**Research/Grants:** Otsuka America Pharmaceutical, Inc.; Myriad Genetics Inc./Rules-Based Medicine, Inc.; National Institute of Mental Health (NIMH)

**Consultant:** Genentech, Inc.; FORUM Pharmaceuticals; Myriad Genetics Inc.
Learning Objective 1

Provide an introduction of the most recent treatment of borderline personality disorder (BPD)
Learning Objective 2

Review the emerging studies of medication combined with psychosocial treatment in the management of BPD
Introduction

- Early use of the term Borderline Disorder began in the early 1950s when Dr. Knight at Menninger Clinic noted patients developed psychotic symptoms in analytic therapy.
- Dr. Kernberg wrote the leading article in 1968 describing the developmental issues leading to BPD.
- Gunderson and Singer published the objective criteria for BPD in the mid-1970s which became included in DSM III.
- Following these steps more academic research developed in treatment, such as DBT, neuroscience research such as imaging, and pharmacological clinical trials.
Implications of *DSM-5*

- *DSM-5* has eliminated Axis II, but maintained Personality Disorders with criteria similar to those of *DSM-III* and *DSM-IV*. Many in the field have discussed how this can continue earlier research and clinical classification.
- Data collected about domains may provide another approach as the examination of personality disorders show many comorbidities.
- Further, domains of personality disorders may map to functional imaging patterns in ways that earlier criteria may not.

The goal of the study was to assess any differences in severity of symptomatology between men and women with the diagnosis of BPD.

The subjects were from a clinical trials sample (N=770; 211 males).

Using interviews and questionnaire data, women with BPD had statistically more hostility and relationship disruption. Men had higher rates of Antisocial Personality Disorder and Narcissistic Personality Disorder. However, in other areas there were no differences – aggression, suicidality, substance abuse, panic disorder.”

PMID: 25562535
Examining Brain Imaging in BPD and Other Personality Disorders

- Structural brain imaging studies were conducted in studies at NIMH in the 1980s and differences from controls were not demonstrated.

- As the structural studies did not reveal differences, a PET scan study was designed and personality disorder and other personality patients from Bethesda Naval Clinic were examined.

PET Imaging of Impulsivity Domain vs. DSM-IV Criteria

Lower metabolism is indicated in blue, higher metabolism by orange

Results

Figure 1. Mask of Amygdala/parahippocampal region derived from group comparison of BPD > Cntl for Overt Fear. Uncorrected P<0.005. Region volume is 664 mm^3. MNI 152 2 mm coordinates for Zmax of region are -28, -6, -24.

Results


**$p = .00011$**

**Overt Fear**

**Masked Fear**

# Evidence-Based Treatments for Borderline Personality Disorder

<table>
<thead>
<tr>
<th>Type of Therapy</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialectical behavior therapy</td>
<td>A behavioral therapy that includes both individual and group therapy, involving didactics and homework on mood monitoring and stress management; the best validated and easiest to learn of the psychotherapies, one that teaches the patient how to regulate feelings and behaviors, with the therapist acting as a coach with extensive availability</td>
</tr>
<tr>
<td>Mentalization-based therapy</td>
<td>A cognitive or psychodynamic therapy that includes both individual and group therapy, in which the therapist adopts a “not-knowing” stance while insisting that the patient examine and label his or her own experiences and those of others (i.e., mentalizing); emphasis on thinking before reacting (a process that may be central to all effective therapies)</td>
</tr>
<tr>
<td>Transference-focused psychotherapy</td>
<td>A twice-weekly individual psychotherapy developed from psychoanalysis that includes interpretation of motives or feelings unknown to the patient and retains a focus on the patient’s misunderstanding of others, especially of the therapist (i.e., transference); the least supportive and hardest to learn of the therapies</td>
</tr>
<tr>
<td>General psychiatric management</td>
<td>A once-weekly psychodynamic therapy developed from the APA guidelines and the basic BPD treatment textbook, focusing on the patient’s interpersonal relationships but also possibly including family interventions and pharmacologic therapy; the least theory-bound and easiest to learn of the therapies but least well evaluated</td>
</tr>
</tbody>
</table>

* APA denotes American Psychiatric Association, and BPD borderline personality disorder.

Aripiprazole in the Treatment of Patients With BPD: A Double-Blind, Placebo-Controlled Study

*Not FDA approved for the treatment of BPD.
Visitwise Mean Changes in ZAN-BPD Total Scores During Both Acute and Open-Label Phases of Study A

*Not FDA approved for the treatment of BPD.
Error bars represent +/- SD, but are shown in only 1 direction for clarity.
Objective: Aim of the study was to assess DBT plus olanzapine (OLZ) or placebo (PBO) in BPD

Method: 60 patients with BPD were randomized to OLZ or PBO while all received DBT in this 12-week study

Results: 70% of patients completed the trial. Improvement was seen in both groups. For the OLZ/DBT group, there was a statistically significant advantage over PBO for depression, anxiety, and impulse/aggression

Conclusions: Combined psychotherapeutic and pharmacologic approaches appear to be effective treatment for BPD

*Not FDA approved for the treatment of BPD.
Differential Effectiveness of Antipsychotics in BPD: Meta-Analyses of Placebo-Controlled, Randomized Clinical Trials on Symptomatic Outcome Domains

● **Objective:** The authors examined antipsychotic trials using meta-analysis to contribute to treatment guidelines

● **Method:** Domains that were assessed*
  - Cognitive perceptual symptoms
  - Impulsive behavior symptoms
  - Affective dysregulation
  - *Studies of schizotypal personality disorder were excluded

● **Results:** Included 11 studies with 1,152 patients. Examination of areas of significant effect are:
  - Cognitive perceptual symptoms
  - Mood lability
  - Global functioning
  - Authors noted most pronounced effect on anger

● **Conclusions:** The authors noted tailoring drugs to domains can be beneficial. The findings “raise questions on current pharmacological algorithms and clinical guidelines.”

Efficacy Results with ZAN-BPD
Total Score in Subjects with BPD

*Not FDA approved for the treatment of BPD.

Interpersonal Sensitivity

*Not FDA approved for the treatment of BPD.

Hostility

*Not FDA approved for the treatment of BPD.

Clinical Connections

- BPD is an illness of over 5% frequency and challenging outcomes – clearly better understanding and evolution of treatment is needed.
- Current assessment issues are adding examination of domains which may have an impact on treatment research and planning.
- Exploration of BPD using functional imaging has initiated characteristics of domains and may lead to more specific approaches.
- A recent medication study has shown some potential usefulness, but the editorial in AJP (Tohen) has clearly indicated the next steps in treatment research.