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Gut Microbiota, Exercise, and Athletic Performance: Current Evidence and Clinical Implications

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Abstract (Structured)

Background. The gut microbiota dynamically regulates energy metabolism, mucosal immunity, and systemic homeostasis [1]. In active populations, exercise-microbiome interactions influence athletic performance, adaptation, and recovery [2, 5].

Aim. To critically synthesize empirical evidence on the gut-muscle and gut-brain-muscle axes, evaluate athletic microbial adaptations, address methodological limitations, and provide clinical guidance for sports nutrition.

Material and methods. A review of literature (2020–2026) was conducted across PubMed, Web of Science, and Scopus, encompassing RCTs, athletic cohort studies, and translational models [1-24].

Results. Exercise modulates microbial taxonomy and metabolic output in an intensity-dependent manner [14]. Training enriches SCFA-producing taxa (*Akkermansia muciniphila*, *Faecalibacterium prausnitzii*) and alters bile acid signaling [12, 23]. Metabolites like deoxycholic acid and butyrate stimulate AMPK-PGC1α and TGR5-cAMP-PKA pathways, enhancing endurance [23]. Exercise reinforces tight junctions (ZO-1, Occludin), reducing endotoxemia (LBP, sCD14) and systemic inflammation [9, 22]. Targeted interventions—pre-sleep casein with probiotics [15], dietary fiber [24], polyphenols [3, 18], and low-FODMAP diets [16]—effectively alleviate gastrointestinal symptoms, boost power, and optimize recovery.

Conclusions. The gut-muscle and gut-brain-muscle axes are pivotal for physical resilience. Combining microbiome profiling with targeted nutrition offers strong potential for precision sports medicine [1, 20].

Key words: gut microbiota; exercise physiology; gut-muscle axis; short-chain fatty acids; athletic performance; probiotics; sports nutrition.

1. Introduction

The human gastrointestinal tract harbors a complex and highly specialized ecosystem comprising trillions of microorganisms, whose collective metabolic capacity profoundly influences host physiology, immune function, and endocrine regulation [1]. Over the past decade, advancements in high-throughput metagenomic sequencing and metabolomics have redefined our understanding of physical activity, establishing that the gut microbiota acts not merely as a passive bystander, but as an active transducer of exercise-induced physiological adaptations [1, 13]. Physical exercise exerts a powerful non-pharmacological stimulus that alters intestinal transit time, splanchnic blood flow, mucosal immunity, and luminal metabolic availability, thereby shaping microbial community structure and function [1, 14].

In athletes and highly active populations, the physiological demands of training and competition create unique metabolic and environmental conditions within the gut [2, 5]. Endurance events, high-intensity interval training (HIIT), and resistance regimes demand substantial energy substrate flux, heightened thermoregulation, and rapid tissue repair. Concurrently, strenuous physical stress can induce transient splanchnic hypoperfusion, mucosal barrier disruption, and exercise-associated gastrointestinal symptoms (Ex-GIS) [5, 16]. Understanding how the gut microbiome modulates energy harvest, systemic inflammatory tone, and organ-level crosstalk is therefore paramount for optimizing performance and preserving long-term athletic health [1, 20].

The primary objective of this review is to provide a comprehensive, critical synthesis of current scientific evidence linking gut microbiota, exercise physiology, and athletic performance. Specifically, this paper: (1) details the biological mechanisms underpinning the gut-muscle and gut-brain-muscle axes; (2) critically evaluates empirical findings across diverse competitive athletic cohorts and extreme endurance conditions; (3) identifies key methodological limitations and evidence gaps in contemporary sports microbiome research; and (4) outlines pragmatic clinical strategies—including targeted probiotykotherapy, fiber supplementation, polyphenol intake, and low-FODMAP protocols—to guide sports nutrition practitioners.

2. Plausible Pathways and Biological Mechanisms

The bidirectional communication between skeletal muscle and the gut microbiota—termed the 'gut-muscle axis'—operates through a sophisticated network of microbial metabolites, immune mediators, and endocrine exerkines [1, 20]. Short-chain fatty acids (SCFAs), primarily acetate, propionate, and butyrate, serve as pivotal signaling molecules generated through microbial fermentation of non-digestible dietary carbohydrates [1, 14]. SCFAs cross the intestinal epithelium and enter systemic circulation, where they activate free fatty acid receptors (FFAR2/GPR43 and FFAR3/GPR41) on skeletal muscle cells. This binding stimulates adenosine monophosphate-activated protein kinase (AMPK) and peroxisome proliferator-activated receptor-gamma coactivator 1-alpha (PGC-1α), key master regulators of mitochondrial biogenesis, glucose uptake, and fatty acid oxidation [1, 20].

Expanding beyond skeletal muscle, recent translational paradigms highlight the integrated 'gut-brain-muscle axis', which governs neuromuscular endurance, central fatigue, and cognitive resilience [20]. Microbial metabolites influence central nervous system (CNS) function via vagal nerve stimulation and blood-brain barrier (BBB) permeability regulation [20]. For instance, exercise-induced microbial remodeling enriches species such as Limosilactobacillus reuteri and Akkermansia muciniphila, which alter circulating bile acid pools and elevate neuroprotective factors including brain-derived neurotrophic factor (BDNF) [8, 12, 20]. In animal models of physical stress and stroke, fecal microbiota transplantation (FMT) from exercised donors transferred anti-inflammatory and cognitive resilience benefits, preserving tight junction proteins (ZO-1, Claudin-5, Occludin) in both colonic mucosa and the BBB [8].

In addition to SCFAs, microbial transformation of primary bile acids into secondary bile acids represents a novel biochemical pathway modulating physical endurance [17, 23]. Recent mechanistic studies demonstrate that gypenosides and exercise inhibit intestinal farnesoid X receptor (FXR) signaling, driving the enrichment of secondary bile acids such as deoxycholic acid (DCA) [23]. Elevated DCA acts as a potent endogenous ligand for the Takeda G-protein-coupled receptor 5 (TGR5) on skeletal myoblasts, activating the cAMP-PKA signaling cascade [23]. This axis promotes myogenic differentiation, accelerates myoblast fusion, and induces a favorable metabolic shift toward slow-twitch, oxidative Type I muscle fibers, markedly extending time-to-exhaustion during aerobic exercise [17, 23].

A central protective mechanism of regular, moderate-to-vigorous exercise involves the attenuation of metabolic endotoxemia and systemic low-grade inflammation [9, 22]. Intense or prolonged physical exertion can compromise the intestinal epithelial barrier, allowing lipopolysaccharides (LPS)—a pro-inflammatory glycolipid component of Gram-negative bacterial outer membranes—to translocate into systemic circulation [9, 11]. Translocated LPS triggers systemic inflammatory cascades by binding to Toll-like receptor 4 (TLR4) on circulating monocytes and tissue macrophages, activating the nuclear factor kappa B (NF-κB) pathway and NLRP3 inflammasome [22]. Chronic exercise training counteracts this endotoxemic cascade by upregulating tight junction protein expression (ZO-1, Occludin), lowering plasma levels of LPS-binding protein (LBP) and soluble CD14 (sCD14), and suppressing pro-inflammatory cytokines such as interleukin-1β (IL-1β), interleukin-6 (IL-6), and C-reactive protein (CRP) [9, 22]. However, microbial composition remains a critical modifier; high relative abundance of Prevotella copri has been specifically correlated with elevated post-exercise pro-inflammatory oxylipin generation from arachidonic acid, accounting for significant inter-individual variance in post-exercise inflammatory recovery [11].

3. Evidence Gaps and Methodological Challenges

Despite compelling mechanistic insights, translating microbiome science into athletic populations presents substantial challenges [1, 4]. Cross-sectional and longitudinal evaluations across distinct athletic disciplines reveal marked microbial heterogeneity. In elite female WorldTour cyclists, shotgun sequencing demonstrated a distinct microbial signature characterized by an elevated Bacteroidota-to-Firmicutes ratio and lower alpha-diversity compared to non-athlete controls, driven by high-carbohydrate, energy-dense dietary patterns [2]. Conversely, studies among Iranian professional runners demonstrated discipline-specific taxonomic patterns, with Akkermansia muciniphila predominantly enriched in speed sprinters (40.95%) compared to endurance (27.02%) and middle-distance runners (23.53%) [10]. Furthermore, metagenomic profiling of college sprint athletes identified Segatella copri and Bifidobacterium adolescentis as signature taxa, strongly correlated with whole grain and dairy consumption [19].

Extreme endurance events represent unique real-world stress models for gut-microbiome dynamics. Investigation of endurance runners completing an 80 km ultra-marathon revealed acute post-race shifts, including significant decreases in Actinobacteriota phyla, Bifidobacteriaceae, and Clostridiaceae families, alongside increases in Oscillospiraceae and

Monoglobaceae [5]. Interestingly, while pre-race baseline bacterial profiles correlated with exercise-associated gastrointestinal symptoms (Ex-GIS), acute post-race taxonomic shifts did not directly predict symptom severity, underscoring the distinction between basal mucosal stability and acute stress responses [5]. Similarly, extreme multi-month running challenges (>30,000 km) demonstrate sustained increases in muscle damage markers (creatine kinase 3–15 fold elevation) alongside dynamic shifts in gut diversity, with Bifidobacterium enriching during active running phases and Akkermansia expanding during physiological recovery [21].

A major obstacle in sports microbiome research stems from methodological limitations and confounding variables [1, 4]. Longitudinal monitoring of elite athletes (e.g., Italian SuperLega volleyball players across a competitive season) using Compositional Data Analysis (CoDA) and ANOVA-Simultaneous Component Analysis (ASCA) revealed that individual athlete identity accounted for the vast majority of variance (over 50% at family and genus levels), overshadowing seasonal training phase effects [4]. Many existing human trials suffer from small cohort sizes, lack of rigorous dietary standardization, reliance on 16S rRNA amplicon sequencing rather than high-resolution shotgun metagenomics, and an inability to isolate exercise effects from specialized dietary habits (high-protein, low-fiber, or supplement-dense regimens) [1, 4].

4. Research Materials and Methods

4.1. Review Strategy and Database Screening. To ensure a rigorous and transparent synthesis, this review followed a structured methodological approach to literature identification, data extraction, and evidence appraisal. Literature searches were executed across PubMed/MEDLINE, Web of Science, and Scopus for articles published from January 2020 through March 2026. Primary search terms included combinations of: 'gut microbiota', 'gut microbiome', 'exercise', 'athletic performance', 'gut-muscle axis', 'short-chain fatty acids', 'endotoxemia', 'probiotics', and 'sports nutrition'. Inclusion criteria comprised original research articles (human RCTs, cohort studies, crossover trials), translational animal experiments, and key position papers published in English. Non-peer-reviewed commentaries and duplicate publications were excluded [1-24].

4.2 Data Synthesis and Analytical Framework. Data extracted from eligible studies included target population characteristics (athletic discipline, training volume, sex, age), intervention specifics (exercise intensity, duration, nutritional co-interventions), sequencing methodology (16S rRNA vs. shotgun metagenomics), microbial diversity metrics, functional metabolomic

profiles (SCFAs, bile acids), inflammatory biomarkers (hs-CRP, LBP, sCD14, cytokines), and performance outcomes (VO2max, anaerobic power, time-to-exhaustion, muscle strength) [1-24].

5. Clinical Implications and Practical Considerations

Accumulating empirical evidence supports the implementation of targeted microbial interventions to optimize athletic performance, accelerate recovery, and mitigate Ex-GIS [1, 15]. A notable double-blind, randomized controlled trial in competitive soccer players evaluated the impact of 4 weeks of pre-sleep casein intake (20 g) combined with an 8-strain multi-species probiotic capsule (4.5 × 10^11 CFU containing Lactiplantibacillus plantarum, Lacticaseibacillus casei, Lactobacillus acidophilus, Lactobacillus bulgaricus, Bifidobacterium infantis, B. longum, B. breve, and Streptococcus thermophilus) [15]. The combined PRO+CAS intervention produced superior gains in anaerobic sprint power (RAST average power, $p = 0.003$), isokinetic lower-body strength (AvRFD-180°/s ext, $p = 0.003$), and muscular endurance (Wall-squat test, $p = 0.001$) compared to casein or probiotics alone, demonstrating clear ergogenic synergy [15].

In broader active populations, a 12-week double-blind RCT investigating multi-species probiotic supplementation (containing L. fermentum LF16, L. rhamnosus LR06, L. plantarum LP01, and B. longum 04) demonstrated significant attenuation of metabolic endotoxemia [9]. Probiotic supplementation markedly reduced circulating LBP ($p < 0.001$), sCD14 ($p = 0.001$), and C-reactive protein ($p = 0.047$), alongside improvements in fasting blood glucose homeostasis [9]. These findings confirm that multi-species probiotic strains effectively fortify intestinal epithelial barrier integrity and dampen systemic inflammatory tone under conditions of physiological stress [9, 15].

Table 1. Summary of Targeted Clinical Interventions Modulating the Gut-Muscle Axis in Athletic and Active Cohorts.

Intervention Strategy	Target Population	Dosage & Protocol	Primary Biological / Microbial Outcome	Performance & Clinical Effect [Ref]
Pre-Sleep Casein + Probiotics	Competitive Soccer Players (n=44)	20 g Casein + 8-strain Probiotic (4.5×10^11 CFU) for 4 weeks	Enhanced nutrient absorption & gut microbial functionality	↑ Anaerobic power (p=0.003), ↑ Lower-body strength & wall-squat [15]
Multi-Species Probiotic	Active Adults / Metabolic Stress (n=80)	4-strain probiotic formulation daily for 12 weeks	↓ LBP (p<0.001), ↓ sCD14 (p=0.001), ↑ SCFA synthesis	Reduced metabolic endotoxemia & systemic CRP inflammation [9]
High-Dose Dietary Fiber	College Basketball Players (n=30)	6.84 g/day soluble fiber supplementation for 8 weeks	Microbial community stabilization & SCFA enrichment	↑ VO2max (+8.78 mL/kg/min), ↑ Anaerobic power (+27.16 W) [24]
Short-Term Low-FODMAP Diet	Endurance Runners (n=16)	48-hour low-FODMAP protocol (3.0 g/day) prior to exercise	Maintained fecal SCFA levels & reduced mucosal stress	Significant reduction in exercise-associated GI symptoms [16]

Notes: LBP = Lipopolysaccharide-Binding Protein; sCD14 = soluble CD14; RAST = Running-based Anaerobic Sprint Test; Ex-GIS = Exercise-Associated Gastrointestinal Symptoms; FODMAP = Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols.

Dietary strategies represent another potent pillar for microbiome modulation [3, 18, 24]. In college basketball players, an 8-week high-dose dietary fiber supplementation protocol (6.84 g/day) stabilized gut microbial community structure, significantly reduced body fat percentage (-1.87%), lowered serum cortisol, and enhanced maximal anaerobic power (+27.16 W) and

VO2max (+8.78 mL/kg/min) [24]. Furthermore, dietary polyphenols act as natural prebiotics, enriching Akkermansia muciniphila and Lactobacillus species while directly mitigating exercise-induced oxidative stress and mucosal inflammation [3, 18]. For endurance athletes suffering from acute Ex-GIS during competition, a 48-hour short-term low-FODMAP diet (3.0 g/day FODMAPs) within a high-carbohydrate loading scheme effectively reduced gastrointestinal distress and mucosal permeability markers during prolonged running, providing a practical acute nutritional protocol [16]. Long-chain omega-3 fatty acids also support barrier function and metabolic recovery [6].

To optimize clinical outcomes, sports dietitians and medical staff should implement a structured gastrointestinal monitoring framework [1, 16]. Athletes presenting with recurrent Ex-GIS, unexplained fatigue, or delayed recovery should undergo routine screening for baseline dietary quality, anti-inflammatory nutrient intake, and systemic inflammatory markers (hs-CRP, LBP) [1, 11]. Multi-species probiotic supplementation should be targeted to intense training blocks, travel, or post-antibiotic recovery periods, while routine diet should emphasize diverse plant fibers and polyphenols to maintain endogenous SCFA production [1, 18, 24].

6. Conclusions and Future Directions

The integration of exercise physiology and gut microbiome research has established that intestinal microorganisms play a central regulatory role in host energetic adaptions, mucosal barrier defense, and systemic inflammatory control [1, 20]. Physical exercise enriches beneficial SCFA-producing taxa, alters bile acid signaling via DCA-TGR5 pathways, and attenuates NLRP3-mediated metabolic endotoxemia [14, 22, 23]. Targeted clinical interventions—combining multi-species probiotics with pre-sleep casein [15], dietary fiber [24], polyphenols [18], and low-FODMAP protocols [16]—offer validated, non-pharmacological avenues to enhance anaerobic power, alleviate Ex-GIS, and accelerate recovery.

Despite significant progress, critical research gaps remain [1, 4]. Future research must prioritize well-powered, multi-center randomized controlled trials incorporating strict dietary controls and long-term (>12 weeks) intervention periods [1, 4]. Transitioning from 16S rRNA gene profiling to high-resolution shotgun metagenomics and integrated multi-omics pipelines (metabolomics, transcriptomics, lipidomics) is essential to establish true strain-level causality and unravel host-microbe-diet interactions [1, 4]. Ultimately, developing phenotype-matched,

personalized exercise and nutritional prescriptions based on baseline microbiome profiling represents the next frontier in precision sports medicine.

Disclosure

The authors declare that no financial or personal relationships inappropriate influenced the writing of this manuscript.

Supplementary Materials

Not applicable.

Author Contributions

Conceptualization: Zuzanna Skoczko- first author of the publication ; Literature Search & Screening: Zuzanna Skoczko, Julia Kobylińska; Data Extraction & Synthesis: Zuzanna Skoczko, Julia Kobylińska, Katarzyna Krzysiak; Writing – Original Draft Preparation: Zuzanna Skoczko; Writing – Review & Editing: Katarzyna Krzysiak. All authors read and approved the final manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

Declaration of the Use of Generative AI and AI-Assisted Technologies in the Writing

During the preparation of this work, the authors used Grammarly for the purpose of improving language and readability. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the substantive content of the publication.

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