Review

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Lithium Stabilization of Impulsivity and Suicidality in Severe Gambling Disorder: A Case Report and Narrative Review

Carolina Pinci [1,2], Tommaso Barlattani [3,*], Riccardo Santini [1], Irene Sferra [1,2], Marika De Simone [2], Simonetta Della Scala [2], Francesca Pacitti [3] and Cinzia Niolu [1]

[1] Department of Systems Medicine, Tor Vergata University of Rome, 00133 Rome, Italy.

[2] Addiction Treatment Service (SerD), Department of Mental Health and Addiction, ASL Roma 6, Italy

[3] Department of Biotechnological and Applied Clinical Sciences (DISCAB), University of L'Aquila, L'Aquila, Italy

* Correspondence: tommaso.barlattani@graduate.univaq.it

Abstract

Gambling disorder (GD) is associated with severe psychosocial impairment, impulsive dyscontrol, affective instability, and increased suicidal risk. Pharmacological options remain limited, particularly for patients whose presentation is dominated by transdiagnostic dimensions such as impulsivity, emotional dysregulation, and suicidal vulnerability. Lithium may be relevant because of its anti-suicidal properties and potential effects on affective instability and behavioral dyscontrol. We describe a 40-year-old man with sports-betting-related GD who presented after a suicidal crisis in the context of financial collapse and marital conflict. He entered a structured multimodal program including psychiatric care, lithium carbonate, individual psychotherapy, psychoeducational and self-help groups, family intervention, and social support. After lithium initiation and titration to 600 mg/day, the patient showed progressive affective stabilization, remission of suicidal ideation, reduced gambling urges, and sustained abstinence, with one brief lapse that was rapidly contained. Psychometric reassessment paralleled the clinical course, showing reduced functional impairment, near-complete resolution of gambling-related cognitive distortions, and a shift from a highly impulsive/dysregulated gambling profile toward an emotionally vulnerable pattern. Although causal inference is limited by the single-case design and multimodal treatment context, this case supports the hypothesis that lithium may help stabilize core vulnerability dimensions in selected GD presentations, particularly impulsivity, affective dysregulation, and suicidality.

Keywords: gambling disorder; lithium; impulsivity; suicidality; behavioral addiction; multimodal treatment

1. Introduction

Gambling disorder (GD) is a behavioral addiction characterized by persistent and recurrent maladaptive patterns of gambling behavior associated with significant psychological, social, and financial consequences [1]. From a diagnostic perspective, GD is classified in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) within the category of Substance-Related and Addictive Disorders, reflecting its phenomenological and neurobiological similarities with substance use disorders [2]. Similarly, the International Classification of Diseases, 11th Revision (ICD-11) conceptualizes gambling disorder as a disorder due to addictive behaviors, characterized by impaired control over gambling, increasing priority given to gambling over other activities, and continuation despite negative consequences [3]. Epidemiological estimates suggest a prevalence of approximately 0.5% in the adult population, with similar or higher rates reported across different countries, highlighting the disorder's global clinical relevance [1]. The etiology of GD

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is multifactorial, involving genetic, environmental, and neurobiological determinants that interact to shape vulnerability and illness trajectories.

Beyond functional impairment, accumulating evidence indicates that individuals with GD are at increased risk for suicidal ideation, suicide attempts, and completed suicide, underscoring the disorder's substantial clinical burden [4–6]. Financial collapse, interpersonal conflict, and experiences of shame and entrapment have been identified as key drivers of gambling-related suicidal crises, positioning suicidality as a critical dimension of GD psychopathology [7]. In addition, GD frequently co-occurs with other psychiatric conditions, including mood, substance-use, and impulse-control disorders, further complicating clinical presentation and treatment planning [1].

From a neurobiological perspective, GD is increasingly conceptualized as a disorder of dysregulated reward processing and impaired cognitive control involving cortico-striato-limbic circuitry. Neuroimaging and translational studies have demonstrated alterations in fronto-striatal networks linking ventral striatal reward responsivity with prefrontal executive regulation, contributing to maladaptive decision-making, heightened cue reactivity, and persistence of gambling behaviors despite adverse consequences [8–10]. These network-level disturbances are thought to give rise to interacting dimensional vulnerabilities—including impulsivity, affective dysregulation, and cue-driven craving—that play a central role in the development, maintenance, and relapse of GD [11]. In line with dimensional models of addiction, GD has been conceptualized as involving a progression from impulsivity-driven reward seeking toward compulsivity-related habitual behavior, reflecting maladaptive reinforcement learning processes and impaired cognitive control [12,13]. Emerging computational approaches further support this framework by demonstrating reinforcement-learning abnormalities and altered value updating in individuals with disordered gambling, highlighting disrupted decision-making mechanisms within reward–control circuitry [14,15].

Despite the severity and complexity of GD, treatment options remain limited. Psychosocial interventions, particularly cognitive behavioral therapy, represent the first-line approach; however, relapse rates remain considerable, and pharmacological strategies have shown heterogeneous and often inconclusive results [16,17]. These limitations highlight the need to explore therapeutic approaches targeting transdiagnostic dimensions underlying GD rather than gambling behavior alone.

Lithium is a well-established mood stabilizer with robust evidence supporting its anti-suicidal properties and capacity to modulate affective instability, impulsive aggression, and behavioral dyscontrol across psychiatric conditions [18,19]. These effects are highly relevant to the dimensional psychopathology of GD, where impulsivity, affective dysregulation, and craving-related urges frequently interact with psychosocial stressors to precipitate behavioral escalation and crisis states. Accordingly, lithium may be conceptualized as a potential intervention targeting core transdiagnostic mechanisms implicated in GD rather than gambling behavior per se.

Emerging neurobiological models provide further support for this hypothesis. Lithium has been shown to influence serotonergic and glutamatergic neurotransmission, enhance prefrontal inhibitory control, and modulate intracellular signaling pathways involved in synaptic plasticity and adaptive learning, including inhibition of glycogen synthase kinase-3 (GSK-3) [20–22]. Through these converging mechanisms, lithium may impact processes implicated in maladaptive reinforcement learning, cue reactivity, and emotional dysregulation that characterize GD, providing a biologically plausible rationale for its investigation in this population.

The present study aims to examine the role of lithium within the broader therapeutic landscape of gambling disorder by presenting a clinical case illustrating recovery from severe gambling behavior within a multimodal treatment framework, and by providing a narrative overview of available therapeutic strategies, with particular emphasis on the potential effects of lithium on gambling-related urges, impulsive dyscontrol, affective instability, and associated suicidal thoughts.

2. Materials and Methods

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This study presents a clinical case report combined with a narrative review of the literature on pharmacological treatments for gambling disorder, with particular emphasis on lithium, impulsivity, and suicidality.MThe case was evaluated and followed within a specialized addiction treatment service. The clinical assessment included a comprehensive psychiatric evaluation and a structured psychometric battery administered at treatment entry and repeated after 18 months. Functional impairment was assessed using the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0). Gambling-related cognitive distortions were measured with the Gambling Beliefs Questionnaire (GBQ), and gambling severity was screened using the Gambling Disorder Screening Questionnaire (GDSQ). Gambling subtypes and underlying vulnerability profiles were characterized with the Gambling Pathways Questionnaire (GPQ). General psychopathology was evaluated through the Symptom Checklist-90-Revised (SCL-90-R), and personality traits and clinical syndromes were assessed using the Millon Clinical Multiaxial Inventory-III (MCMI-III). Lithium serum levels were monitored at regular intervals throughout treatment.The narrative review was conducted by searching PubMed/MEDLINE, PsycINFO, and the Cochrane Library for relevant literature published up to March 2026. Search terms included: “gambling disorder”, “pathological gambling”, “pharmacological treatment”, “lithium”, “mood stabilizers”, “impulsivity”, “suicidality”, and “behavioral addiction”, used individually and in combination. Reference lists of retrieved articles were also examined to identify additional relevant sources. No formal inclusion or exclusion criteria were applied, consistent with the narrative review methodology.

3. Case Presentation

C.M. is a 40-year-old married man with three children who presented to a specialized addiction treatment service in August 2024 following a severe gambling-related psychosocial and financial crisis. The referral occurred shortly after a suicidal crisis during which, in a state of acute psychological distress and alcohol intoxication, he reported an intention to end his life by jumping in front of a train. According to the patient’s report, the act was not carried out because the degree of intoxication prevented him from reaching the railway tracks. The episode occurred after several days of escalating psychological distress associated with the progressive disclosure of gambling-related debts to his family. At the time of presentation, the patient was experiencing significant marital conflict after his spouse discovered extensive financial liabilities accumulated through sports betting over several years. Total debts were estimated at approximately EUR 180,000, partly involving informal lending networks. Following disclosure of the financial situation, the patient temporarily left the family home and moved to his mother’s residence.

C.M. reported a long-standing history of sports betting beginning in early adulthood, with progressive escalation in frequency and financial involvement. Gambling behavior initially occurred sporadically but gradually evolved into increasingly frequent and uncontrolled betting episodes, particularly in attempts to recover previous losses. A first major financial collapse occurred in 2020, when gambling debts reached approximately EUR 100,000. These debts were temporarily repaid through proceeds derived from the sale of a family-owned bar; however, gambling behavior subsequently resumed and progressively worsened. The months preceding referral were characterized by increasing psychological distress, secrecy regarding financial losses, escalating interpersonal conflict, and pervasive feelings of shame and hopelessness. Additional psychosocial stressors included the death of the patient’s father in 2018 following prolonged illness and the recent diagnosis of breast cancer in his sister. Substance-use history was notable for a period of problematic alcohol consumption following his father’s death. For approximately one year, the patient reported daily alcohol intake of 1-1.5 liters of wine or prosecco, typically consumed alone in the evening as a means of coping with emotional distress. Although this pattern gradually diminished over time, episodic binge drinking persisted during periods of acute stress. The patient denied the use of illicit substances.

The initial psychiatric evaluation was characterized by marked affective distress and impaired emotional regulation in the context of severe gambling-related psychosocial destabilization. The

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patient presented with depressed and anxious mood, constricted affect, and persistent ruminative preoccupation with financial debts and marital separation. He reported intense feelings of guilt, shame, and hopelessness, associated with significant psychological tension and sleep disturbance characterized by middle insomnia and nocturnal rumination. At the time of assessment, suicidal ideation was present, mainly in the form of passive death wishes and intrusive thoughts related to self-harm occurring in the context of overwhelming psychological distress. These thoughts were reported in continuity with the recent suicidal crisis described above, although the patient denied active suicidal planning during the evaluation.

Following admission to the service, the patient was enrolled in a structured multimodal treatment program specifically designed for gambling disorder. The intervention involved a multidisciplinary team including psychiatrists, clinical psychologists, physicians, and a social worker. The treatment program combined pharmacological management, individual psychotherapy, psychoeducational group interventions, and social support measures aimed at financial containment and relapse prevention. Regular psychiatric follow-up visits were scheduled to monitor clinical status and pharmacological treatment. In parallel, the patient engaged in individual psychological sessions and weekly psychoeducational group meetings focused on gambling disorder, with the aim of improving insight into addictive behaviors, emotional regulation, and relapse prevention strategies. Family involvement was progressively introduced through joint sessions and psychoeducational interventions, while social support measures were implemented to assist with financial management and debt restructuring. Following baseline laboratory investigations and cardiological evaluation, pharmacological treatment with lithium carbonate was initiated at an initial dosage of 150 mg twice daily. Lithium therapy was progressively titrated based on clinical response and serum lithium concentrations. During the initial titration phase, serum lithium concentration was 0.12 mEq/L. Subsequent monitoring demonstrated progressive stabilization, with values ranging between 0.20 and 0.70 mEq/L during the following weeks. The lithium dosage was gradually increased to 600 mg/day. Continued monitoring showed lithium levels within the lower therapeutic range, including 0.34 mEq/L and 0.25 mEq/L in December 2024, and reaching 0.60 mEq/L in February 2025. The clinical course, including lithium titration and serum level monitoring, is summarized in Table 1.

Following lithium initiation, progressive clinical stabilization was observed. The patient reported improved mood regulation, reduction in anxiety and emotional lability, and attenuation of ruminative preoccupation related to gambling and financial stressors. Sleep quality progressively improved. Importantly, suicidal ideation fully remitted during follow-up, with no further suicidal thoughts reported in subsequent psychiatric evaluations. In parallel, the patient described a progressive reduction in gambling urges and maintained abstinence from gambling behavior. Treatment adherence was high, with regular participation in individual psychotherapy sessions and weekly psychoeducational and self-help groups. Within the multimodal treatment framework, social containment strategies were implemented early in the course of care: financial management was temporarily delegated to the patient's mother and structured debt-management pathways were activated. Over the following months, family involvement progressively increased, and the patient's spouse gradually re-engaged in the therapeutic process through joint sessions and psychoeducation. Functional recovery progressed alongside symptomatic stabilization. From late 2024 into 2025, the patient maintained abstinence from gambling, reported minimal craving, and demonstrated improved planning and role functioning. He obtained new employment and initiated the process of selling the bar while implementing a structured debt-repayment plan with family support.

In July 2025, a brief gambling lapse was documented but was rapidly identified and managed within the therapeutic network without progression to sustained gambling behavior or renewed financial destabilization. The patient remained engaged in treatment, promptly resumed abstinence, and continued follow-up within the same multimodal therapeutic framework. At the most recent follow-up in February 2026, C.M. continued lithium carbonate 600 mg/day with regular monitoring. He maintained abstinence from gambling, denied clinically relevant craving and suicidal ideation, and showed sustained psychosocial improvement, including stable occupational functioning,

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improved family relationships, and an active debt-repayment plan, while continuing periodic family sessions and psychoeducational support.

Table 1. Clinical course, lithium titration, and key outcomes.

Timepoint	Lithium treatment	Serum lithium (mEq/L)	Clinical course
Treatment entry (Aug 2024)	-	-	Severe gambling relapse, financial crisis, and suicidal crisis
Early treatment	Multimodal treatment initiated	-	Psychiatric care, psychotherapy, group intervention, and social support
Lithium initiation (Oct 2024)	Lithium carbonate 300 mg/day	0.12	Affective instability, suicidal ideation, and ruminative distress
Dose titration	Lithium carbonate 600 mg/day	0.20-0.70	Progressive mood stabilization and reduction of anxiety
Follow-up (Dec 2024)	Lithium carbonate 600 mg/day	0.34-0.25	Reduced rumination and sustained abstinence from gambling
Follow-up (Feb 2025)	Lithium carbonate 600 mg/day	0.60	Remission of suicidal ideation and improved affective stability
Mid-course follow-up (Jul 2025)	Lithium carbonate 600 mg/day	-	Brief gambling lapse, rapidly recognized and contained
Latest follow-up (Feb 2026)	Lithium carbonate 600 mg/day	-	Stable mood, no suicidal ideation, sustained abstinence, and ongoing debt-repayment planning

4. Psychodiagnostic Assessment

A structured psychometric assessment was conducted at treatment entry and repeated after 18 months of treatment. Key findings are summarized in Table 2.

Table 2. Summary of key psychometric findings at baseline and 18-month follow-up.

Measure	Baseline	18-month follow-up
WHODAS 2.0 total score	22.5%	13%
WHODAS domains	ADL 53%; understanding/communication 37.5%; participation 34%; mobility 0%; self-care 0%; interpersonal relationships 10%	Understanding/communication 12.5%; mobility 30%; self-care 0%; interpersonal relationships 10%; ADL 22%; participation 6%
GBQ	91/147	2/147

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GDSQ	6	No diagnostic criteria identified
GPQ	Pathway Type 3	Pathway Type 2
SCL-90-R global indices	GSI 0.77 (T=60); PST 27 (T=50); PSDI 2.56 (T=78)	GSI 0.79 (T=60); PST 29 (T=51); PSDI 2.45 (T=76)
Prominent SCL-90-R dimensions	Depression T=82; Obsessive-Compulsive T=66; Anxiety T=51	Somatization T=82; Phobic Anxiety T=67; Depression T=56
MCMI-III personality profile	Dependent BR=90; Depressive BR=85; Borderline BR=79; Negativistic BR=72	Dependent BR=66; Narcissistic BR=63; Depressive BR=42; Borderline BR=34
MCMI-III clinical syndromes	Anxiety BR=97; Major Depression BR=91; Dysthymia BR=89; PTSD BR=79	Anxiety BR=60; Major Depression BR=24; Dysthymia BR=30; PTSD BR=66

At baseline, functional impairment was assessed using the World Health Organization Disability Assessment Schedule (WHODAS 2.0). The patient obtained a total score of 22.5%, indicating moderate functional impairment. Domain scores showed higher impairment in activities of daily living (53%), understanding and communication (37.5%), and participation in social life (34%), while mobility (0%) and self-care (0%) were preserved. Mild impairment was observed in interpersonal relationships (10%). Gambling-related cognitive distortions were evaluated using the Gambling Beliefs Questionnaire (GBQ), yielding a total score of 91/147. Gambling severity was screened using the Gambling Disorder Screening Questionnaire (GDSQ), with a score of 6, consistent with clinically significant gambling disorder. Assessment with the Gambling Pathways Questionnaire (GPQ) classified the patient within Pathway Type 3.General psychopathology was assessed using the Symptom Checklist-90-Revised (SCL-90-R). Global indices at baseline were Global Severity Index (GSI) = 0.77 (T = 60), Positive Symptom Total (PST) = 27 (T = 50), and Positive Symptom Distress Index (PSDI) = 2.56 (T = 78). Across the nine primary symptom dimensions, T-scores were: Somatization = 50, Obsessive–Compulsive = 66, Interpersonal Sensitivity = 40, Depression = 82, Anxiety = 51, Hostility = 56, Phobic Anxiety = 45, Paranoid Ideation = 39, and Psychoticism = 42. Personality traits and clinical syndromes were further explored using the Millon Clinical Multiaxial Inventory-III (MCMI-III). The personality profile showed elevated base-rate scores for Depressive personality (BR = 85), Dependent personality (BR = 90), Negativistic personality (BR = 72), and Borderline personality traits (BR = 79). Among clinical syndrome scales, elevations were observed in Anxiety (BR = 97), Dysthymia (BR = 89), Major Depression (BR = 91), Post-traumatic Stress (BR = 79), and Alcohol Dependence (BR = 69). At 18-month follow-up, the WHODAS 2.0 total score decreased to 13%, indicating a reduction in overall functional impairment. Domain scores were understanding and communication = 12.5%, mobility = 30%, self-care = 0%, interpersonal relationships = 10%, activities of daily living = 22%, and participation in social life = 6%. Gambling-related cognitions showed a marked reduction, with the Gambling Beliefs Questionnaire (GBQ) score decreasing from 91/147 at baseline to 2/147 at follow-up. The Gambling Disorder Screening Questionnaire (GDSQ) did not identify any diagnostic criteria for gambling disorder at follow-up. Reassessment with the Gambling Pathways Questionnaire (GPQ) indicated a shift in classification from Pathway Type 3 at baseline to Pathway Type 2. General psychopathology at follow-up, assessed with the SCL-90-R, showed global indices of Global Severity Index (GSI) = 0.79 (T = 60), Positive Symptom Total (PST) = 29 (T = 51), and Positive Symptom Distress Index (PSDI) = 2.45 (T = 76). Across the nine primary symptom dimensions, T-scores were: Somatization = 82, Obsessive–Compulsive = 59, Interpersonal Sensitivity = 58, Depression = 56, Anxiety = 46, Hostility = 46, Phobic Anxiety = 67, Paranoid Ideation = 44, and Psychoticism = 52. According to the Italian factorial structure of the SCL-90-R, T-scores were: Relational Distress = 55, Somatic Complaints = 85, Anxiety = 62, Aggression/Hostility = 44, Dysphoria

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= 45, Depressive Ideation = 64, Obsessive–Compulsive = 56, and Sleep Disturbances = 57. Personality reassessment with the MCMI-III showed the following base-rate scores: Schizoid = 70, Avoidant = 63, Dependent = 66, Narcissistic = 63, Obsessive–Compulsive = 60, Histrionic = 55, Antisocial = 51, Sadistic = 53, Masochistic = 45, Negativistic = 36, Depressive = 42, Schizotypal = 60, Borderline = 34, and Paranoid = 24. Clinical syndrome scales showed Anxiety = 60, Somatization = 20, Bipolar: Mania = 48, Dysthymia = 30, Alcohol Dependence = 45, Drug Dependence = 60, Post-traumatic Stress = 66, Thought Disorder = 30, Major Depression = 24, and Delusional Disorder = 20. The MCMI-III protocol was considered valid and interpretable.

Overall, the follow-up psychometric assessment indicated substantial improvement across multiple clinical domains. Functional impairment decreased, gambling-related cognitive distortions were almost completely resolved, and no diagnostic criteria for gambling disorder were identified at follow-up. In addition, the shift in GPQ classification from Pathway Type 3 to Pathway Type 2 suggested a modification in the underlying vulnerability profile, with reduced impulsive dyscontrol and a clinical pattern more closely characterized by emotional vulnerability rather than severe behavioral dysregulation. Taken together, these findings indicate a global improvement in gambling-related psychopathology, emotional functioning, and psychosocial adjustment over the course of treatment.

5. Pharmacological Treatment of Gambling Disorder

Current clinical frameworks conceptualize gambling disorder (GD) as a chronic, relapsing behavioral addiction requiring a multimodal approach that integrates psychological, social, and - only in selected cases - pharmacological interventions [1]. In line with this, the first NICE guideline on gambling-related harms emphasizes identification, assessment, and management pathways in which evidence-based psychological therapies (e.g., CBT-based approaches) remain first-line, while pharmacological interventions may be considered adjunctively within specialist care, particularly when targeting comorbidities and high-risk clinical presentations. This guideline positioning reflects the broader evidence base: despite multiple drug classes having been studied, no medication currently has a formal indication specifically for GD, and the pharmacotherapy literature remains characterized by heterogeneity in design, outcomes, and patient selection [23,24].

Recent syntheses underscore that pharmacological strategies for GD have largely been extrapolated from models of addiction neurobiology and impulse-control psychopathology rather than derived from disorder-specific drug development [1,25,26]. In a contemporary narrative review, the pharmacological evidence base spans opioid receptor antagonists (notably naltrexone and nalmefene), serotonin reuptake inhibitors, glutamatergic agents (e.g., N-acetylcysteine, acamprosate, memantine), mood stabilizers (including topiramate, carbamazepine, lithium), and other compounds—yet conclusions remain cautious because results are often mixed and difficult to generalize across clinically heterogeneous samples [25,27]. Complementing these narrative updates, a Cochrane review focusing on randomized pharmacological interventions classified medications into major classes (antidepressants, opioid antagonists, mood stabilizers/anticonvulsants, and atypical antipsychotics) and concluded that evidence is preliminary overall, with the most consistent short-term improvements in gambling symptom severity reported for opioid antagonists (naltrexone, nalmefene) and for olanzapine among atypical antipsychotics, while evidence for other drug classes remained limited or inconsistent across outcomes beyond symptom severity [24].

Within opioid modulation, earlier controlled studies and subsequent reviews highlight signals of efficacy for both nalmefene and naltrexone, particularly when targeting strong urges/craving and potentially in individuals with co-occurring alcohol-use problems [28–31]. At the same time, tolerability and dosing considerations may shape observed benefit, and overall response remains heterogeneous, reinforcing the need for better stratification of treatment targets and patient phenotypes [24,25,27,29]. More broadly, contemporary clinical commentaries reiterate that, while pharmacological trials suggest some potential benefit, robust evidence to support routine use remains insufficient, and non-pharmacological modalities continue to be central to care [23,32].

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The limited and inconsistent pharmacotherapy evidence base is also mirrored by health-system implementation realities. A UK scoping review of intervention research highlights a relative paucity of UK-based gambling treatment outcome studies, underscoring barriers to building a strong local evidence base to inform guideline implementation [33]. Similarly, qualitative work among UK gambling treatment providers suggests that adoption of certain evidence-based addiction treatment principles (e.g., contingency management) in gambling services may be constrained by practitioner perceptions and practical barriers, pointing to the importance of implementation science alongside efficacy research [34]. Primary-care oriented clinical guidance also emphasizes under-detection and the role of front-line clinicians in screening, brief interventions, and referral pathways, highlighting that scalable care models remain crucial given low treatment-seeking rates [35]. Finally, the clinical context in which GD occurs frequently involves comorbidity and complex service needs; for example, observational data in methadone maintenance settings indicate that pathological gambling can be prevalent and clinically relevant within opioid-treatment populations, reinforcing the need for integrated assessment and multidisciplinary care pathways [36].

Overall, current evidence supports a pragmatic conclusion: pharmacotherapy in GD remains best conceptualized as an adjunctive, target-based option within specialist care—most plausibly when guided by transdiagnostic dimensions (e.g., craving/urges, impulsivity, affective instability) and comorbid psychiatric profiles—rather than as a universal first-line treatment [24–26]. Within this context, mood stabilizers have attracted interest due to their established effects on behavioral dyscontrol and affective instability, providing a conceptual basis for the focused examination of lithium presented in the following section [37].

5.1. Mood Stabilizers in GD and Evidence on Lithium

Mood stabilizers have attracted interest in gambling disorder (GD) due to their established effects on affective instability, impulsive aggression, and behavioral dyscontrol—dimensions frequently implicated in the clinical expression of GD. This dimensional rationale is supported by contemporary evidence indicating that lithium may modulate impulsivity and aggressive dyscontrol across psychiatric conditions, with recent clinical and translational studies linking lithium exposure to reduced impulsivity and altered emotional processing relevant to behavioral regulation [19,38]. Early pharmacological conceptualizations of pathological gambling emphasized overlap with impulse-control and bipolar-spectrum disorders, providing a rationale for investigating agents traditionally used in mood regulation [27,39]. In this context, mood stabilizers have been explored as potential modulators of core vulnerability dimensions rather than disorder-specific treatments targeting gambling behavior per se.

Among mood stabilizers, lithium represents one of the earliest and most directly investigated compounds in pathological gambling. A randomized single-blind clinical trial by Pallanti and colleagues evaluated lithium carbonate versus valproate in non-bipolar pathological gamblers over a 14-week period, demonstrating significant reductions in gambling severity across both treatment arms as measured by the Yale–Brown Obsessive Compulsive Scale modified for pathological gambling (PG-YBOCS) [37]. Response rates exceeding 60% were observed in the lithium group, supporting the potential efficacy of mood stabilization strategies in reducing gambling symptomatology even in the absence of formal bipolar diagnosis. Importantly, this study represented the first controlled evaluation of mood stabilizers in pathological gambling, establishing a preliminary empirical foundation for subsequent investigations.

Subsequent controlled research further examined lithium within specific clinical subgroups characterized by affective instability and bipolar-spectrum features. In a placebo-controlled trial, sustained-release lithium was associated with reductions in both gambling severity and affective instability among pathological gamblers presenting bipolar spectrum characteristics, suggesting that mood stabilization may indirectly attenuate gambling behavior through modulation of emotional reactivity and impulsive decision-making processes [40]. These findings contributed to a dimensional

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interpretation of lithium's therapeutic effects in GD, consistent with models conceptualizing gambling behavior as emerging from interacting affective and impulsive vulnerabilities.

Beyond lithium, other mood stabilizers—including valproate and topiramate—have been explored with heterogeneous results. Preliminary studies of valproate have reported reductions in gambling severity comparable to lithium in early comparative trials, whereas investigations of topiramate have yielded mixed findings regarding efficacy and tolerability [26,27]. Consistent with these findings, broader pharmacological syntheses of gambling disorder treatments have highlighted mood stabilizers as a potentially relevant but empirically underdeveloped class, with available studies suggesting possible benefits in selected subgroups while remaining limited by small sample sizes and methodological variability [39]. Overall, systematic and meta-analytic syntheses indicate that evidence supporting mood stabilizers in GD remains limited by heterogeneous study designs and variability in participant comorbidity profiles, precluding definitive treatment recommendations while nevertheless highlighting a signal of potential benefit in clinically selected populations [26,27].

More recent literature has continued to emphasize the relevance of mood-stabilizing strategies within transdiagnostic frameworks of behavioral addiction. Contemporary reviews and network meta-analytic work underscore that pharmacological interventions in GD demonstrate variable efficacy across mechanistically distinct classes, with mood stabilizers representing a theoretically coherent yet empirically underdeveloped domain warranting further investigation [24,26]. Within this landscape, lithium remains uniquely positioned given its established anti-suicidal properties, effects on impulsive aggression, and capacity to modulate affective instability—features closely aligned with clinical dimensions associated with severe gambling presentations.

Collectively, available evidence suggests that lithium may exert beneficial effects on gambling behavior through dimensional mechanisms encompassing emotional stabilization, reduction of impulsive drives, and attenuation of affectively triggered gambling episodes. Although the empirical base remains limited, convergence across controlled trials, comparative studies, and conceptual frameworks supports consideration of lithium as a candidate intervention in carefully selected individuals with GD, particularly those presenting prominent affective dysregulation, impulsivity, or suicidal vulnerability within multimodal treatment contexts.

5.2. Neurobiological Rationale for Lithium in GD

Contemporary models conceptualize gambling disorder (GD) as a behavioral addiction emerging from dysfunctional interactions between reward-related striatal circuitry and prefrontal systems mediating inhibitory control, decision-making, and emotion regulation. Early clinical–neurobiological accounts emphasized the high psychiatric comorbidity of pathological gambling, including suicidality, and highlighted overlaps with impulse-control and bipolar-spectrum psychopathology [41]. More recent pharmacotherapy syntheses indicate that medication effects in GD are heterogeneous and are best interpreted within a target-based framework addressing dimensional constructs such as craving, impulsivity, and affective instability rather than disorder-specific mechanisms [25,27,42]. Within this framework, lithium is of particular interest because it combines established effects on affective instability, impulsive/aggressive dyscontrol, and suicidal vulnerability—domains strongly associated with severe GD presentations and relapse risk.

From a mechanistic perspective, lithium's potential relevance to GD can be conceptualized across converging neurocognitive and intracellular pathways implicated in reward–control dysfunction. At the neurocognitive level, gambling behavior critically depends on decision-making under risk and reward sensitivity, processes commonly assessed through paradigms such as the Iowa Gambling Task and Cambridge Gambling Task. Observational evidence suggests that lithium exposure may be associated with improved decision-making performance in euthymic bipolar patients [43], while a recent double-blind crossover study demonstrated that short-term lithium administration can rapidly modify emotional processing biases, including enhanced positive emotional encoding, with more limited effects on impulsivity and reward-seeking behavior [38].

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These findings provide a translational link between lithium and cognitive–affective processes that are central to gambling persistence, cue-driven escalation, and relapse vulnerability.

At the molecular level, inhibition of glycogen synthase kinase-3 (GSK-3) represents one of the most consistently supported intracellular mechanisms of lithium action. Lithium can inhibit GSK-3 via competition with magnesium, thereby modulating downstream signaling pathways involved in synaptic plasticity and learning-related processes [44]. Importantly, contemporary neurobiological models of GD emphasize maladaptive reinforcement learning, altered valuation, and cue-driven behavioral persistence supported by dysregulated striatal–prefrontal circuitry. Computational studies in disordered gambling have identified reinforcement-learning abnormalities associated with maladaptive choice behavior, while neuroimaging meta-analyses converge on alterations in fronto-striatal and limbic networks implicated in reward processing and decision-making [45]. Additionally, cue-reactivity paradigms demonstrate that craving in GD is associated with activity and connectivity changes within insula, ventral striatum, and prefrontal regions, supporting the embedding of cue-driven urges within reward–control network dysfunction [9,46].

Within this GD framework, GSK-3 is positioned as a biologically plausible intracellular bridge linking lithium pharmacodynamics to addiction-relevant circuitry. GSK-3 regulates signaling pathways implicated in synaptic plasticity, stress-responsive neuroadaptation, and learning processes that can support cue-conditioned responding and habit-like behavioral persistence. Preclinical evidence further links GSK-3β signaling to contextual cue–reward memory processes relevant to addiction-like phenotypes [47], while mechanistic syntheses highlight lithium's capacity to inhibit GSK-3 both directly and through upstream signaling cascades, with downstream effects on dopaminergic–glutamatergic interactions and activity-dependent plasticity [22]. Consistent with this perspective, contemporary integrative reviews of lithium pharmacodynamics emphasize its multimodal intracellular actions—including GSK-3 inhibition, neurotrophic modulation, and regulation of synaptic plasticity—as central mechanisms underlying lithium's effects on behavioral regulation and emotional stability [20]. Together, these findings support the hypothesis that lithium-mediated GSK-3 inhibition may influence dimensional processes central to GD, including maladaptive reward learning, cue-reactivity and craving, and impaired top-down regulatory control.

This mechanistic plausibility is consistent with clinical observations and focused trials indicating that lithium may reduce gambling severity and affective instability, particularly among individuals with bipolar-spectrum features [40,48], as well as with early comparative evidence in non-bipolar pathological gamblers [37]. A qualitative systematic review examining bipolar disorder–GD comorbidity concluded that lithium remains the only pharmacological agent supported by relatively higher-level evidence in this clinical context, emphasizing the importance of phenotypic stratification [49], while case-based reports underscore potential utility when treatment selection is guided by temperament and bipolar-spectrum vulnerability [50].

Taken together, these converging neurocognitive and intracellular mechanisms support a coherent translational hypothesis: lithium may be particularly relevant in GD presentations characterized by affective instability, impaired top-down control, and suicidality, with therapeutic effects potentially mediated through modulation of decision-making and emotional processing alongside plasticity-related intracellular signaling pathways. Nevertheless, mechanistic inference remains indirect, and future studies integrating behavioral, neuroimaging, and molecular endpoints are needed to clarify lithium's role within the neurobiology of gambling disorder.

Table 3. Neurobiological targets of lithium and their potential relevance for gambling disorder.

Lithium target	Mechanism	Relevance for gambling disorder	References
Suicidality	Anti-suicidal effect through mood stabilization and stress-system modulation	GD is associated with elevated risk of suicidal ideation and attempts	[18,19]

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Impulsivity / behavioral dyscontrol	Modulation of serotonergic signaling and reduction of impulsive aggression	Impulsivity contributes to loss of control during gambling episodes	[12,19]
Affective dysregulation	Mood stabilization via serotonergic and glutamatergic pathways	Emotional distress often precipitates gambling behavior	[20]
Reward learning	Inhibition of GSK-3 and modulation of fronto-striatal circuitry	GD involves maladaptive reinforcement learning and reward processing	[8,22]
Decision-making	Modulation of emotional processing and cognitive control	GD is characterized by impaired decision-making under risk and reward	[38,43]

6. Discussion

The present case illustrates the clinical trajectory of a patient with severe gambling disorder (GD) characterized by profound psychosocial destabilization, affective dysregulation, and a recent suicidal crisis. Within a structured multimodal treatment framework, the introduction and stabilization of lithium carbonate were associated with progressive remission of suicidal ideation, marked reduction of gambling urges, sustained behavioral abstinence, and significant improvements in functional and psychometric measures over long-term follow-up.

Contemporary models conceptualize GD as a disorder emerging from the interaction between dysregulated reward processing, impaired cognitive control, and emotional vulnerability within fronto-striatal networks [1,8]. In this framework, gambling behavior is increasingly interpreted not merely as a behavioral habit but as the clinical expression of interacting transdiagnostic dimensions, particularly impulsivity, affective instability, stress reactivity, and maladaptive reinforcement learning [11,12]. These dimensions are also closely linked to the elevated prevalence of suicidal behavior observed in individuals with gambling disorder [4,5].

Within this dimensional perspective, lithium represents a pharmacological agent of particular theoretical interest. Lithium is widely recognized for its anti-suicidal properties and its ability to modulate impulsive aggression, emotional dysregulation, and behavioral dyscontrol across psychiatric conditions [18,19]. These mechanisms are directly relevant to the psychopathological profile often observed in severe GD, where impulsivity and affective instability frequently interact with psychosocial stressors to precipitate gambling escalation and crisis states.

In the present case, the patient initially displayed a clinical presentation consistent with high impulsive and emotional vulnerability. Psychometric evaluation at baseline classified the patient within Pathway Type 3 on the Gambling Pathways Questionnaire (GPQ), a subtype characterized by pronounced impulsivity, emotional dysregulation, and higher psychiatric comorbidity. This profile is generally associated with greater clinical severity and poorer outcomes. The patient's clinical history was congruent with this profile, including impulsive loss of control during gambling episodes, episodic alcohol misuse in response to emotional distress, and the occurrence of a suicidal crisis during a period of overwhelming psychosocial stress.

Notably, reassessment at 18-month follow-up demonstrated a shift toward Pathway Type 2, a subtype primarily characterized by emotional vulnerability rather than severe impulsive dyscontrol. The transition from a more impulsive/dysregulated gambling profile toward a predominantly emotionally vulnerable pattern may be interpreted as being congruent with a reduction in impulsive dyscontrol and improved affective regulation, domains that are theoretically and clinically relevant

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to lithium's mechanism of action [19,20]. This change in vulnerability profile occurred alongside remission of suicidal ideation, stabilization of mood symptoms, and sustained behavioral abstinence.

Further evidence of clinical improvement was reflected in the marked reduction of gambling-related cognitive distortions. The Gambling Beliefs Questionnaire score decreased at follow-up, indicating near-complete resolution of maladaptive beliefs associated with gambling behavior. Similarly, the Gambling Disorder Screening Questionnaire no longer identified any diagnostic criteria for GD at follow-up. In parallel, functional impairment decreased substantially as reflected by improved WHODAS scores, suggesting recovery across multiple domains of daily functioning.

The clinical course also included a brief gambling lapse during follow-up. The patient reported having taken approximately EUR 800 from his son, which he gambled and unexpectedly won. Importantly, the episode was immediately disclosed to the treatment team and to family members, and the patient rapidly resumed abstinence without progression to sustained gambling behavior or financial destabilization. Although a direct causal attribution cannot be made, the rapid containment of the lapse despite the positively reinforcing effect of a gambling win is clinically consistent with a background process of affective and behavioral stabilization. In this regard, recent literature suggests that lithium may modulate impulsive dyscontrol and emotional processing, while contemporary recovery models in gambling disorder emphasize that promptly disclosed and therapeutically contained lapses should be distinguished from full relapse [19,20,32,51].

From a neurobiological perspective, lithium may exert relevant effects on addiction-related processes through modulation of intracellular signaling pathways involved in synaptic plasticity and emotional regulation. In particular, inhibition of glycogen synthase kinase-3 (GSK-3) represents one of the most consistently supported mechanisms of lithium action. GSK-3 is a central regulator of synaptic plasticity, reinforcement learning, and stress-related neuroadaptation—processes that are increasingly implicated in the neurobiology of addictive behaviors [22]. Lithium-mediated modulation of these pathways may influence dopaminergic and glutamatergic signaling within fronto-striatal circuits, potentially stabilizing reward-processing dynamics that sustain compulsive gambling behavior.

Although pharmacological treatment of GD remains limited by heterogeneous evidence, several reviews and meta-analyses have suggested that medications targeting underlying affective or impulsive dysregulation may indirectly reduce gambling behavior [25–27]. Lithium occupies a unique position within this pharmacological landscape because it combines well-established anti-suicidal effects with stabilization of impulsive and affectively driven behaviors. The present case therefore contributes to emerging literature suggesting that lithium may represent a clinically relevant adjunctive strategy in selected GD presentations characterized by severe emotional dysregulation and suicidal vulnerability.

Importantly, the clinical improvements observed in this case occurred within a multimodal treatment program, including psychotherapy, psychoeducational group interventions, social support measures, and family involvement. Such integrated approaches are increasingly recommended for gambling disorder, reflecting the complex biopsychosocial nature of the condition and the need for flexible and sustained treatment strategies capable of supporting long-term recovery [32,51].

Several limitations should be acknowledged. As a single-case report, causal inference regarding the specific contribution of lithium cannot be established. The observed clinical improvement likely reflects the combined effects of pharmacological stabilization and intensive psychosocial intervention. In addition, follow-up psychometric assessments for some instruments are still ongoing. Nevertheless, the temporal association between lithium stabilization, remission of suicidal ideation, reduction in gambling urges, and improvement in vulnerability dimensions measured by the GPQ suggests that lithium may have played a clinically meaningful role in the stabilization of impulsive and affectively driven gambling behavior in this patient.

Taken together, this case highlights the potential relevance of lithium within a dimensional treatment framework for gambling disorder. In individuals presenting with severe GD accompanied by impulsivity, emotional dysregulation, and suicidal risk, lithium may represent a promising

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adjunctive intervention capable of stabilizing core vulnerability mechanisms that sustain gambling behavior. Further controlled studies integrating clinical, neurobiological, and dimensional assessments are warranted to clarify the potential role of lithium in the treatment of gambling disorder.

7. Conclusions

This case highlights the potential clinical relevance of lithium within a dimensional treatment framework for gambling disorder. In a patient presenting with severe GD accompanied by affective dysregulation, impulsive loss of control, and suicidal ideation, lithium treatment—implemented within a structured multimodal intervention—was associated with sustained clinical stabilization, remission of suicidal thoughts, and long-term abstinence from gambling behavior. Psychometric findings further suggested a modification of underlying vulnerability dimensions, with a shift from a predominantly impulsive–dysregulated gambling profile toward a pattern characterized mainly by emotional vulnerability. These changes occurred alongside substantial reductions in gambling-related cognitive distortions and functional impairment. Although causal inference cannot be established from a single case, the present observations support the hypothesis that lithium may contribute to the stabilization of impulsive and affectively driven gambling behaviors. Further controlled studies are warranted to clarify the potential role of lithium as an adjunctive pharmacological strategy in selected gambling disorder presentations characterized by emotional dysregulation and suicidal risk.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org. Table 1. Clinical course, lithium titration, and key outcomes; Table 2. Summary of key psychometric findings at baseline and 18-month follow-up; Table 3. Neurobiological targets of lithium and their potential relevance for gambling disorder.

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Abbreviations

GD	Gambling Disorder
DSM-5-TR	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision
ICD-11	International Classification of Diseases, 11th Revision
CBT	Cognitive Behavioral Therapy
NICE	National Institute for Health and Care Excellence
GSK-3	Glycogen Synthase Kinase 3
PG-YBOCS	Pathological Gambling version of the Yale-Brown Obsessive Compulsive Scale
GPQ	Gambling Problems Questionnaire
GDSQ	Gambling Disorder Screening Questionnaire

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GBQ Gambling Beliefs Questionnaire

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