Advances in Diagnosis, Neurobiology, and Treatment of Mood Disorders

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Borderline Personality Disorder: Evidence-Based Clinical, Diagnostic and Management Issues

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The presenter was a member of the DSM-5 Committee’s Personality Disorders Work Group, and is currently a member of the APA’s DSM-5 Steering Committee, but his pronouncements do not represent the Association’s opinion.

No relevant financial information to disclose in connection with this presentation.

Generic names and off-label use of some medications will be described.
Overall Learning Objectives

- Identify clinical signs and symptoms described in DSM-5 for borderline personality disorder
- Review recent neurobiological and psychometric test findings in research on borderline personality disorder
- Translate the latest evidence on the pharmacological and non-pharmacological management of borderline personality disorder into practice
What percentage of patients with BPD previously were inaccurately diagnosed with bipolar disorder?

A. 15%
B. 25%
C. 40%
D. 50%
Outline

- Brief history of the BPD concept
- BPD in DSM-5 (Sections II and III)
- Nosological and clinico-diagnostic debates
- Course, outcome and prognosis
- Recent research contributions
- Treatment/Management approaches
- Conclusions
Brief History of Borderline Personality Disorder (BPD)

- Mid- to late 19th. Century: “Monomania” and “Moral insanity”.
- Kraepelin’s era: “Fundamental states” and pathological/constitutional characters.
- Schneider’s Characterology and “psychopathic personalities”.
- First half of 20th. Century: Psychoanalysis and “character neuroses”.
- Initial delineations and Kernberg’s contributions (1950s and 1960s).
- DSM III to 5: Categorical descriptions.
Basic Epidemiology of BPD

- **Prevalence**
  - Roughly ~20% of clinical samples
  - 15% of inpatients (51% with PD) and 8% of outpatients (27% with PD)
  - 1.2 - 5.9% in community samples

- **Gender**
  - Approximately ~75% female in clinical samples
  - More equal M:F ratio in community samples

- **Heritability**
  - Small number of twin studies show 55% heritability and a single latent factor accounting for the co-occurrence of interpersonal, emotional, behavioral and cognitive components\(^1,2,3\)

# Debates About Personality Disorders in DSM-5

<table>
<thead>
<tr>
<th>Feature</th>
<th>Section II</th>
<th>Section III</th>
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<tbody>
<tr>
<td>Structure</td>
<td>Categorical</td>
<td>“Hybrid” (Categorical/dimensional)</td>
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<td>Presentation</td>
<td>Descriptive criteria</td>
<td>Functional levels</td>
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<tr>
<td>Definition</td>
<td>Enduring pattern of inner experience and behavior that deviates markedly from expectations of the individual’s culture, is pervasive and inflexible, onset in adolescence or early adulthood, stable over time, leads to distress or impairment.</td>
<td>Impairments in personality functioning (self → identity and self-direction; interpersonal → empathy and intimacy), and presence of pathological personality traits (identified from 25, grouped in five domains).</td>
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<tr>
<td>Distribution</td>
<td>By clusters</td>
<td>Specific disorders</td>
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<tr>
<td>Number</td>
<td>Ten</td>
<td>Six</td>
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Six Types of PD in *DSM-5* (Section III)

- Antisocial
- Borderline
- Schizotypal
- Obsessive-compulsive
- Avoidant
- Narcissistic

## Definition and Characteristics of Borderline Personality Disorder in **DSM-5**

<table>
<thead>
<tr>
<th>Section II</th>
<th>Section III</th>
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<td>Instability of interpersonal relationships, self-image and affects, and marked impulsivity, beginning by early adulthood and present in various contexts:</td>
<td>A. Moderate or greater impairment in personality functioning with difficulties in 2 or more of the following areas:</td>
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<tr>
<td>1. Frantic efforts to avoid real or imagined abandonment.</td>
<td>1. Identity: Impoverished, poorly developed, unstable self-image, self-criticism, emptiness, dissociative states.</td>
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<td>2. Interpersonal relationships alternating between extremes of idealization and devaluation.</td>
<td>2. Self-direction: Instability in goals, aspirations, values, career plans.</td>
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<td>3. Disturbed identity or self-image.</td>
<td>3. Empathy: Inability to recognize feelings and needs of others, hypersensitivity, negative perceptions.</td>
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<td>4. Impulsivity in several areas.</td>
<td>4. Intimacy: Intense, unstable and conflicted close relationships; mistrust, neediness, anxious preoccupation with real or imagined abandonment; extremes in interpersonal relations.</td>
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<td>6. Affective instability.</td>
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<td>7. Chronic feelings of emptiness.</td>
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<td>8. Inappropriate, intense, constant anger.</td>
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<td>9. Transient, stress-related paranoid ideation or severe dissociative symptoms.</td>
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BPD’s Interpersonal Coherence

Subtypes of BPD

- Affective
- Impulsive
- Aggressive
- Empty
- Dependent
- Narcissistic?

Research on BPD in DSM-5, Section III

- A recent empirical study (Morey L., et al., 2013) of 334 clinicians found that, in 14 of 18 comparisons, DSM-5 Section III proposal is perceived as more clinically useful than DSM-IV with respect to:
  - Ease of use
  - Communication of clinical information to other professionals
  - Communication of clinical information to patients
  - Comprehensiveness in describing pathology
  - Treatment planning

- Confirmations of this finding from U.S., Europe, Middle East and Asian researchers.

DSM-5 Section III proposal better addresses PD complexity:

- Advantages of single item rating of personality functioning
- Substantial reduction of specific number of diagnostic criteria by 43%
- Empirically reduces co-morbidity
- Accounts for co-morbidity when it actually exists
- Captures clinical heterogeneity
- Replaces the vague PDNOS, the most frequently assigned DSM-IV PD diagnosis, with more specific and informative clinical information (e.g., PD-TS)

Nosological and Clinico-Diagnostic Debates About BPD (I) Relationship with Bipolar Disorder

- 40% of patients who do have BPD and do not have bipolar disorder have previously been inaccurately diagnosed with bipolar disorder.¹

- One in five people experience BPD-BD comorbidity.²

- Comorbidity BPD/BD as expression of “emotional frailty” and predictor of worse outcome³ vs. no impact of bipolar on BPD course, modest impact of BPD on bipolar course.

- Clinical practice compromised by difficulties in a reliable differentiation between BD and BPD.⁴

- Childhood sexual abuse, depersonalization, relationship difficulties, sensitivity to criticism and absence of BP family history are powerful predictors of BPD vs. BD.⁵

Nosological and Clinico-Diagnostic Debates About BPD (II) Relationship with Bipolar Disorder

- MDE patients with comorbid BPD were significantly younger and reported a high prevalence of mixed features and Bipolar Disorder, with complex course and reduced treatment response.¹

- Psychosocial morbidity (e.g., history of SUD, higher suicidality and poorer global functioning) greater in BPD than BD patients.²,³

- In euthymic bipolar patients, 23.1 % associated with Cluster B PDs, the majority of them, BPD.⁴

- “Lack of premeditation” and “lack of perseverance” (i.e., impulsivity, affective lability and intensity) score higher among BPD patients compared to BD’s, using self-report questionnaires.⁵

Comorbid depression does not impact the accuracy of BPD assessments\(^1\)

Comorbidity BPD-Mood Disorders extremely common
- MDD: 50%
  - Atypical vs melancholic poorly studied
- BPI/II: 20%
  - Poorly studied in BPII and spectrum

BP/BPD course independent, but MDD markedly impacted by BPD ("Treatment-resistant")\(^2\)

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Nosological and Clinico-Diagnostic Debates About BPD (IV) Relationship with Other Disorders

- BPD patients with comorbid PTSD reported significantly higher levels of global psychological distress at baseline and end of treatment, compared to non-PTSD counterparts.\(^1\)
- Hospital admissions for self-harm related to significant association of BPD with PTSD and significant dysregulation and relational problems.\(^2\)
- Relevance of CSA in occurrence of PTSD in patients with BPD.\(^3\)
- Significant negative impact of comorbid ADHD and BPD in impulsivity, additional psychopathology, lower intellectual and attentional functioning and increased psychosocial difficulties.\(^4\)
- In a community sample, childhood abuse was positively associated with emotional dysregulation and need for approval as mediators of BPD.\(^5\)
- Gender bias as a relevant factor in diagnosis of BPD vs. NPD.\(^6\)

CSA = Child sexual abuse

Nosological and Clinico-Diagnostic Debates About BPD (V) Relationship with Other Disorders

- One of five chronic non-cancer patients (CNCP) treated with prescribed opioids screened positive for BPD and were at elevated risk for suicidal behavior¹

- OCD patients with BPD (21.8% of a Brazilian sample) exhibited higher rates of several comorbid psychiatric disorders, greater frequency of compulsions involving interpersonal domains (e.g., reassurance seeking), increased severity of depression, anxiety and OCD, more motor and non-planning impulsivity and greater “cognitive” compulsivity, compared to OCPD and SPD²

- Depressive symptoms associated with BPD emerge in the context of interpersonal sensitivity and relationship stability, and therefore, the holding environment of a hospital can result in rapid improvement³

- Dysthymic disorder and double depression have a higher proportion of comorbid PDs than MDD. Only BPD seems to be consistently high within and across different regions of the Asian continent⁴

OCPD = Obsessive compulsive personality disorder; SPD=Schizotypal personality disorder
Nosological and Clinico-Diagnostic Debates About BPD (VI) Relationship with Other Disorders

- Insecure attachment common in BPD and Somatoform Disorder but hyperactive emotion dysregulation is prominent in BPD whereas deactivation is evident in SD\(^1\)

- Schizophrenic and BPD patients share problems in social cognition, understanding of feelings, intentions and thoughts of other people, the social cognitive subdomain of the ToM, but Scz women perform markedly below\(^2\)

- BPD affected one fifth of male offenders in probation in Sweden, with significantly more current psychiatric co-morbidity, particularly ASPD (91%), MDD (82%), substance dependence (73%), ADHD (70%) and alcohol dependence (64%)\(^3\)

- Expressive suppression and cognitive reappraisal associated with dissociation in BPD patients with diagnosis of Eating Disorder and history of Non-suicidal Self-Injury (NSSI)\(^4\)

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Nosological and Clinico-Diagnostic Debates About BPD (VII) Relationship with Other Disorders

- Cyclothymic Disorder (BPD = Ultra-rapid cycler)
- Anxiety Disorders
- “Premorbid” condition in Autism Spectrum Disorders
- New diagnosis in *DSM-5*: Disruptive Mood Dysregulation Disorder (DMDD)
- Other PDs and psychotic disorders.

BPD’s Longitudinal Course

Number of Criteria (CLPS) $^1$

% Remitted (MSAD) $^2$

Years of follow-up

N = 362

N = 175

MSAD = McLean Study of Adult Development
Recent Clinical Research Findings on BPD (I)

- Unlike BPD patients seen in MH settings, those in PC settings tend to present more unsubstantiated chronic pain of various types, as well as somatic preoccupation.\(^1\)
- “Meaning in life” feelings, highly negatively, correlated with BPD symptoms and non-suicide self-injuries.\(^2\)
- Anger rumination significantly predicts aggression proneness, over and above emotional dysregulation.\(^3\)
- BPD patients considered “difficult” and routed out of care by treating physicians through a variety of direct and indirect means (de jure medicalization resulting in de facto demedicalization).\(^4\)

Recent Clinical Research Findings on BPD (II)

- BPD patients are more susceptible to confusing dream content with actual waking events; DRC associated with unstable sleep and wake cycles, dissociative symptoms, fantasy proneness, nightmares, cognitive disturbances and thin boundaries.\(^1\)

- Sexual difficulties in BPD patients: from sex avoidance to promiscuity through “being symptomatic after sex”; in long-term follow-up, 95\% reach remission.\(^2\)

- Impulsivity and Non-conformity/Aggression: childhood personality traits that predict BPD in adulthood.\(^3\)

- “Narcissistic wounds” subtype of mental pain is a sensitive specific diagnostic indicator of BPD.\(^4\)

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Recent Test Findings in Research on BPD Psychological/Psychometric

- Using the Metacognition Assessment Interview, BPD patients show difficulties in two mindreading functions, differentiation and integration, strongly related to severity of the psychopathology.¹

- Even “including contexts” induce lower feelings of social connection and activate feelings of rejection in BPD patients, whose expectations of idealized interpersonal inclusion my nullify the opportunity of experiencing “real” relationships.²

- No or questionable compliance detected in BPD patients taking a Performance Validity test, showing also lower premorbid intellectual functioning.³

- BPD patients show prolonged, slower recovery following errors (PES) than BD patients.⁴

Recent Test Findings in Research on BPD Neurobiological/Biochemical

- Following a social stress test, salivary cortisol levels significantly decreased in female, and increased in male BPD patients, POMS and STAI items increased, vigor scores decreased in both, compared to controls.\(^1\)

- Oxytocin is involved in attachment security and methylation of the OT receptor may play a role in the epigenetic modulation of early adversity; it also interacts with vasopressin, testosterone, dopamine & serotonin, important players in social reward and stress responsivity.\(^2,3\)

- Increased testosterone levels and cortisol awakening responses in BPD patients.\(^4\)

- BPD patients have abnormally higher mean value of serum prolactin, compared to healthy controls (interaction between ST system, SI and impulsivity)\(^4\)

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Recent Test Findings in Research on BPD Neurophysiological/Endocrine

- BPD patients show more complexity of self- and other-representation and insensitivity to hyperactivation on crucial areas of social cognition (medial PFC, T-P junction, several regions of the frontal pole, precuneus and middle TG.¹
- Close links between abnormal sensory processing and self-identity: BPD patients experience lower pleasantness and higher disgust ratings for bitter (quinine) and sweet (juice) tastes; the latter is related to self-disgust.²
- State-dependent deficits in the cortical processing of bodily signals in patients with BPD who presented significantly reduced HEP amplitudes, in turn negatively correlated with emotional dysregulation.³
- Altered neural mechanisms underlying self-referential thinking in female BPD patients, with higher activation in right DMPFC, bilateral motor/premotor regions, LIFG and left PCC, all related to emotion regulation functions.⁴

Recent Test Findings in Research on BPD Neuroimaging (I)

- Blunted bilateral responses of DLPFC and hyperresponsivity of the left amygdala (with smaller gray matter volume) and PCC during the processing of negative emotional stimuli strengthen dysfunctional PF and limbic brain regions as hallmark of BPD’s emotional dysregulation.¹,²,³

- Gender differences: Reduced amygdala and hippocampal gray matter volume in female BPD patients BUT in males, reduced gray matter in ACC, increased in putamen, reduced striatal activity during an aggression task, and a more pronounced deficit in central ST responsivity (> impulsivity).⁴

- Increased DPFC activation and relatively decreased VLPFC and hippocampal activation –frontolimbic circuitry-- associated with clinical improvement after psychotherapy.⁵

Recent Test Findings in Research on BPD Neuroimaging (II)

- Greater posterior caudate volumes and O-F surface area anomalies in Cluster B PDs, and parallel findings in patients with comorbid SUDs

- Gender Increased DPFC activation and relatively decreased VLPFC and hippocampal activation—frontolimbic circuitry—associated with clinical improvement after psychotherapy

Recent Test Findings in Research on BPD Genetic (1)

- Significant aberrant (higher) methylation processes: lower for rDNA gene’s promoter region, and higher for the promoter of the proline rich membrane anchor 1 gene (PRIMA1) in BPD patients, suggesting a role in the pathogenesis of the disorder\(^1\)

- Three polymorphisms from 4 noradrenergic genes showed association with BPD and seemed modulated by childhood trauma BUT the findings didn’t survive Bonferroni correction\(^2\)

- Role of H-P-A genes (and childhood trauma): Two FKBP5 polymorphisms and haplotype combinations of FKBP5 and CRHR1; two other FKBP5 alleles were more frequent in BPD patients with history of physical abuse and emotional neglect; and two CRHR2 variants in those with sexual and physical abuse\(^3\)

- FFI-BPD is 44 % heritable, and 71 % of the genetic influences are shared between FFI-BPD and a BPD self-report measure\(^4\)

Good Management of BPD: General Aspects

- Main features
  - Psychoeducation, interpersonal focus, active family participation
  - Case management and multi-disciplinary approaches emphasized
  - Pragmatic integration of psychotherapy (individual ands group) and psychopharmacological approaches.

- Opening and continuously improving a patient-centered communication; not using the BPD label may not sidestep the stigma\(^1\)

- Adverse effects of “labelling” on the clinician’s judgment (more negative ratings); behavioral descriptions of difficulties are less likely to result in negative judgments and predictions\(^2\)

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Pharmacological Treatment of BPD

- 75% of BPD patients are prescribed psychotropic medications.
- Clear delineation of goals, setting of accurate/realistic expectations (i.e., decrease mood lability, normalize sleep, decrease transient psychotic symptoms) and holding of reasonable limits.
- Measure effectiveness through use of a methodical approach to medication trials: Don’t add without subtracting.
- Avoid or reduce polypharmacy, which can be associated with iatrogenic harm and contribute to functional impairment.¹
- Main effects sought and found on overall psychological distress, interpersonal sensitivity, impulsive-disruptive behaviors, depression and hostility.
- Mixed results of few experimental trials of intranasal oxytocin (less stress and mild prosocial effects vs “paradoxical” reactions).²

Pharmacotherapy of BPD at a Glance

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<th>Anti-psychotics</th>
<th>Anti-depressants</th>
<th>Mood stabilizers</th>
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<tbody>
<tr>
<td>Anger</td>
<td>++</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>↓ Mood</td>
<td>O</td>
<td>O</td>
<td>+</td>
</tr>
<tr>
<td>Anxiety</td>
<td>O</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>+</td>
<td>O</td>
<td>+++</td>
</tr>
<tr>
<td>Cognitive-Perceptual</td>
<td>++</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Functioning</td>
<td>+</td>
<td>O</td>
<td>++</td>
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A Spectrum of Psychotherapeutic Approaches to BPD

Cognitive Behavioral

DBT

STEPPS

Psychodynamic

MBT

SFT

TFP

GPM

DBT = Dialectic behavior therapy; STEPPS = Systems Training for Emotional Predictability and Problem Solving; SFT = Solution focused therapy; GPM = Good psychiatric management; MBT = Mentalization-based treatment; TFP = Transference-focused psychotherapy

Empirically Validated BPD Psychotherapies

- **Dialectical Behavioral Therapy (DBT)** – Linehan et al., 1993, 2006
- **Schema Focused Therapy (SFT)** – Giesen-Bloo et al., 2006
- **Transference Focused Psychotherapy (TFP)** – Clarkin et al., 2007; Levy et al., 2006
- **Systems Training for Emotional Predictability & Prob. Solving (STEPPS)** – Blum et al., 2008
- **General Psychiatric Management (GPM)** – McMain et al., 2009 (after Gunderson & Links)
Notes on Other Psychotherapy Approaches

- Fostering Self-Compassion and Loving-Kindness as accompanying strategies.\(^1\)
- Motive-oriented therapeutic relationship (MOTR): effective brief modality that enhances process of early engagement.\(^2\)
- Systems Training for Emotional Predictability and Problem Solving (STEPPS) effective in global symptoms and impulsiveness in BPD/ASPD patients.\(^3\)
- Family- and parental co-therapy improves attachment capacities and sensitivity to children’s emotional communication.\(^4\)
- Long-term combined psychotherapy at 6-years’ follow-up: greater reduction of distress and improvement in Identity Integration and Self-control.\(^5\)

Socio-Cultural Perspectives on BPD

- Stigma, a universally strong issue.\(^1,2\)
- Subtle ways of professionals’ rejection or disgust when facing the diagnosis.
- Issues of social marginalization, discrimination, poverty, rural and urban settings.
- Pathogenic relevance of all types of violence, childhood victimization, abandonment, etc. in the family and community contexts.
- Misperceptions and mistaken interpretations of social behaviors as symptoms.\(^3,4,5\)

Outcome Issues

- 35% of patients make serious suicidal attempt, 10% die from suicide.
- Most patients improve even if their problems persist (work matters).
- Impulsive symptoms decline more rapidly than affective symptoms.
- After 10 years, more than one third of patients have stable full-timework and family life.
- By 16-year follow-up, 95% of BPD patients with sexual difficulties had achieved remission.

Conclusions

● BPD as a relevant example of the multifaceted complexity of contemporary Psychiatry.
● Theoretical and nosological changes throughout the history of the concept.
● Current clinical description resulting from numerous debates and voluminous research.
● Increasing diagnostic resources to establish similarities and differences with other disorders.
● Well evidenced results of, preferentially, combined treatment approaches and follow-up outcomes.
● Need of further research in diagnostic, treatment and socio-cultural areas.
What percentage of patients with BPD previously were inaccurately diagnosed with bipolar disorder?

A. 15%
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C. 40%
D. 50%