Probiotics, Dopamine, and Emotional Dysregulation in ADHD: Clinical Promise or Premature Hope?

Etty Christina Baboe[1,2] and Royke Tony Kalalo[1,2,*]

[1]*Department of Psychiatry, Dr Soetomo General Academic Hospital, Surabaya, Indonesia*

[2]*Department of Psychiatry, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia*

Abstract: Interest in the gut-brain axis has increased rapidly as evidence links intestinal microbiota with neuro-developmental outcomes in children. Emotional dysregulation remains a major unmet need in attention-deficit hyperactivity disorder (ADHD), often persisting despite stimulant therapy. This narrative review examines whether probiotics may offer clinical benefit by modulating dopaminergic, inflammatory, and microbial pathways relevant to ADHD. A literature search of PubMed and Google Scholar identified clinical trials, observational studies, and meta-analyses published between 2015 and 2025 evaluating probiotics in ADHD or related emotional symptoms. Findings suggest that multi-strain probiotics may improve irritability, mood lability, and selected cognitive domains, although effects on core ADHD symptoms remain inconsistent. Most studies are short in duration, involve small samples, and differ in probiotic strains and outcomes measured. Current evidence indicates that probiotics are safe and biologically plausible adjuncts, but they are not yet ready for routine clinical use. Larger standardized trials with longer follow-up are required.

Keywords: ADHD, probiotics, gut-brain axis, emotional dysregulation, microbiome, child psychiatry, adjunctive therapy.

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) affects millions of children worldwide and is characterized by persistent inattention, hyperactivity, and impulsive behavior [1]. Beyond these core symptoms, emotional dysregulation is increasingly recognized as a major contributor to impairment. Irritability, rapid mood shifts, frustration intolerance, and explosive reactions often create greater functional disruption than attention or behavioral symptoms alone [2]. These emotional difficulties are associated with poor academic performance, strained peer relationships, and increased family conflict [3].

Standard treatments, including stimulant medications and behavioral therapy, often fail to fully address emotional dysregulation in children with ADHD [4]. This therapeutic gap has encouraged exploration of additional biological mechanisms that may influence emotional regulation and broader child health outcomes. One area of growing interest is the gut-brain axis, an interactive network through which the intestinal microbiota interacts with neural, endocrine, and immune pathways involved in emotion and cognition [5]. As diet is a major determinant of microbiome composition in early life, probiotics have increasingly been viewed as nutritional interventions rather than solely experimental psychobiological agents. Experimental and clinical studies suggest that specific bacterial strains may influence neurotransmitter availability, inflammation signaling, and stress regulation. Children with ADHD have been reported to exhibit differences in microbial composition compared with their neurotypical peers [5, 6]. These findings have prompted an investigation into whether probiotic supplementation may serve as an adjunctive nutritional strategy for improving emotional and cognitive symptoms in ADHD.

MATERIALS AND METHODS

This article is presented as a narrative review. Studies were identified through focused searches of major biomedical databases and manual screening of reference lists from key publications. Selection was guided by relevance to pediatric ADHD and neurodevelopmental conditions, probiotic or microbiome-related nutritional interventions, and outcomes related to emotional regulation, executive function, or child health. Formal quality scoring was not performed, consistent with a narrative review approach, but studies were assessed for methodological clarity and clinical applicability. Table **1** from the original manuscript summarizes the included clinical studies and is preserved unchanged.

*Address correspondence to this author at the Department of Psychiatry, Faculty of Medicine Universitas Airlangga, Dr Soetomo General Academic Hospital, Jl. Mayjen. Prof. Dr. Moestopo, 47, Surabaya, Jawa Timur, 60286, Indonesia; Tel: +62-31-5914042;
Fax: +62-31-5915551; E-mail: drroykekalalo@fk.unair.ac.id

Table 1: Key Clinical Studies of Probiotics in ADHD

Study (Year)	Population	Intervention	Duration	Main outcomes	Findings
Sepehrmanesh *et al.*, 2021	Children with ADHD aged 8-12	Multi-strain mix (*L. reuteri, L. acidophilus, L. fermentum, B. bifidum*)	8 weeks	ADHD Rating Scale, inflammatory markers	Reduced ADHD scores and improved inflammatory profile compared with placebo
Rojo-Marticella, 2025	Children with ADHD and ASD (n = 80), aged 5-16 years	Multi-strain probiotic (*Lactiplantibacillus plantarum* and *Levilactobacillus brevis* (10^9 CFU daily)	12 weeks	Conners 3rd Ed, SRS 2, CPT 3 or K CPT 2, quality of life, sleep	No significant overall group differences; age stratified analyses showed improved hyperactivity impulsivity in younger children with ADHD and ASD, reduced impulsivity on CPT in ASD, and improved quality of life in ASD
Parhiz *et al.*, 2026	Children with ADHD aged 7-12 years (n = 84)	Multi strain probiotic (*Lactobacillus acidophilus*, *Bifidobacterium lactis*, *Bifidobacterium longum*)	8 weeks	Executive function (BRIEF questionnaire)	Significant improvement in executive function in the probiotic group compared with placebo after adjustment for confounders
Wang *et al.*, 2024	Children with ADHD, aged 6-12	*B. bifidum* Bf 688	12 weeks	Continuous Performance Test, microbiome	Improved reaction time and favorable microbiome shifts
Pärtty *et al.*, 2015	Infants randomized at birth, followed to age 13	*L. rhamnosus* GG	6 months	ADHD and ASD diagnosis	Fewer ADHD and ASD diagnoses in probiotic group
Elhossiny *et al.*, 2023	Children and adolescents with ADHD on atomoxetine, aged 6-16 years	*L. acidophilus* LB plus atomoxetine	12 weeks	Conners Parent Rating, cognition	Greater improvement in symptoms and cognition compared with atomoxetine alone
Liang *et al.*, 2024	Seven trials involving 379 ADHD participants (mean age 10.37 years, range 4-18 years)	Mixed strains	8 to 12 weeks	ADHD symptoms	No consistent benefit on core symptoms, probiotics safe and well tolerated

FINDINGS

Multi-Strain Probiotic Trials

Several multi-strain formulations have demonstrated promising clinical effects. Sepehrmanesh *et al.* reported that children receiving a combination of Lactobacillus reuteri, Lactobacillus acidophilus, Lactobacillus fermentum, and Bifidobacterium bifidum for eight weeks experienced reductions in ADHD symptom scores and improvements in inflammatory and antioxidant markers. These dual behavioral and biological effects suggest that multi-strain formulations may simultaneously influence multiple pathways [7] In a 12-week randomized trial of children with ADHD and autism spectrum disorder, a multi-strain probiotic containing Lactiplantibacillus plantarum and Levilactobacillus brevis showed no significant overall group differences, but age-stratified analyses demonstrated improvements in hyperactivity-impulsivity in younger children and improved quality of life in autism spectrum disorder [9]. In an 8-week randomized trial of children aged 7-12 years with ADHD, a multi-strain probiotic containing Lactobacillus acidophilus, Bifidobacterium lactis, and Bifidobacterium longum significantly improved parent-reported executive function compared with placebo after adjustment for confounders [10].

Single-Strain Trials

Single-strain probiotics show strain-specific effects. Wang *et al.* investigated Bifidobacterium bifidum Bf-688 for twelve weeks and found improvements in sustained attention and reaction time, accompanied by shifts in microbial composition. While encouraging, the effects were limited to cognitive performance and did not generalize to broad symptom improvement [11]. In a preventive context, Parťty *et al.* provided Lactobacillus rhamnosus GG during infancy and reported a lower prevalence of ADHD and autism diagnoses in adolescence. Although not a treatment trial, it suggests that early microbiome shaping may influence long-term neurodevelopment [12].

Adjunctive Therapy Trials

Adjunctive approaches combine probiotics with conventional medication. Elhossiny *et al.* studied children receiving atomoxetine and found that adding Lactobacillus acidophilus LB produced greater improvements on the Conners Parent Rating Scale and selected cognitive tasks than medication alone [13]. This suggests a potential role for probiotics in enhancing treatment response, particularly in emotional and cognitive areas less responsive to medication.

Meta-Analyses and Systematic Reviews

Liang *et al.* concluded that probiotics do not consistently improve core ADHD symptoms but noted excellent safety and tolerability. Heterogeneity in strains, durations, and outcome measures was identified as a major limitation [14].

DISCUSSION

This narrative review highlights that probiotics may play a supportive role in managing emotional dysregulation in ADHD, particularly when viewed as nutritional interventions within a child health framework, an area of significant unmet clinical need. Although stimulant medications remain the primary treatment for core symptoms, they have a limited impact on irritability, mood instability, and emotional reactivity. These emotional challenges often persist despite adequate medication adherence and contribute to behavioral crises and family stress [2,4]. From a pediatric perspective, emotional dysregulation in childhood ADHD is associated with poorer peer relationships, academic difficulties, caregiver burden, and increased risk of later mental health problems, underscoring its relevance to long-term child development rather than short-term symptom control alone. The possibility that probiotics may improve these domains is therefore clinically relevant. The biological rationale for probiotic use is supported by several mechanisms. Microbial strains influence the production and metabolism of neurotransmitters such as dopamine, which plays a central role in reward processing and emotional regulation [8]. However, these observations are derived primarily from preclinical models and associative human studies and do not establish a direct causal effect of probiotics on neurotransmitter function or ADHD symptoms. Probiotics also reduce inflammatory cytokines and modulate the hypothalamic-pituitary-adrenal axis, potentially improving stress tolerance. Accordingly, these mechanisms should be interpreted as biologically plausible pathways rather than proven clinical effects [1,5, 8]

In children, these pathways intersect with critical periods of neurodevelopment during which immune signaling, stress responsivity, and emotional regulation systems are still maturing; and are frequently implicated in ADHD and may partially explain why emotional symptoms show greater responsiveness than core behavioral symptoms [5,6] From a child nutrition perspective, probiotics represent a low-intensity intervention capable of influencing neurodevelopmental processes through diet-microbiome interactions, rather than direct pharmacological modulation. These effects should be viewed as supportive and adjunctive rather than therapeutic [5, 6, 8]

However, existing evidence is limited by methodological constraints. Sample sizes are often small, treatment durations are short, and probiotic strains are highly variable. Many commercial formulations differ from those tested in clinical research, which complicates translation to practice. This gap is particularly relevant for families, as probiotics are widely marketed as over-the-counter supplements despite limited pediatric efficacy data. In addition, the heterogeneity of ADHD suggests that not all children will respond similarly. Emotional dysregulation itself represents a distinct dimension within ADHD, and children whose symptoms arise from heightened stress reactivity may be more likely to benefit. This highlights the importance of identifying clinically meaningful subgroups within pediatric ADHD rather than assuming a uniform response.

Despite these limitations, probiotics appear safe, inexpensive, and acceptable to families. Their excellent tolerability makes them appealing as potential adjunctive therapies while stronger evidence accumulates. From a public health and nutrition standpoint, interventions with low-risk profiles and high accessibility are particularly attractive in pediatric populations, especially when long-term pharmacological exposure is a concern. Future research should prioritize adequately powered pediatric trials with standardized probiotic formulations, age-specific outcome measures, and longer follow-up periods. Additional priorities for nutrition-focused research include determining optimal strain combinations and dosing strategies, evaluating probiotics within the context of habitual diet and overall

nutritional status, and examining interactions with lifestyle factors such as sleep and physical activity. Pragmatic trials embedded in routine pediatric care settings may further clarify feasibility, adherence, and real-world effectiveness. Integrating microbiome and inflammatory biomarkers may also help identify which children are most likely to respond. At a policy level, clearer guidance is needed to help clinicians and families distinguish between evidence-supported probiotic interventions and untested commercial products. Until stronger evidence emerges, probiotics should be discussed within a framework of nutritional support and ongoing research rather than routine clinical recommendations. Such work would support the development of evidence-based nutritional strategies that complement existing ADHD treatments and address domains currently underserved by pharmacotherapy.

CONCLUSION

Probiotics offer a biologically plausible and safe adjunctive approach for improving emotional dysregulation in ADHD. While findings from multi-strain and adjunctive therapy trials are encouraging, evidence remains insufficient to support routine clinical use. Larger, longer, and more standardized trials are required to determine efficacy and identify appropriate candidates. Until then, probiotics may be considered an experimental but potentially valuable complement to standard ADHD treatments, particularly for children with prominent emotional symptoms.

CONFLICT OF INTEREST

All authors have reported no conflict of interest relevant to the contents of this paper to disclose.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization: ECB, RTK

Literature Search and Data Extraction: All authors

Analysis and Interpretation of Evidence: All authors

Manuscript Writing: All authors contributed to drafting the manuscript

Critical Revision: All authors reviewed and revised the manuscript for important intellectual content

Final Approval: All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

ETHICAL APPROVAL

N/A.

REFERENCES

[1] Faraone SV, Bellgrove MA, Brikell I, Cortese S, Hartman CA, Hollis C, *et al*. Attention-deficit/hyperactivity disorder. Nat Rev Dis Primers 2024; 10(1): 11. Erratum in: Nat Rev Dis Primers 2024; 10(1): 29. https://doi.org/10.1038/s41572-024-00495-0

[2] Grossman A, Avital A. Emotional and sensory dysregulation as a possible missing link in attention deficit hyperactivity disorder: a review. Front Behav Neurosci 2023; 17: 1118937. https://doi.org/10.3389/fnbeh.2023.1118937

[3] Peasgood T, Bhardwaj A, Biggs K, Brazier JE, Coghill D, Cooper CL, *et al*. The impact of ADHD on the health and well-being of ADHD children and their siblings. Eur Child Adolesc Psychiatry 2016; 25(11): 1217-1231. https://doi.org/10.1007/s00787-016-0841-6

[4] Nazarova VA, Sokolov AV, Chubarev VN, Tarasov VV, Schiöth HB. Treatment of ADHD: drugs, psychological therapies, devices, complementary and alternative methods as well as trends in clinical trials. Front Pharmacol 2022; 13: 1066988. https://doi.org/10.3389/fphar.2022.1066988

[5] Lewis N, Villani A, Lagopoulos J. Gut dysbiosis as a driver of neuroinflammation in attention-deficit/hyperactivity disorder: a review of current evidence. Neuroscience 2025; 569: 298-321. https://doi.org/10.1016/j.neuroscience.2025.01.031

[6] Dicks LMT. Gut bacteria and neurotransmitters. Microorganisms 2022; 10(9): 1838. https://doi.org/10.3390/microorganisms10091838

[7] Sepehrmanesh Z, Shahzeidi A, Mansournia MA, Ghaderi A. Clinical and metabolic response to probiotic supplementation in children with ADHD. Int Arch Health Sci 2021; 8(1): 22-30.

[8] Cickovski T, Mathee K, Aguirre G, Tatke G, Hermida A, Narasimhan G, *et al*. Attention deficit hyperactivity disorder (ADHD) and the gut microbiome: an ecological perspective. PLoS One 2023; 18(8): e0273890. https://doi.org/10.1371/journal.pone.0273890

[9] Rojo-Marticella M, Arija V, Canals-Sans J. Effect of probiotics on the symptomatology of autism spectrum disorder and/or attention deficit/hyperactivity disorder in children and adolescents: pilot study. Res Child Adolesc Psychopathol 2025; 53(2): 163-178. https://doi.org/10.1007/s10802-024-01278-7

[10] Parhiz A, Samani P, Kamali M, Shekari Y, Naghshi N, Faghihshojaei N, *et al*. Probiotic supplementation and executive function in children with attention-deficit/hyperactivity disorder. Neuropsychopharmacol Rep 2026; 46(1): e70084. https://doi.org/10.1002/npr2.70084

[11] Wang LJ, Yang CY, Kuo HC, Chou WJ, Tsai CS, Lee SY, *et al*. Effects of Bifidobacterium bifidum Bf-688 on ADHD in children: a gut microbiome randomized controlled trial. Prog Neuropsychopharmacol Biol Psychiatry 2024; 122: 110732.

[12] Pärtty A, Kalliomäki M, Wacklin P, Salminen S, Isolauri E. Early probiotic use associated with lower risk of ADHD and autism spectrum disorders at 13 years of age. Pediatr Res 2015; 77(6): 823-828. https://doi.org/10.1038/pr.2015.51

[13] Elhossiny RM, Elshahawy HH, Mohamed HM, Abdelmageed RI. Lactobacillus acidophilus LB as adjunctive management of attention-deficit/hyperactivity disorder in children and adolescents. Child Adolesc Psychiatry Ment Health 2023; 17: 116. https://doi.org/10.1186/s12888-023-05324-4

[14] Liang S-C, Sun C-K, Chang C-H, Cheng Y-S, Tzang R-F, Tzang R-F, *et al*. Efficacy of probiotics for attention-deficit/hyperactivity disorder symptoms: a systematic review and meta-analysis. BJPsych Open 2024; 10(2): e56. https://doi.org/10.1192/bjo.2023.645