***Mount Sinai Mood and Personality Program offers treatment studies in dialectical behavioral therapy and medication trials.***

# Current Psychological and Psychopharmacologic Treatments of Borderline Personality Disorder

**By Marianne Goodman M.D. and Larry Siever M.D.**

Borderline personality disorder (BPD) is a severe, chronic, disabling condition characterized by pervasive difficulties in interpersonal relationships, instability of mood states, and impulsive aggressive behavior. 69-75% of individuals with the disorder have self-destructive behaviors including self-mutilation, suicide attempts, abuse of alcohol and drugs and completed suicide rates ranging between 3-9% [1]. The life-threatening quality of this symptomatology requires extensive use of health care resources, and successful treatment is often difficult to achieve.

This chapter on BPD treatment strategies begins by providing necessary background on factors which influence choice of intervention and outcome; including psychopathology, illness course, traumatic antecedents and biological basis underlying this disorder. Next, current empirically validated treatment studies and American Psychiatric Association (APA) treatment guidelines for BPD are reviewed. Lastly, shortcomings and inadequacies of the treatment literature are highlighted.

## Psychopathology

There are three main dimensions of symptomatology in borderline personality disorder: (1) affect dysregulation; (2) impulsive aggression; and (3) identity disturbance. The affective domain comprises emotional experiences ranging from intense bouts of anger lasting hours, rapid fluctuations of mood states and episodes of profound dysphoria and anguish that is relieved at times by attempts at self-injury.

Impulsive aggressive behaviors are violent actions directed toward the self or others, including self-injurious behavior (e.g. cutting), domestic violence, assault, destruction of property, and suicide. These behaviors account for a substantial portion of the morbidity and mortality associated with the disorder. Forms of impulsive aggression directed at self, such as repetitive skin cutting or burning, have been demonstrated in up to 80% of individuals with borderline personality disorder.

Identity disturbance symptoms may include an unstable sense of self, chronic feelings of emptiness, and changing views of career, friendships, and values. Individuals with borderline personality disorder are prone to cognitive distortions and can experience a variety of dissociative symptoms including depersonalization, derealization, and, during times of stress, vulnerability to transient psychotic experiences.

The cluster of BPD symptoms results in inordinate dysfunction in interpersonal relationships. Individuals with BPD have stormy connections with people, are sensitive to criticism and rejection, easily disappointed, and frequently exert frantic efforts to avoid being left or abandoned.

These three dimensions, affective instability, impulsive aggression and identity disturbance likely have different etiologies and specific treatments have been developed to target each.

## Prevalence

Borderline personality disorder affects 2% of the general population, and young women are at greatest risk for the disorder. Additionally, 11% of psychiatric outpatients and 19% of psychiatric inpatients, carry the diagnosis of BPD [2]. There is speculation that females with BDP present to mental health systems whereas males with BDP are more commonly found within the forensic system, and, consequently, have poor access to treatment.

## Course

Key features of a personality disorder are its pervasiveness across a several areas of functioning, stability over time and relatively early onset in development. This applies to borderline personality disorder, which tends to present in early adulthood and remain stable over time. The extreme behaviors of suicidality and impulsivity, however, may diminish somewhat with increasing age and treatment.

## Role of childhood trauma

Several studies of clinical populations of borderline personality disorder [3] note extremely high abuse rates--over 90%. Some clinicians have interpreted these findings to suggest that BPD is a "complex" form of posttraumatic stress disorder (PTSD). They posit that chronic childhood neglect and abuse, in particular childhood sexual abuse, contribute to the development of insecure attachments to caregivers that lead to problems in self-regulation of emotions, feelings, and impulses. These ideas suggest that BPD treatment be informed by an understanding of the sequelae of childhood trauma, and should incorporate PTSD treatment paradigms.

## Biological underpinnings

Over the last fifteen years, research on borderline personality disorder psychopathology has moved from a phenomenological to a biological perspective secondary to advances in psychopharmacology, neuroimaging and genetics. The major biological theory of borderline personality disorder implicates the neurotransmitter serotonin (5-HT) which is involved in appetite, impulse control, sleep, sexual drive, and mood regulation. Individuals with BPD have been shown to have diminished brain serotonin levels. Biological data in individuals carrying a diagnosis of BPD suggests decreased levels of 5-HT metabolites in the cerebrospinal fluid, altered post-synaptic serotonin receptor levels, and abnormally diminished responses to 5-HT stimulating agents [4]. Moreover, genetic studies have been performed that examine genes that determine activity of the serotonergic system including receptors, synthetic enzymes, and uptake sites. These genes have been associated with behavioral traits of BPD. Differences in allelic variation of the enzyme tryptophan hydroxlyase, the rate limiting step in the synthesis of 5-HT and the 5-HT 1-B receptor, which may influence the amount of presynaptic release of 5-HT have been associated with impulsive aggression in borderline personality disorder [5]. Variations in the genes of the 5-HT system likely have small to modest effects but contribute to the reduced responsiveness of the 5-HT system. These findings have directly informed advances in psychopharmacologic treatment of BPD, namely the selective serotonin reuptake inhibitors (SSRI) and suggest possible future directions for drug choice and development.

With the use of neuroimaging paradigms including PET scanning, reduced ventral prefrontal cortex activity in BPD has been reported. The prefrontal cortex is heavily innervated by the 5-HT system. After administration of an agent that stimulates the brain's serotonergic system, BPD patients showed less robust activity in the orbital frontal and cingulate cortex compared to control subjects [6]. The orbital frontal cortex is a region that modulates aggression

and lesions to this area have been associated with profound personality changes, aggression, and anger. The cingulate cortex is part of the limbic system that evaluates incoming emotional stimuli in the service of preparing for action. Thus, the orbital frontal and cingulate serve as a brake for the more primitive parts of the brain that generate aggression. The reduced serotonergic brain activity and responsivity translates to less inhibition of aggressive urges and more overt aggressive behavior seen clinically in BPD as displays of anger, assaults, self-mutilation, and suicide attempts. Treatment implications from these data suggest that interventions, which increase the functionality of ventral frontal and cingulate brain areas, may be effective for minimizing the impulsive aggression of BPD.

The affective instability of BPD is believed to be in part due to greater baseline limbic irritability. Administration of procaine, which stimulates paralimbic structures, such as the amygdala and cingulate cortex, causes increased irritability and mood shifts in subjects with BPD compared to control subjects [7]. EEG studies and recording of brainstem auditory evoked potentials in borderline personality disorder suggest cerebral dysfunction, particularly involving reactivity of the limbic system. Taken together, these studies suggest that paralimbic structures may play a critical role in the affective processing and emotional liability of borderline personality disorder, although more direct tests of activation of these regions are needed.

At present, little is known about the biological basis of identity disturbance symptomatology in BPD.

## Treatment

Patients with BPD are problematic to treat, as their difficulties with interpersonal relationships extend to the clinicians that are attempting to offer help. The self-destructive behaviors, anger, mood instability, and pervasive fear of abandonment all interfere with a clinician's ability to establish a therapeutic alliance and sustain a successful treatment. Moreover, patients with BPD are large utilizers of psychiatric care compared to other disorders, they require longer inpatient stays [8] and more contact in outpatient settings [9]. Despite this increased use of services, both traditional psychotherapies and pharmacotherapy have been only partially successful in ameliorating BPD symptomatology. Numerous approaches exist including individual, group, partial hospital and family therapy, however empirical data supporting efficacy is minimal.

## Psychological

### Psychodynamic/Psychoanalytic

The psychological treatment of BPD has been strongly influenced by psychoanalytic thinkers such as Kernberg. He theorized that BPD is the result of internalized early pathological object relations that are maintained by defense mechanisms such as splitting [10]. He contends that a young infant is unable to see his mother both as a good, nurturing figure and a disappointing, hateful, depriving person as to do so would cause overwhelming anxiety. Children split these experiences into separate parts, a defense called "splitting". With normal development, children outgrow this psychological response, however individuals with BPD do not. This manifests in later life as distortion of relationships with idealization or devaluation, denial of present or past feelings, vacillation of opposite feeling states, feelings of inadequacy and self-hatred. Furthermore, in BPD, projective identification; the attribution of repressed aspects of oneself on to another person, further impairs the quality of interpersonal relationships and integrated sense of self. Treatment efforts are aimed at understanding the splitting and projective identification through intensive psychoanalytic psychotherapy and exploration of transference

issues and current reality. Unfortunately, evidence to bolster this treatment approach is limited primarily to case studies.

There is however, one empirical study of psychoanalytically oriented treatment of BPD in a partial hospitalization [11]. Subjects received weekly individual therapy, expressive therapy, community meeting and three times a week group psychotherapy and monthly medication management. The comparison group received standard treatment in the general psychiatric service, averaging two individual therapy sessions a month, and twice monthly visits form a community psychiatric nurse. The authors conclude that the partial hospitalization treatment produced significant benefits in decreasing self-mutilation, depression, anxiety, suicide attempts and interpersonal problems. However, it is difficult to discern whether this efficacy is due to increased intensity of clinician visits, medication status and effect or the treatment modality itself.

**Dialectical Behavioral Therapy (DBT)**

The psychological treatment approach with the most convincing outcome data is DBT. This is a manualized cognitive behavioral treatment approach developed by Dr. Marsha Linehan to treat chronically suicidal individuals, many of which met criteria for BPD. DBT presumes that BPD arises from emotional dysregulation problems coupled with an invalidating environment [12].

The approach combines behavioral interventions including skills training, exposure, and problem solving with cognitive techniques of mindfulness, and stresses the importance of the client-therapist connection. Patients receive weekly skills training taught in a group setting, weekly individual therapy, and telephone consultation as needed. Additionally, there is a weekly therapist consultation group where clinical matters are discussed and support and guidance is offered to the treatment provider.

The first stage of DBT treatment focuses on achieving behavioral control and is accomplished through a hierarchical approach. These include the following steps: 1) decreasing life threatening and suicidal threats, 2) diminishing treatment interfering behaviors including non-compliance and premature dropout, 3) addressing patterns of behavior that adverse impact on quality of life, and 4) increasing behavioral skills. Later stages of treatment focus on- resolution of PTSD symptomatology and response, improving self-respect, and increasing the ability to experience joy. The original study of DBT [13] concluded that one year of standard DBT treatment is significantly superior to treatment as usual (TAU) in reducing suicidal and parasuicidal behavior. DBT subjects were more likely to stay in individual therapy and utilized fewer inpatient psychiatric hospital days. DBT did not differ from TAU in symptoms such as depression, suicidal ideation and hopelessness.

Koons et al [14] adapted Linehan's approach to a Veteran Administration (VA) setting, comparing a modified DBT to treatment as usual in a VA outpatient clinic. Her subjects were female veterans with BPD but were not required to have recent or past parasuicidal behavior. Additionally the treatment time frame was modified to six months from the traditional year reported in the original Linehan studies [13]. In the Koons study [14], DBT treatment as compared to TAU, resulted in a minimization of suicidal ideation, anger, and depression. In a pilot study [15] using a non-randomized design, 6 months of DBT was compared to 6 months of TAU (n=30). Their findings were notable for diminished self- mutilation acts and urges, as well as suicidal thoughts. Interestingly, there were no differences in self-reported symptoms of depression, global functioning and hopelessness. Both of these studies point to the feasibility of 6-month treatment duration. Of note most DBT studies have been conducted in women, with minimal data available regarding the application of this treatment approach for men.

Furthermore, the DBT approach has also been successfully adapted to other settings and patient populations including inpatient hospitals [16,17,18], criminal justice settings [19] and to

outpatient populations of BPD substance abusers [20,21], depressed and suicidal adolescents with BPD or BPD traits [22] and binge-eating disordered individuals [23].

These replication studies are important in demonstrating DBT efficacy is not limited to the site where it was developed and that the techniques can be mastered and employed successfully in other institutions. Limitations of this approach include that there is no data for DBT efficacy after stage 1 treatment. Moreover, the confounding effect on treatment efficacy of concomitant medication use with DBT has not been resolved.

## Additional Cognitive Behavioral Therapy approaches

A psychoeducational, cognitive-behavioral systems based treatment for BPD, Systems Training for Emotional Predictability and Problem Solving (STEPPS) has been developed by Blum and colleagues[24]. This is a manualized cognitive behavioral program consisting of twenty, two hour sessions that include both patients and family members or significant others, which fosters the acquisition of skills to manage specific problematic emotions and behaviors. Specific emotion management training skills include: distancing, communication, challenging of maladaptive thoughts and distraction. A sampling of behavior management skills covered in the treatment include goal setting, exercise and improvement of physical health, strengthening interpersonal relationship and avoidance of abusive behavior. STEPPS enhances the efficacy of ongoing treatment that the patient is already receiving.

A one-year, twice monthly extension program called STAIRWAYS (Setting goals, *T*rusting and taking risks, *A*nger management, *I*mpulsivity control, *Relationship* behavior, *W*riting a script, *A*ssertiveness training, *Y*our Journey and *S*chemas revisited) exists for graduates of the STEPPS program.

Assessment of the STEPPS program in an uncontrolled, retrospective analysis suggests that the program is well received by patients and therapists who deliver the care. This pilot study encourages further research to demonstrate efficacy and validity of the approach.

## Cognitive Analytic Therapy

There is one study in the literature targeting the treatment of dissociation and personality fragmentation using cognitive analytic therapy (CAT) [25]. This treatment blends concepts of object relations theory with cognitive behavioral features, aiming to increase patient's self-awareness of their dissociative processes. The treatment is based on Ryle's [26] conceptualization of BPD as a "multiple self-states" model, with partially dissociated self-states that influence symptom formation. Subjects receive 16 sessions, which focus on integrating self-states by techniques of a reformulation letter, and a self-states sequential diagram. The relationship with a therapist is informed by psychoanalytic concepts such as transference. Using a patient series within subject design, 5 patients with BPD received 16 sessions of CAT. Pre and post treatment assessments were notable for reductions in BPD symptom severity in all 5 participants, with less consistent results for dissociative symptomatology and interpersonal adjustment. Although its uncontrolled nature and small size limit this study, it offers a novel treatment approach that may prove to be promising particularly for BPD with more severe personality fragmentation.

## Pharmacotherapy

Given the heterogeneity of the disorder and that the diagnosis of BPD requires any 5 of 9 DSM-IV criteria, pharmacologic treatment has evolved to treat *particular dimensions* of BPD rather than the disorder in its entirety. The dimensions include affective instability, impulsive aggression and identity disturbance.

## Treatment Studies of affective instability in BPD

### Antidepressants

Early studies of treatment in BPD examined the effects of tricyclic antidepressants and monoamine oxidase inhibitors on affective symptoms of anger, depression and mood lability of BPD. Open label studies on tricyclic antidepressants (TCAs) [27] and a double-blind trial with amitriptyline [28] found some improvement in these domains. Nonetheless, these benefits were limited by a high lethality in overdose, difficult side effect profile and in a sub-group of BPD patients, a paradoxical effects of increased hostility and affective instability.

The use of monoamine oxidase inhibitors (MAOIs) in treating affective lability and rejection sensitivity in BPD is supported by a double blind phenelzine vs. TCA study [29] and a five condition cross-over study involving alprazolam, tegretol, phenelzine, triflurperazine and placebo [30]. In both of these studies, MAOIs were superior to other agents in alleviating depression, hostility, and anger. However, concerns about overdose lethality and interactions with tyramine containing foods limit the use of these medications.

The use of selective serotonin reuptake inhibitors (SSRIs) has gained popularity and is particularly effective in the treatment of depressive and anger symptoms of BPD [31,32]. Moreover, studies on depressed subjects without a personality disorder [33] and normal individuals [34] highlight the role of SSRIS in reducing mood symptoms such as anger, hostility and irritability.

### Mood stabilizers

Depakote has been found to be effective in treating mood symptoms in two recent reports [35,36]. In a ten week double-blind, placebo-controlled trial of depakote on 16 individuals with BPD, significant changes in global measures, Clinical Global Impressions-Improvement Scale (CGI-I) and Global Assessment Scale (GAS) as well as core BPD symptoms of irritability, suicidality, depression and aggression were noted. Despite these improvements, there was a high dropout rate of 58 percent [35].

A longer, six month double-blind placebo-controlled trial of depakote with women with comorbid BPD and bipolar II noted improvements in interpersonal sensitivity, anger and hostility as measured by the Symptom Checklist 90 (SCL-90) and overall aggression as measured by the modified Overt Aggression Scale (MOAS). In contrast to the Hollander study (2001), the medication was well tolerated [36].

Lithium and carbamazepine have also been investigated as potential mood stabilizers in BPD. A double blind placebo controlled crossover study comparing lithium and a TCA noted improvements in mood symptoms of anger and irritability with lithium [37]. Two double blind studies of carbamazepine support its use with episodic behavioral dyscontrol [30,38].

An open case series of lamotrigine with 8 patients diagnosed with BPD and serious histories of suicide, drug use, and promiscuity noted significant improvement with GAF scores rising an average of 40 points during a 3-4 month period and complete absence of impulsive, sexual and suicidal behaviors in three of the subjects [39]. Lamotrigine, an anticonvulsant found to have mood stabilizing and antidepressant properties operates through direct action at voltage dependent NA+ channels, stabilizing neuronal membranes and inhibiting the release of glutamate and aspartate [40]. The authors hypothesize that subsets of BPD patients suffer with severe affective dysregulation described as “ultra-rapid” cycling and have links to a bipolar II diagnosis. The mechanism responsible for decreasing the severity of impulsive aggression in these anticonvulsant agents is unknown. Additional placebo controlled studies are needed as is research to determine which sub-populations of BPD patients will respond to these interventions.

In summary, these data suggest that affective dysregulation is best treated with SSRIs, with depakote or carbamazepine as a second choice. In certain BPD sub-groups, use of a MAOI may be considered if the likelihood of overdose is low and ability to regulate diet is possible.

**Treatment studies of impulsivity and aggression in BPD**:

The deepening understanding of the neurobiology of impulsive aggression in BPD has impacted treatment. The most logical extension of the serotonin hypothesis is the use of selective serotonin reuptake inhibitors (SSRIs). To date three double blind placebo controlled studies [31,32,41] have found efficacious results with fluoxetine on aggressive behaviors in patients with personality disorders. The most recent [32], was a study consisting of 40 non-depressed personality disordered outpatients, (one third met criteria for BPD) who were medicated with fluoxetine over a 14 week trial. The starting dose was 20mg for the first month, with increases to 60mg by month 3 if there was not a 75% diminution of aggressive symptomatology. However, most patients required between 20-40mg. 80% of patients randomized to medication were responders at 12 weeks. The primary difference between responders and non-responders was time in treatment with responders staying in the research study 10 weeks compared to non-responder's 7 weeks. The difficulty in maintaining patients in treatment was felt not to be related to side-effects but rather the underlying impulsivity and difficulties with engagement that characterizes this population.

Additional SSRI agents including citalopram [42] and sertraline [43] have undergone open trials with positive results.

Other agents that have been shown to be useful in treating impulsive aggression in BPD patients include mood stabilizers and atypical antipsychotics. In the previously discussed double-blind placebo controlled divalproex study [35], patients assigned to drug responded with an average Aggression Questionnaire (AQ) score 32 points below that of controls. There were no changes on any of the Overt Aggression Scale- modified (OAS-M) for either patients or controls.

There is growing interest in olanzapine, an atypical antipsychotic with mood stabilizing properties. An open label pilot study [44] in subjects with BPD and dysthymia demonstrated significant improvements in anger, psychoticism, interpersonal sensitivity and depression. Similarly, a six month placebo-controlled, double blind trial of olanzapine on 28 females with BPD, noted significant improvements in self-reported changes as measured by the by the Symptom Checklist 90 (SCL-90) in anxiety, paranoia, anger, hostility and interpersonal sensitivity but not in depression. The medication was well tolerated with no reported movement disorders, however a modest weight gain occurred in subjects taking the olanzapine [45].

Case reports and open label series have reported for other atypical antipsychotic medications in BPD including clozapine [46,47,48] and risperidone [49,50], to ameliorate severe self mutilation and reduce impulsive behaviors. These patients either exhibited extreme self mutilating behaviors, had concurrent Axis1 diagnosis of atypical psychotic disorder, or several previous trials of neuroleptics and likely represent a sub-population of patients with BPD with a psychotic diathesis.

Lastly, the class of opioid antagonists is being investigated as a treatment for impulse-control disorders. Studies aiming to reduce repetitive self-injurious behaviors have targeted the nonselective opioid antagonist naltrexone [51,52,53] in open-label trials with beneficial reductions in dissociative phenomena, and urge related symptoms. It is unclear how alterations of the endogenous opiate system interface with the serotonergic system in the etiology of impulsive aggressivity in BPD.

**Treatment Studies of identity disturbance and psychotic symptoms in BPD**

The etiology and biological underpinnings of this dimension of BPD rare only beginning to be identified precluding a mechanism based treatment. There are no pharmacologic interventions that target psychological symptoms such as unstable sense of self, chronic emptiness or changing views of the self. However, dissociative symptoms and transient psychotic episodes have been treated with low dose atypical antipsychotics and naltraxone. The treatment of dissociative symptoms using these agents has been conducted in the context of impulsive aggressive behaviors (e.g. self-mutilation, parasuicidal and suicidal acts) and is discussed under that heading.

**Clinical guidelines**

The Clinical Practice Guidelines for BPD [54] published in 2001, represents the first effort to establish evidence based treatment recommendations for this disorder. Despite a limited number of rigorously designed studies (i.e. randomized controlled treatment trials) for this disorder, the guidelines state " the primary treatment for BPD is psychotherapy, complemented by symptom-targeted pharmacotherapy" (p.4)[54]. The guidelines further suggest that the psychotherapies with some efficacy are psychoanalytic, psychodynamic and DBT and that pharmacotherapy with a SSRI is the initial treatment of choice for symptoms of affective dysregualtion and impulsive behavioral dyscontrol and low dose atypical neuroleptics are the treatment of choice for cognitive and perceptual problems. These recommendations were based on only 5 randomized controlled studies on psychotherapy for BPD *in female subjects only* and 21 randomized trials for pharmacotherapies for BPD. This is in comparison to over 75 randomized controlled psychotherapy studies in depression. Clearly the literature on BPD treatment is limited in scope and the guidelines will change with growing literature and future research.

**Conclusions** -

BPD is a challenging disorder to treat. Patients with this disorder are large utilizers of medical and psychiatric care, however their symptoms of self-destruction, anger, mood instability and impaired interpersonal relationships hinder the development of a therapeutic alliance and successful treatment outcome. The treatment literature of BPD is characterized by only a few rigorously designed studies, which form the basis for APA treatment guidelines for the disorder. Reasonably strong empirical findings support the use of SSRIs and DBT, with more limited but promising evidence for mood stabilizers such as depakote and the atypical antipsychotic olanzapine.

The treatment literature has numerous limitations. Beyond the small sample sizes of the studies and short duration of treatment (DBT being the exception), most of the research has been conducted on female subjects only. There is little to no data on the role of co-morbid axis I illness, long term efficacy of these interventions and no studies to date on combining medication and psychotherapy modalities and only one preliminary report on comparison of drug with DBT [55].

Future treatment approaches may aim to target the specific BPD dimensions of affective instability, impulsive aggression and identity disturbance with combined pharmacologic and psychotherapeutic modalities for maximum efficacy ( see table 1).

Table 1

combined pharmacologic and psychotherapeutic modalities for treatment of specific BPD dimensions

| Affective Instability | Impulsive Aggression | Dissociation/Identity disorder |
|---|---|---|
| SSRI/mood stabilizer | SSRI | Low-dose neuroleptic |
| DBT | DBT | Cognitive analytic therapy |

We are hopeful that the continuing neurobiologic advancements in BPD etiology, and development of more effective pharmacologic interventions coupled with wider delivery and further validation of psychotherapy approaches, will produce more significant symptomatic relief. Although the BPD treatment field is young, the next phase will include more sophisticated, well designed combination studies, further refinement of individual strategies, as well as a neurobiologic understanding of psychotherapeutic interventions.

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**Contributed by Marianne Goodman M.D., Larry Siever M.D.**