The Role of Brexpiprazole in Treating Irritability in Borderline Personality Disorder: A Hypothesized Mechanism of Action

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INTRODUCTION

Borderline Personality Disorder (BPD) is a severe and enduring psychiatric condition characterized by affective instability, impulsivity, chronic interpersonal dysfunction, and high levels of irritability and anger. These symptoms often result in functional impairment, recurrent psychiatric crises, and increased healthcare utilization. Despite the clinical burden, there are no FDA-approved pharmacologic treatments for BPD, and off-label medication use is common.

Brexpiprazole, an atypical antipsychotic with partial agonism at dopamine D2 and serotonin 5-HT1A receptors and antagonism at serotonin 5-HT2A and alpha-1 adrenergic receptors, is currently approved for major depressive disorder and schizophrenia.

Given its pharmacologic profile, brexpiprazole may exert modulatory effects on neural circuits implicated in affective dysregulation. This poster proposes a hypothesized mechanism of action (MoA) by which brexpiprazole may attenuate irritability in individuals with BPD and presents a brief case series to illustrate real-world clinical observations.

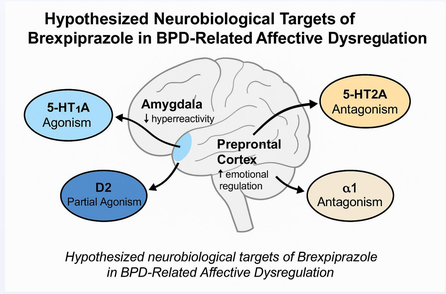
Core Symptoms of BPD

- Affective Instability: Intense, rapidly shifting moods
- Chronic Feelings of Emptiness
- Impulsive Behaviors
- Fear of Abandonment
- Unstable Relationships
- Distorted Self-Image or Sense of Identity
- Inappropriate, Intense Anger or Difficulty Controlling Anger
- Recurrent Suicidal Behavior or Self-Harming Acts

METHODS

This hypothesized MoA analysis is based on a targeted review of brexpiprazole's receptor pharmacodynamics and the neurobiological mechanisms underlying BPD-related affective dysregulation.

Emphasis was placed on corticolimbic circuitry, particularly the amygdala and prefrontal cortex.



Hypothesized neurobiological targets of Brexpiprazole in BPD-Related Affective Dysregulation

To support clinical plausibility, a retrospective review was conducted on three adult patients (n=3) with DSM-5–confirmed BPD treated in a community-based outpatient psychiatric clinic.

All presented with prominent irritability, impulsive aggression, and difficulty with affect modulation.

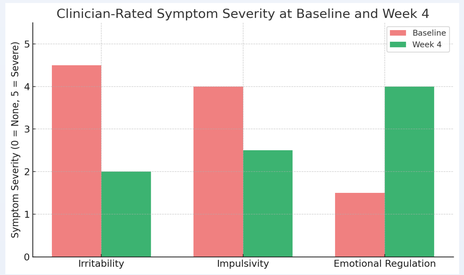
Each patient was initiated on low-dose brexpiprazole (0.5 mg to 1 mg daily) and monitored for symptom changes over a 6-week period.

RESULTS

All three patients reported clinically meaningful improvements in irritability, with decreased verbal outbursts, improved frustration tolerance, and enhanced capacity for emotional regulation. Symptom improvement was observed within 2 to 4 weeks of treatment initiation. No extrapyramidal symptoms, sedation, or metabolic adverse effects were reported. One patient demonstrated marked improvement in interpersonal boundaries, suggesting broader affect stabilization.

Patient	Age/Sex	Baseline Symptoms	Brexpiprazole Dose	Observed Change	Onset
A	28/F	Irritability, verbal outbursts	0.5 mg QHS	↓ Frequency of outbursts, calmer mood	2 weeks
B	33/M	Impulsivity, agitation	1 mg QHS	↑ Frustration tolerance, ↓ aggression	4 weeks
C	41/F	Mood lability, anger episodes	0.5 mg BID	↓ Interpersonal conflict, stable mood	3 weeks

Table 1. Summary of clinical characteristics and treatment outcomes for three adult patients (n=3) with DSM-5–confirmed BPD treated with low-dose brexpiprazole.



Graph 1. Symptom severity rated 0 (none) to 5 (severe). Red bars = baseline; green bars = week 4. Lower scores reflect improvement, except Emotional Regulation, where higher scores may indicate better control.

DIAGRAMS

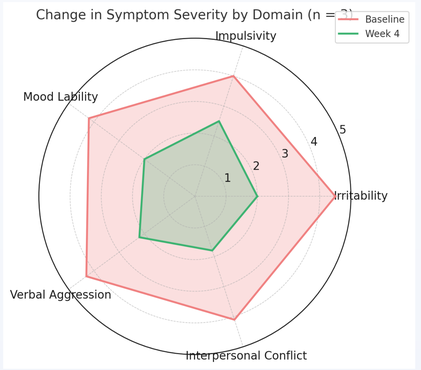


Figure 1. Clinician-rated symptom severity from 0 (none) to 5 (severe). Red area = baseline; green area = week 4. Reduction across all domains reflects improvement in symptoms over time.

Selected Observations (Patient Voice)

"I feel like I can pause before reacting." — Patient A

"I'm not yelling at people as much anymore." — Patient B

"I finally feel like I can control how I respond to things." — Patient C

Note: Quotes reflect patients' perceived improvements in emotional regulation and reactivity by week 4, highlighting subjective gains alongside clinician-rated outcomes.

CONCLUSIONS

Brexpiprazole may represent a novel pharmacologic option for managing irritability and affective dysregulation in BPD.

Its multimodal receptor activity is hypothesized to normalize dysregulated corticolimbic pathways. In this limited case series (n=3), low-dose brexpiprazole was well tolerated and associated with early subjective and functional improvements.

These findings support further investigation into its role as an adjunctive treatment in BPD, particularly in patients with prominent irritability and poor response to first-line psychotherapies.

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