disorder. DSM-IV criteria for BPD—which
include substance abuse, disordered eating behavior, abnormalities in mood state, and psychosis-like phenomena—all predispose toward the co-occurrence of Axis I disorders of similar symptomatology.33

Symptom overlap between bipolar disorder and BPD includes emotional instability, impulse dyscontrol, cognitive dysfunction, and the potential for exacerbation of symptoms with antidepressant use.35 Additionally, cyclothymia occurs frequently in patients with BPD,46 and patients with cyclothymic bipolar II often are misclassified as having BPD because of their extreme mood instability.37-40 BPD and bipolar II disorder share the trait of affective lability. In contrast, the symptoms of impulsiveness and aggressiveness usually are seen in patients with BPD.29

PATHOPHYSIOLOGY

Disturbances in various neurotransmitter systems are implicated in mental disorders. Although an oversimplification, research suggests that psychosis is mediated predominantly by glutamate and dopamine, mood and dysphoria are mediated by serotonin and norepinephrine, anxiety is mediated by γ-aminobutyric acid, and memory is orchestrated by acetylcholine.44 In neurochemical and pharmacologic challenge studies, reduced serotonergic activity is associated with impulsive aggression in patients with personality disorders.41 Treatment studies suggest that impulsive aggression improves with selective serotonin reuptake inhibitors independently of the resolution of depression.42 Affective instability also may be related to abnormalities in the central adrenergic and cholinergic systems and appears to respond to mood stabilizers, such as lithium and carbamazepine.

Compared with healthy controls, patients with BPD showed significantly blunted metabolic responses in the orbital frontal, adjacent ventral medial, and cingulate cortices after administration of the serotonin-releasing agent fenfluramine.44 These results are consistent with findings of reduced serotonergic modulation of orbital frontal, ventral medial frontal, and cingulate cortices in patients with impulsive-aggressive personality disorders.85,46

PHARMACOTHERAPY

Although psychotherapy remains the cornerstone of BPD treatment, the high rates of symptom overlap and comorbidity with Axis I disorders suggest that many patients with BPD may benefit from pharmacotherapy. Furthermore, the American Psychiatric Association practice guideline recommends symptom-targeted pharmacotherapy.

BPD is multidimensional and may have different pathophysiologic characteristics associated with each component of the disorder, requiring different treatments. Neurotransmitter mediation of perception, cognition, affect, and impulse suggests a role for pharmacotherapy in 3 to 4 symptom domains. Cognitive-perceptual symptoms may be treated with antipsychotics; affective dysregulation, with antidepressants/anticonvulsants; and impulse behavior dyscontrol, with antidepressants, mood stabilizers, or antipsychotics.

ANTIDEPRESSANTS

Although antidepressants are the most widely used medications for patients with BPD, only 2 double-blind, placebo-controlled studies have been conducted in this patient population. Salzman et al studied fluoxetine (mean dose, 40 mg/d) in 22 patients with mild to moderate BPD in a 13-week, double-blind, placebo-controlled study.47 Fluoxetine therapy significantly improved symptoms of anger and depression compared with placebo. In a study of 38 nonschizophrenic, nonbipolar female patients with BPD, fluvoxamine significantly improved rapid mood shifts compared with placebo but had no effect on symptoms of anger or impulsivity.48 Furthermore, fluvoxamine was associated with a high incidence of adverse effects, including nausea and fatigue.

MOOD STABILIZERS

Two randomized, double-blind, placebo-controlled trials of divalproex have been conducted in patients with BPD and bipolar disorder. Frankenburg and Zanarini studied divalproex (serum level, 50-100 mg/L) in 30 women with BPD and bipolar II disorder during a 6-month period.49 Significant improvement was seen in interpersonal sensitivity, anger/hostility, and aggression, but no change in depressive symptoms was noted. Hollander et al found significant improvement in overall clinical condition and functioning in patients with BPD with divalproex (serum level, 80 mg/L) compared with placebo.50

ANTIPSYCHOTICS

The atypical antipsychotics aripiprazole, olanzapine, ziprasidone, quetiapine, and risperidone are indicated for the treatment of bipolar disorder. In
addition, atypical antipsychotics have been used in treating patients with BPD. Small open-label studies have shown the efficacy of clozapine and risperidone for a variety of symptoms in patients with BPD.

In a 6-month, double-blind, randomized, placebo-controlled trial, Zanarini and Frankenburg studied 28 women with BPD. Compared with placebo, olanzapine significantly improved symptoms of anxiety but was associated with a high incidence of weight gain. In another double-blind, placebo-controlled, 12-week study of 40 patients with BPD, olanzapine produced significant improvement in overall clinical condition. However, particular dimensions of symptoms were not delineated in this study. In addition, olanzapine therapy was associated with significant increases in body weight beginning the second week of treatment.

Although atypical antipsychotics are beneficial in patients with BPD, certain agents are associated with adverse effects, such as weight gain and increased risk for metabolic disturbances (diabetes, hyperprolactinemia). The clinical impact of drug-related adverse effects may be magnified in patients with BPD, who are highly intolerant of adverse effects, leading to compromised treatment outcomes due to poor tolerability of prescribed agents and poor compliance with therapy. The newer antipsychotics, such as ziprasidone and aripiprazole, induce relatively benign adverse effects (low weight gain, no increase in prolactin levels, low incidence of extrapyramidal symptoms) and may offer another treatment option for patients with BPD, although studies must be conducted in this area.

**OTHER AGENTS**

Omega-3 fatty acid is commonly found in seafood. Cross-national studies have indicated that greater consumption of seafood is associated with lower rates of bipolar disorder and major depression. Zanarini and Frankenburg studied the effect of omega-3 fatty acid (1 g/d) in an 8-week, placebo-controlled, double-blind study involving 30 women with BPD. The researchers saw significant improvements in aggression and depression with the dietary supplement compared with placebo. These preliminary results suggest some potential benefit of this compound in patients with BPD and may warrant further investigation.

**SUMMARY**

BPD is a heterogeneous disorder that substantially overlaps with Axis I disorders, including bipolar disorder. Pharmacotherapy is an increasingly viable treatment option for patients with BPD, although there is a need for large, randomized, controlled trials in this patient population. Newer atypical antipsychotic agents, in particular, may be safe, effective options for the treatment of patients with BPD.

**REFERENCES**

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