

Case Report

Utilization of probiotics modulating the gut-brain axis in bipolar disorder and ADHD: a case report

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Received: 09 May 2025

Revised: 23 June 2025

Accepted: 24 June 2025

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ABSTRACT

Bipolar disorder (BD) and attention-deficit/hyperactivity disorder (ADHD) frequently co-occur, complicating treatment due to overlapping symptoms and limited efficacy of conventional pharmacotherapy. Emerging evidence indicates gut dysbiosis in neuropsychiatric pathophysiology via the gut-brain axis, suggesting probiotics as a potential adjunctive intervention. However, their utility in comorbid BD-ADHD remains unexplored. A 15-year-old male with comorbid BD and ADHD exhibited persistent manic symptoms (YMRS:42/60) and hyperactivity despite treatment with aripiprazole and lamotrigine. While manic symptoms improved post-treatment (YMRS:9/60), ADHD-related impulsivity and behavioral dysregulation remained, as shown by the Vanderbilt ADHD scales. Adjunctive probiotics were initiated due to familial preference against stimulant medication. Over 18 months, clinical improvement in both ADHD-related symptoms and residual behavioral dysregulation, as evidenced by follow-up scale scores. This case highlights probiotics as a potential adjunctive therapy for comorbid BD-ADHD, potentially modulating the gut-brain axis pathways to address residual symptoms unresponsive to conventional pharmacotherapy. Further controlled trials are needed to validate microbiota-targeted interventions in complex neuropsychiatric comorbidities.

Keywords: Probiotics, ADHD, Bipolar, Vanderbilt, YMRS, Gut-brain axis

INTRODUCTION

Bipolar disorder (BD) and attention-deficit/hyperactivity disorder (ADHD) are complex, chronic neuropsychiatric conditions that frequently co-occur, resulting in an earlier onset, increased symptom severity, and poorer long-term functional outcomes compared to either disorder alone.^{1,2}

The comorbidity of BD and ADHD presents significant diagnostic and therapeutic challenges, as overlapping symptoms can obscure diagnosis and complicate treatment strategies.³ Although pharmacological interventions such as mood stabilizers and stimulants are commonly used, they often yield only partial efficacy and

may produce adverse effects, especially when treating patients with both conditions simultaneously.² The gut-brain axis, a bidirectional communication network linking the gastrointestinal tract and the central nervous system, has emerged as an area to understand neuropsychiatric disorders.⁴ Emerging evidence suggests that gut microbiota dysbiosis may contribute to systemic inflammation, neurotransmitter dysregulation, and behavioral abnormalities, which are hallmark features of conditions such as BD and ADHD.^{5,6} Probiotics, live microorganisms with potential benefits for gut microbiota composition, have shown promise in modulating this axis, offering a novel adjunctive therapeutic avenue for mental health conditions.⁷

In BD, gut dysbiosis has been associated with increased pro-inflammatory cytokines, oxidative stress, and mood instability.⁸ A randomized controlled trial demonstrated that adjunctive probiotic supplementation reduced rehospitalization rates in patients with acute mania, suggesting microbiota modulation as a viable strategy.⁸ Preliminary evidence indicates that probiotics may reduce depressive and anxiety symptoms, modulate stress responses, and enhance cognitive function through microbial modulation of neuroactive compounds.^{9,10} Similarly, ADHD has been linked to altered gut microbial diversity and intestinal permeability, with preclinical studies implicating microbiota-derived metabolites in dopaminergic and noradrenergic dysfunction.¹¹

The intersection of BD and ADHD presents unique clinical challenges, including overlapping symptoms (e.g., impulsivity) and shared pathophysiological mechanisms, such as chronic low-grade inflammation.⁶ Adjunctive probiotic supplementation may address these mechanisms by restoring gut barrier integrity, reducing systemic inflammation, and enhancing neurotransmitter production.¹² However, existing literature have not investigated this approach in comorbid populations.

This case report explores the feasibility and potential benefits of adjunctive probiotic supplementation in patients with BD and comorbid ADHD, focusing on gut-brain axis modulation as a therapeutic target. We aim to provide preliminary evidence to guide future randomized trials by bridging this gap.

CASE REPORT

The patient is a 15-year-old male with a documented history of both ADHD and bipolar disorder (BPD), who exhibited persistent manic episodes and hyperactivity despite long-term pharmacologic treatment. The patient was initially brought in for emergency evaluation after engaging in risky and disinhibited behaviors, including briefly driving a school bus for a block, sitting in a stranger's car, and talking to unfamiliar individuals. He had also been sent home from school for disruptive actions, such as breaking a microphone and sitting in the principal's chair.

Following clinical assessment, the Young Mania Rating Scale (YMRS) and Vanderbilt ADHD Diagnostic Rating Scale (completed by parents and teachers) were administered. Figure 1 illustrates the YMRS scores over time, with the Y-axis representing symptom severity (range: 0-60) and the X-axis denoting time.

Higher scores indicate greater manic symptom burden. Figure 2 depicts the Vanderbilt ADHD scale scores for hyperactivity (items 10-18, parent/teacher-reported) and functional performance (items 48-54 parent-reported; items 36-43 teacher-reported). The Y-axis represents time, while the X-axis uses "1" (meets criteria) and "-1" (does not meet criteria) to denote symptom severity.

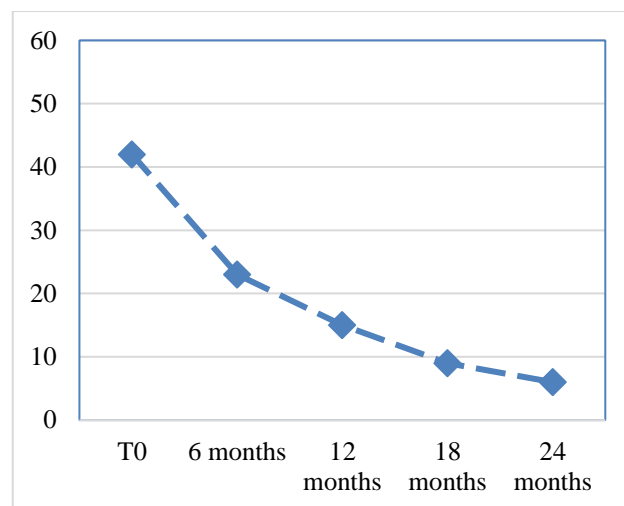


Figure 1: Young mania rating scale.

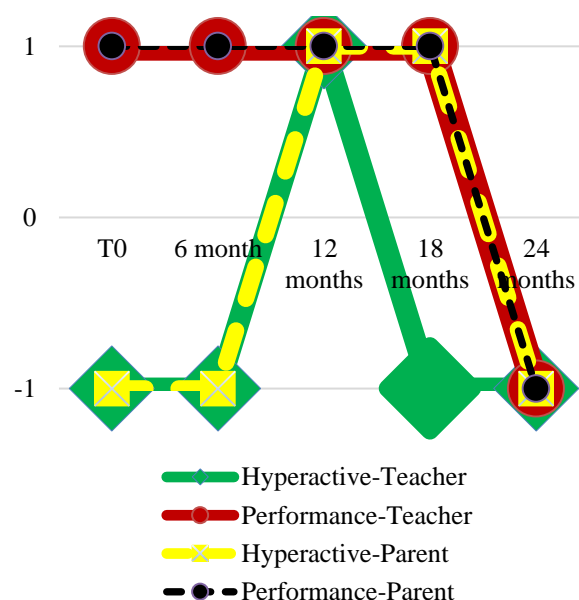


Figure 2: Vanderbilt assessment scale- teacher/parent informant.

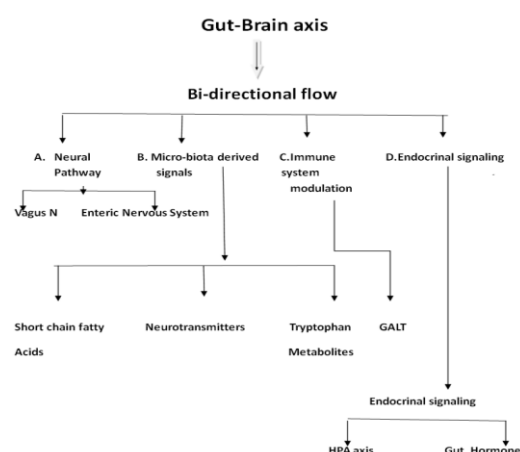


Figure 3: The gut-brain axis mechanism.

Based on the findings, his symptoms were initially attributed primarily to mania, and treatment was initiated with aripiprazole and lamotrigine. The patient's YMRS score was 42/60 (Figure 1), consistent with significant manic symptomatology. After treatment with Lamotrigine 100 mg orally once daily and Aripiprazole 10 mg orally once daily, the score steadily decreased, culminating in a final assessment score of 9/60 (Figure 1) on YMRS. However, hyperactive, talkative, and impulsive behaviors persisted, suggesting an incomplete therapeutic response, which could not be fully explained by mood instability alone.

At this stage, ADHD symptomatology was reassessed using the Vanderbilt scale (Figure 2), revealing ongoing behavioral dysregulation. In light of emerging evidence supporting the role of the gut microbiome in modulating neuropsychiatric symptoms, a probiotic regimen was introduced alongside the existing stimulant and mood stabilizer therapy because the family did not want him on more medicines.^{4,15-17}

Over 18 months (Figure 2), the patient demonstrated marked clinical improvement in both ADHD-related symptoms and residual behavioral dysregulation, as evidenced by follow-up scale scores. This case highlights a potential adjunctive role for probiotics in managing comorbid psychiatric conditions, particularly when conventional treatment yields only a partial response.^{1,9,18}

DISCUSSION

The gut-brain axis (GBA) serves as a complex and interactive communication network linking the central nervous system (CNS) with the gastrointestinal (GI) system. This combination of neural, hormonal, immune, and microbial pathways plays an essential role in managing psychiatric conditions. The gut-brain axis operates through four primary pathways.

Neural pathways

The vagus nerve is the primary conduit for neural communication between the gut and brain, which senses microbial metabolites and conveys these signals to the brainstem and hypothalamus. The enteric nervous system (ENS) regulates gastrointestinal motility and secretion while independently interacting with the CNS.^{4,13}

Microbial-derived signals

Gut microbiota produces various bioactive molecules that impact brain function. Short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate cross the blood-brain barrier (BBB) and modulate neuroinflammation and neurotransmitter synthesis.^{14,16} Some bacteria synthesize neurotransmitters, including GABA, serotonin (5-HT), dopamine, and acetylcholine, influencing mood, cognition, and behavior.^{15,17} Microbiota also regulate tryptophan metabolism, affecting serotonin synthesis and

the kynurenine pathway, critical to emotional and immune regulation.¹⁶

Immune system modulation

The gut-associated lymphoid tissue (GALT) is essential in immune surveillance. It can influence BBB permeability, regulate systemic inflammation, and modulate neuroimmune activity, affecting behavior and psychiatric symptomatology.^{4,19,20}

Endocrine signalling

Gut-derived hormones such as ghrelin, leptin, and peptide YY contribute to energy regulation and appetite control and play roles in cognitive processing and emotional regulation. The hypothalamic-pituitary-adrenal (HPA) axis also mediates the body's stress response. Activating this axis leads to cortisol release, which alters gut barrier function and microbiota composition, further influencing mental health.^{17,21}

CONCLUSION

This case illustrates how modulation of the gut microbiome through probiotics may serve as a promising adjunctive treatment for complex psychiatric disorders, particularly in patients with overlapping symptom domains. The observed reduction in both manic and ADHD symptoms following the introduction of probiotics supports the evolving understanding that the gut microbiota influences CNS function through multiple, interconnected pathways.

By restoring microbial balance, probiotics may enhance neurotransmitter regulation, reduce inflammation, and support neural homeostasis, offering a novel therapeutic strategy in psychiatry. While further research and controlled trials are needed, this case adds to the growing body of evidence advocating for integrating gut-targeted interventions in neuropsychiatric care.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Parikh P, Singh SK, Suthar HJ, Oza M, Mineo A. Utilization of probiotics modulating the gut-brain axis in bipolar disorder and ADHD: a case report. *Int J Community Med Public Health* 2025;12:3789-92.