

REBUILDING THE EVIDENCE ON THE USE OF LITHIUM
FOR BORDERLINE PERSONALITY DISORDER

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Since its initial psychodynamic characterization and subsequent inclusion as a categorical diagnosis in DSM-III, Borderline Personality Disorder (BPD) has occupied a close relationship with affective disorders, especially when considering the presence of overlapping symptoms, the high comorbidity rates of BPD with mood disorders, and the lack of diagnostic stability of BPD overtime (Akiskal, 1981). In addition, the emotional, interpersonal, and cognitive symptoms result in different presentations for this condition, with great variability in terms of psychopathology (Stone, 2019). Nonetheless, there is a consensus, supported by previous guidelines, that the pharmacological treatment of BPD is just ancillary and usually restricted to the treatment of comorbidities or specifically targeted symptoms such as anxiety, depressed mood, impulsivity, or psychotic-like states. On the other hand, psychotherapy modalities, such as dialectical behavioral therapy, are usually regarded as the standard of care for the treatment of this condition (National Collaborating Centre for Mental Health, 2009).

The relationship between BPD and mood disorders, particularly bipolar disorder (BD) and bipolar spectrum conditions has been an object of great speculation. Psychopathological features such as impulsivity, affective instability, mood changes, and anger outbursts are shared by both conditions. The distinction becomes even harder when different conceptualizations, such as the opposing views of cyclothymia/cyclothymic disorder as a mood disorder versus a temperament, are taken into consideration. Otherwise, a possible distinction between symptoms in both conditions is related to a pervasive pattern of affective instability in BPD, often triggered by environmental/interpersonal stressors. In

contrast, in BD symptoms tend to occur as a direct consequence of a mood episode. Other differences between BPD and BD are related to patterns of familial aggregation and the role of psychopharmacology, which is well established in BD (Sanches, 2019).

Lithium is considered a cornerstone in the treatment of BD. Beyond its classic anti-maniac action, lithium is effective in the prevention of mania and depression, in addition to its effect in acute bipolar depression. Moreover, available literature indicates other positive effects of lithium in different conditions, including adjunctive treatment for major depressive disorder, impulsivity, and suicide prevention (Malhi et al., 2017; Sheard, 1975). Some of these effects are related to usual symptoms of BPD, such as suicidality and aggressive-impulsive behaviors, and could justify its rational use in this condition.

Surprisingly, just one small clinical trial evaluated the use of lithium in patients with BPD (Links et al., 1990). In a double-blind crossover trial, subjects were randomly assigned to receive lithium, desipramine, or placebo. Only ten patients completed at least two arms of the study. The outcomes assessed included reductions in affective symptoms and the treatment perception of the therapist and patient. The authors found no significant effects of lithium or desipramine concerning improvements in depressive symptoms. However, lithium demonstrated positive effects in the treatment of anger and suicidality. Regarding their subjective perception, therapists reported better improvements for lithium compared to desipramine/placebo.

In this scenario, one can hypothesize that lithium might play a role in the management of BPD (Table 1). More specifically, it suggests that BPD patients with certain peculiarities re-

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garding symptoms and comorbidities might particularly benefit from the use of lithium, to individualize treatments and achieve improvements in clinical response and remission rates. For example, lithium may be a medication of interest in the case of BPD with comorbid bipolar spectrum disorders, which are present in approximately 20% of the cases of BPD and vice-versa (Fornaro et al., 2016). In addition, patients with BPD presenting with marked impulsivity, mood shifts, and anger outbursts may respond differently to pharmacological agents compared to patients primarily experiencing chronic feelings

suicidal attempts experienced by patients with BPD. Tolerability is another important aspect since lithium is associated with several potential side effects (nausea, diarrhea, tremors, polyuria, abdominal pain, weight gain, among others) which could be potentiated in cases where patients are taking one or more concomitant medications, such as antidepressants and antipsychotics (Gitlin, 2016), commonly utilized in the treatment of BPD. In addition, no specific evidence is available about the optimal lithium levels recommended for patients with BPD and their association with long-term negative effects of

Table 1. Potential benefits/disadvantages and treatment considerations considering the use of lithium in BPD

Potential Benefits	Potential Disadvantages	Practical and Psychosocial Considerations
Comorbidity with Bipolar Spectrum Disorders	Risk of acute and chronic intoxication	Family Support
Marked presence of impulsive and aggressive behaviors	Poor tolerability due to side effects (i.e. nausea, diarrhea, tremors, polyuria, polydipsia, abdominal pain, weight gain)	Regular access to medical treatment
Self-harm behaviors	Narrow effect-toxicity index	Psychoeducation about the pharmacological treatment (possible benefits and risks), including family members
Suicidality	Long-term treatment impairments (kidney, thyroid, parathyroid)	Regular blood level monitoring and tolerability assessment
	Lack of evidence regarding possible therapeutic serum levels	

of emptiness, fear of abandonment, and unstable relationships (Stone, 2019).

Furthermore, suicidality and self-injury behaviors are common symptoms of BPD. Research findings show that 60-70% of BPD patients make suicide attempts, with rates of completed suicide around 10% (Black et al., 2004). Lithium is significantly associated with decreases in the rate of suicide compared to placebo. In the past 50 years, several studies have been addressing the anti-suicidal effects of lithium. The effects of lithium on suicide may be related not only to reductions in the risk of mood episode relapses but also to decreasing impulsivity and aggressive behaviors (Cipriani et al., 2005). In a longitudinal study, the rates of self-harm and unintentional injury among patients with BD were significantly lower in those receiving lithium compared to valproate, quetiapine, and olanzapine (Hayes et al., 2016). Nevertheless, to date, no studies have analyzed a possible anti-suicidal effect of lithium in BPD.

Impulsivity is another core symptom of BPD. It may present itself as a spectrum of behaviors and actions, such as reckless sexual behavior, use of substances, reckless driving, self-injury, and aggressive outbursts (Barker et al., 2015). A review of the use of lithium in patients with a history of antisocial behavior and with aggressive/self-harm behaviors due to organic conditions showed significant effects in reducing the frequency and severity of aggressive outbursts. They also pointed to a tendency of ability to control angry feelings (Rifkin et al., 1972).

Safety concerns represent a major topic of interest that needs to be addressed and balanced against lithium's potential benefits to this population. First, lithium has a narrow therapeutic index, therefore caution is required concerning the risk of intoxication, as a result of inadvertent or intentional overdose, given the high rates of

lithium treatment, such as its effects on thyroid and renal function. Another potential concern is how individuals with BPD may respond to lithium therapy, as it can paradoxically lead to reactions that suggest slight mood destabilization, for example (Calil et al., 1990).

In summary, available evidence supporting the use of lithium in BPD is scant and limited by small sample sizes, high rates of heterogeneity, and other methodological limitations. Moreover, most of the evidence on the putative use of lithium for the management of BPD are extrapolations from studies analyzing its efficacy in different conditions that share psychopathological features with BPD, especially BD. Despite these limitations, no marked advances in the pharmacological treatment of BPD have been made over the past several decades. Therefore, the role of lithium in the management of BPD represents a topic of high interest for clinical research.

References

- Akiskal, H. S. (1981). Subaffective disorders: Dysthymic, cyclothymic and bipolar II disorders in the "borderline" realm. *The Psychiatric Clinics of North America*, 4(1), 25–46.
- Barker, V., Romaniuk, L., Cardinal, R. N., Pope, M., Nicol, K., & Hall, J. (2015). Impulsivity in borderline personality disorder. *Psychological Medicine*, 45(9), 1955–1964. <https://doi.org/10.1017/S0033291714003079>
- Black, D. W., Blum, N., Pföhl, B., & Hale, N. (2004). Suicidal behavior in borderline personality disorder: Prevalence, risk factors, prediction, and prevention. *Journal of Personality Disorders*, 18, 226–239.
- Calil, H. M., Zwicker, A. P., & Klepac, S. (1990). The

- effects of lithium carbonate on healthy volunteers: Mood stabilization? *Biological Psychiatry*, 27(7), 711–722. [https://doi.org/10.1016/0006-3223\(90\)90586-q](https://doi.org/10.1016/0006-3223(90)90586-q)
- Cipriani, A., Pretty, H., Hawton, K., & Geddes, J. R. (2005). Lithium in the prevention of suicidal behavior and all-cause mortality in patients with mood disorders: A systematic review of randomized trials. *The American Journal of Psychiatry*, 162(10), 1805–1819. <https://doi.org/10.1176/appi.ajp.162.10.1805>
- Fornaro, M., Orsolini, L., Marini, S., De Berardis, D., Perna, G., Valchera, A., Ganança, L., Solmi, M., Veronese, N., & Stubbs, B. (2016). The prevalence and predictors of bipolar and borderline personality disorders comorbidity: Systematic review and meta-analysis. *Journal of Affective Disorders*, 195, 105–118. <https://doi.org/10.1016/j.jad.2016.01.040>
- Gitlin, M. (2016). Lithium side effects and toxicity: Prevalence and management strategies. *International Journal of Bipolar Disorders*, 4(1), 27. <https://doi.org/10.1186/s40345-016-0068-y>
- Hayes, J. F., Pitman, A., Marston, L., Walters, K., Geddes, J. R., King, M., & Osborn, D. P. (2016). Self-harm, unintentional injury, and suicide in bipolar disorder during maintenance mood stabilizer treatment: A UK population-based electronic health records study. *JAMA Psychiatry*, 73(6), 630–637. <https://doi.org/10.1001/jamapsychiatry.2016.0432>
- Links, P. S., Steiner, M., Boiago, I., & Irwin, D. (1990). Lithium therapy for borderline patients: Preliminary findings. *Journal of Personality Disorders*, 4(2), 173–181. <https://doi.org/10.1521/pedi.1990.4.2.173>
- Malhi, G. S., Gessler, D., & Outhred, T. (2017). The use of lithium for the treatment of bipolar disorder: Recommendations from clinical practice guidelines. *Journal of Affective Disorders*, 217, 266–280. <https://doi.org/10.1016/j.jad.2017.03.052>
- National Collaborating Centre for Mental Health (UK). (2009). *Borderline personality disorder: Treatment and management*. British Psychological Society (UK).
- Rifkin, A., Quitkin, F., Carrillo, C., Blumberg, A. G., & Klein, D. F. (1972). Lithium carbonate in emotionally unstable character disorder. *Archives of General Psychiatry*, 27(4), 519–523. <https://doi.org/10.1001/archpsyc.1972.01750280083014>
- Sanches, M. (2019). The limits between bipolar disorder and borderline personality disorder: A review of the evidence. *Diseases*, 7(3), 49. <https://doi.org/10.3390/diseases7030049>
- Sheard, M. H. (1975). Lithium in the treatment of aggression. *The Journal of Nervous and Mental Disease*, 160(2–1), 108–118. <https://doi.org/10.1097/00005053-197502000-00005>
- Stone, M. H. (2019). Borderline personality disorder: Clinical guidelines for treatment. *Psychodynamic Psychiatry*, 47(1), 5–26. <https://doi.org/10.1521/pdps.2019.47.1.5>