Various theoretical orientations have converged upon the conceptualization of borderline personality disorder (BPD) as a disturbance in mental representations of self and other, contributing to core difficulties in identity, intimacy, empathy, and self-directed motivation.\textsuperscript{1-3} In BPD, this core psychopathology contributes to the characteristic syndrome of impulsivity, aggression, suicidality, transient dissociation or psychosis, affective instability, chronic emptiness, identity diffusion, and tumultuous interpersonal dysfunction oscillating between idealization and devaluation.\textsuperscript{4} BPD symptoms are most severe in the context of interpersonal stressors such as perceived rejection or abandonment. Affective dysregulation and impulsive aggression often contribute to self-destructive behavior,\textsuperscript{5} with worsening symptoms, frank dissociation, and worsening suicidality occurring in the context of interpersonal stressors.\textsuperscript{6-8} The prevalence of BPD may be as high as 5\% to 6\%, with high comorbidity with mood, anxiety, and substance abuse disorders.\textsuperscript{9-10} Patients with BPD have suicide rates 50 times that of the general population\textsuperscript{11} and utilize more mental health resources than individuals with other psychiatric disorders.\textsuperscript{12,13}

**Keywords:** borderline personality disorder; personality disorder; psychopharmacology; impulsivity; aggression; interpersonal

**Introduction**

The best available evidence for psychopharmacologic treatment of borderline personality disorder (BPD) is outlined here. BPD is defined by disturbances in identity and interpersonal functioning, and patients report potential medication treatment targets such as impulsivity, aggression, transient psychotic and dissociative symptoms, and refractory affective instability. Few randomized controlled trials of psychopharmacological treatments for BPD have been published recently, although multiple reviews have converged on the effectiveness of specific anticonvulsants, atypical antipsychotic agents, and omega-3 fatty acid supplementation. Stronger evidence exists for medication providing significant improvements in impulsive aggression than in affective or other interpersonal symptoms. Future research strategies will focus on the potential role of neuropeptide agents and medications with greater specificity for 2A serotonin receptors, as well as optimizing concomitant implementation of evidence-based psychotherapy and psychopharmacology, in order to improve BPD patients’ overall functioning.

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BPD arises in the context of variable interactions between specific genetic risk factors and developmental factors related to early care-giving, eliciting a pattern of psychopathological personality traits and potential differences in neurobiological functioning. With the increasing recognition over the past several decades of the underlying neurobiology associated with BPD, treatment has shifted from the exclusive use of psychotherapy to the development of strategic approaches for evidence-based psychopharmacology. Although developmental heterogeneity and individual differences within BPD complicate general psychopharmacologic management strategies, BPD patients manifest persistent, intrapsychic pain and interpersonal hypersensitivity, subjectively experienced as aversive and/or aggressive reactions to what might otherwise be mild interpersonal stressors. Not surprisingly, some BPD symptoms are more amenable to treatment than others. When patients are followed prospectively, interpersonal affective symptoms, such as intolerance of aloneness and conflicted feelings about dependency, are slowest to remit, while symptoms reflecting impulsive behavior, self-injury, and aggression tend to resolve more quickly. Although impulsive aggression and suicidality are often acute presenting symptoms motivating concern and psychopharmacologic consultation, paradoxically, these symptoms may be most apt to resolve. Meanwhile, interpersonal affective symptoms reflective of core psychopathology persistently contribute to chronic functional impairment, intrapsychic pain, and difficulty maintaining social support.

Methods

The following review discusses the results of a search of the PubMed database, utilizing the MeSH terms “borderline personality disorder” or “borderline personality disorder: drug therapy” (with limits restricted to articles in English, on humans, clinical trials, and reviews). The focus is primarily on highest-level original research (ie, randomized controlled trials, either with placebo control or comparing multiple active medications). Moreover, this review adds studies published since the author’s last comprehensive review of pharmacotherapy for personality disorders. Additional, recently published systematic reviews add consensus data in the psychopharmacologic treatment of BPD. The primary aim of this review is to present the most up-to-date, evidence-based clinical approach to psychopharmacologic management of BPD. Secondary aims include detailing current difficulties and future directions in research on BPD psychopharmacology.

General considerations

The evidence base for psychopharmacological treatment of BPD is limited by relatively small sample sizes, high rates of placebo response, and brief trial durations. Most trials in the past have lasted 3 months or less, or else suffered from high dropout rates. Because of high comorbidity of BPD with Axis I disorders, subjects often report other disorders whose presence may complicate response to the study medication. Without this comorbidity, however, results would not be generalizable to clinical practice. BPD trials are also prone to high placebo response rates, meaning that open-label trial data should be interpreted with caution. Nevertheless, clinicians can provide optimal evidence-based treatment by implementing the specific medications studied in randomized placebo-controlled trials, along with evidence-based psychotherapy.

An older literature characterized BPD subjects with a distinct diagnostic nosology, or included subjects with highly comorbid or other personality disorder diagnoses. Findings may therefore be difficult to apply to current practice. Clinicians should exercise caution in attempting to apply research findings to severely ill BPD patients, as many medication trials recruited only outpatients, who further were excluded if they expressed acute suicidality or had made a recent suicide attempt. Impulsive aggression has been targeted more effectively with medications relative to other symptoms, as evident in the conclusions of recent systematic reviews. This suggests that these symptoms, though acutely dangerous, may be more amenable to treatment than identity and interpersonal dysfunction, whose functional neurobiology is less well understood. As noted above, impulsive aggression is more apt to resolve spontaneously, compared with interpersonal affective symptoms.

There are no medications approved by the US Food and Drug Administration (FDA) for the treatment of BPD, and very limited data exist for any single medication improving overall BPD severity. This has led to symptom-based approaches to psychopharmacologic man-
agement, often resulting in unnecessary polypharmacy, despite little benefit from this in the main trial studying such a practice. Instead, practicality dictates targeting patients’ most distressing symptoms with the most efficacious and tolerable medications, and repeated evaluation of risks versus benefits of continued pharmacotherapy. Others interpret limitations in the evidence base to advocate use of medication only during crises. Coordination between psychopharmacologist, psychotherapist, and others involved in patients’ treatment is often necessary for targeted, timely intervention and ongoing re-evaluation of attendant risks versus benefits of treatment.

Several recent articles are considered only briefly here. An open-label comparison of sertraline and olanzapine in patients with BPD who were also receiving methadone maintenance treatment for opioid dependence showed that both agents were effective, but comorbidity limited the findings’ generalizability. Another study was a randomized, double-blind comparison of olanzapine and haloperidol, with both agents demonstrating similar efficacy but distinct side-effect profiles. There have also been recent positive, open-label trials with duloxetine, quetiapine, oxcarbazepine, the traditional herb yi gan san, and other medications, but lack of randomized, double-blind methodology significantly limits applicability of these results. One could speculate about potential benefits of these medications on noradrenergic, serotonergic, γ-aminobutyric acid (GABA)-ergic, and glutamatergic neurotransmission. The lack of placebo control methodology and the propensity of BPD trials for high placebo response rates makes open-label trials difficult to interpret.

**Antidepressants**

Four attachment classifications have been identified in developmental research on the enduring impact of early attachment relationships on representations of self and others in relationships. BPD is associated with a higher prevalence of the disorganized attachment classification, characterized by dissociative lapses in reason with respect to significant past and present attachment relationships. Serotonergic genetic polymorphisms, mainly related to the serotonin transporter, are associated with disorganized attachment classification in the context of trauma and adverse care-giving environments. Despite neurobiological evidence of a disturbance in serotonin signaling associated with BPD and associated phenomena such as impulsivity, aggression, and suicidality, the clinical significance of these findings in terms of psychopharmacologic enhancement of serotonergic neurotransmission has recently been called into question. In contrast to the 2001 American Psychiatric Association (APA) guidelines for treatment of BPD, recent systematic reviews have highlighted a limited role for antidepressants in the treatment of BPD, due to more modest therapeutic effects on these symptom domains relative to other medication classes. Nevertheless, antidepressants are often used to treat commonly comorbid anxiety and mood disorders. Selective serotonin reuptake inhibitors (SSRIs) have minimal effect on impulsive aggression in BPD, but may have modest effects in decreasing anxiety, depression, and possibly affective lability (the latter, particularly with fluvoxamine). Older BPD trials showed lack of effectiveness of tricyclic antidepressants, likely because anticholinergic sequelae may worsen effortful control of

| Medication | Dosing | Effects |
|------------|--------|---------|
| MAOIs      |        |         |
| Phenelzine | 15-90 mg/d | Improvements primarily in depression, impulsive aggression. Some patients experience uncomfortable activation. |
| Tranylcypromine | Mean dose 40 mg/d | Improvements primarily in affective symptoms, interpersonal sensitivity, but limited data. |
| SSRIs      |        |         |
| Fluoxetine | 20-80 mg/d | Mild improvements in affective symptoms, anger, impulsive aggression. Effects may be pronounced in males, patients with high levels of impulsive aggression. |
| Fluvoxamine | 150-250 mg/d | Mild improvement in affective instability, not impulsivity. |
| Paroxetine | 20-40 mg/d | Possible decrease in suicidality without significant effect on depression, though limited data. |

Table I. Antidepressants demonstrating efficacy in borderline personality disorder. MAOI, monoamine oxidase inhibitor; SSRIs, selective serotonin reuptake inhibitors.
impulsivity, aggression, and suicidality. Histologically, monoamine oxidase inhibitors (MAOIs) have been considered the treatment of choice for patients with atypical depression characterized by rejection sensitivity and affective reactivity. Consistent with the high rates of rejection sensitivity associated with BPD, MAOIs demonstrated robust improvements (particularly in aggression and anxiety) in older trials. However, lower tolerability profiles of MAOIs and potential adverse reactions (e.g., hypertensive crises during dietary indiscretion) have limited their utility for BPD patients with severe impulsivity or suicidality. Refer to Table I for a summary of pertinent positive findings within the antidepressant class.

Because antidepressants have not demonstrated significant high-level evidence of therapeutic benefit, these medications currently lack strong recommendations in treating BPD. Serotonin regulates amygdala hyper-reactivity in BPD, thought to be a central neurobiological correlate of affective instability. Interpersonal hypersensitivity in BPD may be associated with the combination of lack of amygdalar and psychophysiological habituation to social affective stimuli on the one hand, and blunted empathic understanding of these stimuli on the other. Nevertheless, current antidepressants may not efficiently target the receptors or mesocorticolimbic brain regions associated with clinically significant amygdala hyper-reactivity. Limited therapeutic effectiveness of antidepressants in BPD may be related to lack of serotonin receptor specificity, since 5-HT but not 5-HT antagonism is associated with decreasing impulsivity. Complex, coordinated agonism and antagonism of 5-HT and receptors is needed for adaptive, deliberate decision-making. Similarly, pharmacologic alteration of 5-HT signaling yields distinct effects on animal models of impulsive aggression, depending on brain regions targeted, whether signaling is tonic or phasic, and concomitant modulation by GABAergic, glutamatergic, or neuropeptide signaling.

**Antipsychotics**

BPD patients demonstrate higher plasma and cerebrospinal fluid levels of the dopamine metabolite homovallinic acid. Dopamine receptor genetic polymorphisms interact with traumatic attachment stressors to yield attachment insecurity and disorganization, thought to be central to development and intergenerational transmission of interpersonal dysfunction in BPD. The functional neurobiology of attachment insecurity and disorganization remain unclear, but impulsivity and transient psychotic symptoms associated with BPD provide further evidence for targeting dopamine neurotransmission.

Dopaminergic signaling has distinct effects on cognition, reward processing, and impulsivity, depending on whether it affects D, D, receptor, brain region, and tonic versus phasic patterns of synaptic release. Older trials demonstrated significant improvements in anger for haloperidol, and suicidality for flupenthixol decanoate, as well as inconsistent effects on psychosis, irritability, and affective symptoms. Despite improvement with some classical neuroleptics on individual symptoms, the antipsychotic class as a whole was associated with worsening overall severity of BPD in a recent meta-analysis. Classical neuroleptics may improve anger and impulsive aggression, but patients must be closely monitored for notable risks of extrapyramidal symptoms, tardive dyskinesia, and worsening overall functioning.

Atypical antipsychotics are prescribed more often, due to greater tolerability and broader therapeutic benefits associated with serotonergic and noradrenergic activity beyond classical neuroleptics’ stronger D receptor antagonism. Atypical antipsychotics are efficacious in the treatment of impulsive aggression. Across trials, this therapeutic effect is driven primarily by olanzapine and aripiprazole. These antipsychotics significantly improved affective instability, impulsivity, psychosis, and interpersonal dysfunction, leading to clinical consensus of breadth of efficacy in BPD.

Despite one trial failing to establish statistically significant improvement with low-dose olanzapine, a larger, multisite sample recently showed significant but modest decreases in overall BPD severity, with further improvements seen in open-label continuation. Similarly broad benefits are seen in trials of aripiprazole improving impulsivity, aggression, affective instability, self-injury, and interpersonal symptoms. Aripiprazole has a long half-life and favorable metabolic profile, which may contribute to ease in administration and effectiveness. The coordinated serotonergic and dopaminergic activity of aripiprazole as a partial agonist at D and 5-HT receptors, and antagonist at 5-HT receptors, may be more efficacious in treating impulsivity and aggression in BPD. Despite similar noradrenerg-
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Anticonvulsants

Affective symptoms associated with BPD, particularly those related to intolerance of aloneness and dependency, are refractory relative to impulsive aggression and self-injurious behavior. 18-21 Despite phenomenological similarity between BPD and the bipolar spectrum, characteristic, associated interpersonal and identity disturbances distinguish affective instability in BPD. 97-101 Although older studies indicated lithium as efficacious for BPD, 33,102 risks associated with toxicity or noncompliance and the need for frequent monitoring have limited its clinical utility.

Temporal aspects of affective instability in BPD appear to be similar to rapid-cycling variants of bipolar disorder, motivating more frequent use of other mood stabilizers. Despite early documentation of clinical benefit from carbamazepine, its efficacy in trials was inconsistent and possibly associated with worsening depressive symptoms. 103-105 Valproate, lamotrigine, and topiramate offer greater therapeutic benefits in treating affective instability and impulsivity in BPD. 22,29 As a class, anticonvulsant medications offer moderate-to-large effects on impulsive aggression, affective instability, and overall functioning, with potentially greater effect size than associated with atypical antipsychotic treatment. 22,29 Trials with topiramate suggest a broad spectrum of therapeutic benefit, particularly in anger and interpersonal functioning. 106-110 However, adverse cognitive sequelae may interfere with psychotherapy for some BPD patients, and potential weight loss may become troubling for patients with comorbid eating disorders. Lamotrigine treatment improves impulsivity, affective symptoms, 41,112 but it requires lengthy titration to avoid life-threatening rash and toxicity. Valproate appears to be particularly efficacious in BPD patients with prominent impulsive aggression, rather than affective instability. 113 Table III shows pertinent positive results within the class of mood stabilizer/anticonvulsant medications. These medications stabilize excitatory neurotransmission, but they differ greatly in mechanism of action and effects on glutamatergic and GABAergic signaling, so specific mechanisms of therapeutic response in BPD remain unclear. The long-term risk versus benefit analysis for...

| Medication                    | Dosing       | Effects                                                                 |
|-------------------------------|--------------|-------------------------------------------------------------------------|
| Clasical neuroleptics         |              |                                                                         |
| Fluphenazine decanoate; flupenthixol depot | Variable     | Improvements in suicidality, self-injurious behavior. Requires regular injections, limited data on effectiveness. |
| Haloperidol                   | Mean doses 3-7.8 mg/d | Improvements in paranoia, anger, possibly anxiety/affective symptoms. Superior to tricyclic antidepressant but not MAOI. Possibly worsening overall status due to worsening sedation, depression, side-effects. |
| Loxapine                      | Mean dose 14.5 mg/d | Improvements in depression and anger (relative to chlorpromazine), but limited data. |
| Thiothixene                   | Variable     | Improvements primarily in cognitive-perceptual symptoms, psychoticism, but limited data. |
| Atypical antipsychotics       |              |                                                                         |
| Aripiprazole                  | 15 mg/d      | Improvements in affective symptoms, aggression, paranoia, overall functioning |
| Olanzapine                    | 2.5-10 mg/d  | Improvements in affective instability, impulsivity, aggression, interpersonal sensitivity, and overall borderline personality disorder severity. High risk of weight gain, metabolic effects. |

Table II. Antipsychotics demonstrating efficacy in borderline personality disorder. MAOI, monoamine oxidase inhibitor.
these medications in BPD needs to be determined case by case, particularly with respect to recognized risks of teratogenicity for women of child-bearing age.

Other medications

Alprazolam and other benzodiazepines are strongly discouraged in treating BPD, due to risks of worsening impulsivity and suicidality. BPD patients may be at increased risk for benzodiazepine dependence, in an effort to self-medicate chronic, refractory affective symptoms by fostering dissociative symptomatology. Targeting noradrenergic signaling has been less frequently studied in psychopharmacological treatment of BPD. The α-adrenergic agonist clonidine proved effective in treating comorbid post-traumatic stress disorder (PTSD) and BPD, but this effect seemed specific to PTSD symptoms. Consistent with increasing recognition of omega-3 fatty acids in mood stabilization, one trial demonstrated tolerability and efficacy of omega-three ethyl-eicosapentaenoic acid (EPA) supplementation, decreasing aggression and affective symptoms in patients with moderate to severe BPD.

Neuropeptides

Recent psychopharmacological research in BPD has involved neuropeptides such as opioids and oxytocin, which modulate broadly-distributed neural networks associated with coordinating complex behavior. Other relevant neuropeptides include vasopressin and neuropeptide Y. Recent neurobiological research has suggested endogenous opioid modulation as a potential avenue for treatment of BPD. Endogenous opioid signaling is involved in consummatory reward processing, pain modulation, social affiliation, rejection sensitivity, and maternal-infant attachment, which may have implications for impulsivity, self-injurious behavior, and interpersonal dysfunction in BPD. Dysregulated opioid signaling is also associated with affective instability in BPD. Despite promise in terms of potential implications in the developmental psychopathology of BPD, opioid medications have not demonstrated consistent therapeutic benefit.

An early open-label study of the opioid antagonist naltrexone showed early promise in treating dissociative symptoms in BPD. Stabilization of opioid signaling may improve self-injury, dissociation, impulsivity, and interpersonal functioning. Moreover, opioid antagonism may prevent adverse effects of dissociation on behavioral conditioning, suggesting a potential synergistic role with psychotherapy to improve interpersonal hypersensitivity. Nevertheless, both opioid agonists and antagonists have shown limited efficacy in preliminary research with BPD patients. A more recent, placebo-controlled trial of naltrexone also failed to demonstrate statistically significant improvement in dissociative symptoms. Therefore, opioid medications lack clear role in treating BPD, and they are associated with substantial risks of dependence (primarily for agonists) and other potential adverse effects.

Oxytocin is associated with empathic processing, self-similarity evaluation, attuned parental care-giving, and affiliative bonding. This has led to similar considerations for treating interpersonal dysfunction in BPD. Nevertheless, placebo-controlled administration of intranasal oxytocin led BPD patients to cooperate less than healthy controls, an adverse effect mediated by higher levels of attachment anxiety. A separate small, placebo-controlled study indicated subtle effects of oxy-

| Medication         | Dosing                             | Effects                                                                 |
|--------------------|------------------------------------|------------------------------------------------------------------------|
| Carbamazepine      | Therapeutic blood levels           | Potential improvement in impulsivity, but also possible worsening in melancholic depression. |
| Divalproex sodium  | Highest tolerated dose             | Improvements (primarily in patients with high impulsive aggression), in interpersonal sensitivity, irritability, and aggression. |
| over 80 µg/mL      |                                    |                                                                        |
| Lamotrigine        | Highest tolerated dose, target 200 mg/d | Improvements in anger, affective instability, impulsivity. Risk of potentially life-threatening rash. |
| Lithium carbonate  | Therapeutic blood levels           | Improvement in affective instability, possibly overall functioning, but limited data. |
| Topiramate         | Target dose 200-250 mg/d           | Improvements in anger, anxiety, interpersonal dysfunction, self-reported quality of life. Associated with weight loss. |

Table III. Mood stabilizers demonstrating efficacy in borderline personality disorder.
tocin in decreasing social stress reactivity, particularly for patients with history of childhood trauma and attachment insecurity. Seemingly divergent effects of oxytocin on social stress on the one hand, and cooperative behavior on the other, suggest that it may have opposing roles in different social cognitive processing networks in BPD. Further research is needed before advising clinical use of oxytocin in psychopharmacological management of BPD.

Future directions

Olanzapine\textsuperscript{88-90} and fluoxetine\textsuperscript{135} have been studied in conjunction with evidence-based psychotherapy for BPD, but respective treatment effects of psychotherapy versus medication remained unclear in these trials. Whether different medications differ in their capacity to synergize with psychotherapy in treating specific BPD symptoms or overall functioning has never been rigorously studied. Many BPD patients are treated with a combined approach, and yet there is limited information for rational clinical decision-making. Further understanding of the neurobiological effects of psychotherapy, relative to mechanisms of action of specific medications may eventually predict which BPD patients will respond to which approach and how to combine different treatments. BPD patients show lack of psychophysiological and amygdala indicators of habituation to repeated interpersonal affective stimuli of positive or negative valence.\textsuperscript{136} Working through interpersonal experiences in psychotherapy may be difficult for BPD patients, and adjunctive medication treatment targeting this capacity for habituation may optimize overall treatment efficacy. Dependent on neuroplasticity and changes in receptor density, habituation is fundamentally affected by glutamatergic N-methyl-D-aspartate (NMDA) signaling, suggesting a role for glutamatergic medications in improving impulsivity, interpersonal symptoms, and cognition in BPD.\textsuperscript{137} Enhancing learning and psychophysiological habituation modulated by NMDA signaling could synergize psychopharmacology and psychotherapy, analogous to strategies proposed for PTSD with respect to enhancement of fear extinction and interference of traumatic memory consolidation.\textsuperscript{141,143} This type of combination strategy has not been studied in randomized controlled trials. Endocannabinoid neurotransmission has also been implicated in impulsivity,\textsuperscript{138} suicidality,\textsuperscript{137} affective instability, and psychosis,\textsuperscript{139} perhaps partly via its role in modulating dopaminergic signaling.\textsuperscript{139} Medications active on CB receptors have also been hypothesized to facilitate extinction and interfere with consolidation of traumatic memories, if used in conjunction with psychotherapy.\textsuperscript{140} Psychopharmacological applications of cannabinoid medications remain theoretical at best, and associated risks remain too uncertain.

Opioid dysregulation may be associated with affective instability, impulsive self-injury, dissociation, and intolerance of aloneness in BPD, while abnormalities in oxytocin signaling may be associated with empathic dysfunction, pervasive shame, and attachment insecurity. Nevertheless, individual differences in genetics, developmental history, and immediate interpersonal context may contribute to inconsistent effects of neuropeptides on interpersonal functioning. Thus, in addition to genetic differences, compensatory postsynaptic receptor changes in response to prior cumulative opioid exposure and developmental environment may change the manifestations associated with neuropeptide signaling at any given moment.

Interactions between monoamine and neuropeptide signaling modulate impulsive aggression,\textsuperscript{86,88} but these interactions have not been studied sufficiently to suggest a psychopharmacological strategy for BPD that combines both neurotransmitter systems. Although full opioid agonists and antagonists have not yielded promising clinical results, the effect of partial agonists (eg, buprenorphine) on BPD symptoms has never been studied. Despite specific affinity of many opioid medications on mu receptor binding, kappa opioid receptor signaling may mediate immediate and cumulative effects of repeated trauma on worsening depression and anxiety.\textsuperscript{137} Kappa antagonists have recently been considered as novel antidepressants or anxiolytics in animal models,\textsuperscript{141,144} which may more accurately reflect affective instability in response to interpersonal stressors and attachment insecurity associated with BPD. Limited psychopharmacological research exists with respect to effects of neuropeptides other than opioids and oxytocin in BPD. Further research may provide novel psychopharmacologic options.

Conclusions

Symptoms of BPD include impulsivity, aggression, affective instability, transient psychotic symptoms, and interpersonal dysfunction, occurring as manifestations of core disturbances in representations of self and other.\textsuperscript{137} This
Treatment research

core is associated with complex interactions between genetic risk factors and developmental attachment stressors. Specific neurobiological effects of these risk factors in BPD remain ill-defined. The most up-to-date evidence suggests that anticonvulsant agents such as topiramate, valproate, or lamotrigine, and atypical antipsychotics such as aripiprazole and olanzapine, are most effective in treating BPD. Consistent with their benefits on impulsivity, a recent review recommended anticonvulsants and atypical antipsychotics for decreasing alcohol craving and consumption in BPD patients with comorbid alcoholism. Of the antidepressants, MAOIs and fluvoxamine may offer greater therapeutic benefits on impulsivity, a recent review recommended antidepressants on BPD symptoms are more modest. Antidepressant medications may nevertheless be helpful to treat comorbid mood and anxiety disorders, and they may be more efficacious in treating male BPD patients with prominent impulsive aggression. There are no medications approved for treatment of BPD as a whole, and targeted, transient use of medication for specific symptom domains is advised. Identity disturbance and interpersonal affective symptoms are less apt to improve with medication alone. Most available medications target impulsivity and aggression, symptoms that are most likely to resolve. Experimental use of glutamatergic medications or alteration of endocannabinoid signaling may enhance affective habituation during processing of interpersonal stressors in psychotherapy. Neuropeptide research may inform understanding of interpersonal dysfunction and identity disturbance characteristic of BPD. There exists potentially great variability in oxytocin and opioid signaling across individuals with BPD, or within a single patient over time. Opioid partial agonists or kappa antagonists may be an efficacious psychopharmacological intervention in BPD, but no direct evidence exists for such a practice clinically. At best, these psychopharmacological strategies remain theoretical and require further research on safety and efficacy prior to drawing any conclusions.

Although antidepressants have shown limited efficacy in treating BPD, they are well-tolerated and greater receptor specificity may be needed for effective serotonergic treatment of impulsive aggression. Atypical antipsychotics and anticonvulsants provide broader and more prominent benefit on some BPD symptoms, but are also associated with potential risks. Thus far, basic research has been difficult to translate into novel psychopharmacologic treatments for BPD. Further research on the functional neurobiology of BPD may improve understanding of chronic, refractory symptoms and assist in predicting treatment response. By relying on the best available evidence, clinicians can assist BPD patients in alleviating debilitating symptoms.

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| Tratamiento psicofarmacológico del trastorno de personalidad borderline | Traitement psychopharmacologique de la personnalité borderline |
|---|---|
| En este artículo se describe la mejor evidencia disponible acerca del tratamiento psicofarmacológico del trastorno de personalidad borderline (TPB). El TPB está definido por alteraciones en la identidad y en el funcionamiento interpersonal, y los pacientes refieren potenciales tratamientos medicamentosos orientados al manejo de la impulsividad, la agresividad, los síntomas psicóticos y disociativos transitorios, y la inestabilidad afectiva refractaria. Aunque recientemente se han publicado unos pocos ensayos terapéuticos controlados y randomizados para el TPB, hay múltiples revisiones que han coincidido en la eficacia de anticonvulsivantes específicos, antipsicóticos atípicos y suplementos de ácido graso omega-3. Hay una mayor evidencia para los fármacos que ofrecen un control significativo de la agresividad impulsiva respecto a los síntomas afectivos u otros síntomas interpersonales. Las estrategias de futuras investigaciones se centrarán en el papel potencial de los neuropéptidos y los medicamentos con mayor especificidad sobre los receptores serotoninérgicos 2A, como también en la optimización de la implementación concomitante de la psicoterapia y la psicofarmacología basadas en la evidencia, con el objetivo de mejorar el funcionamiento global de los pacientes con TPB. | Les meilleures données disponibles pour le traitement psychopharmacologique de la personnalité borderline (PB) sont exposées ici. La PB est définie par des perturbations de l’identité et du fonctionnement interpersonal ; l’impulsivité, l’agressivité, les symptômes transitoires dissociatifs et psychotiques et l’instabilité affective réfractaire présentés par les patients sont autant de cibles potentielles médicamenteuses. Peu d’études randomisées contrôlées sur les traitements pharmacologiques de la PB ont été publiées récemment alors que de nombreuses analyses s’accordent sur l’efficacité d’anticonvulsivants spécifiques, de molécules antipsychotiques atypiques et d’une supplémentation en acide gras oméga 3. Les médicaments capables d’améliorer significativement l’impulsivité agressive sont plus documentés que ceux dédiés aux symptômes affectifs ou interpersonnels. Les stratégies de recherche à venir s’intéresseront au rôle potentiel des neuropeptides et des médicaments plus spécifiques des récepteurs 2A à la sérotonine, comme à l’optimisation de l’apport concomitant d’une psychothérapie et d’une psychopharmacologie basées sur les preuves, afin d’améliorer le fonctionnement global des patients PB. |

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