



QUALITY IN SPORT

eISSN 2450-3118 · Open Access · Peer-reviewed

apcz.umk.pl/QS Nicolaus Copernicus University in Toruń



OWCZARENKO, Konstancja and SZADA-BORZYSZKOWSKI, Kacper. Gut–Immune–Muscle Axis as a Framework Linking Exercise Stress, Intestinal Dysfunction, and Overtraining Syndrome in Athletes: A Narrative Review. *Quality in Sport*. 2026;68:74432. <https://doi.org/10.12775/QS.2026.68.74432>

ARTICLE TIMELINE

Received: 18.07.2026. Revised: 02.08.2026. Accepted: 02.08.2026. Published: 13.08.2026.

The journal has been awarded 20 points in the parametric evaluation by the Polish Ministry of Higher Education and Science (Annex to the announcement of 05.01.2024, No. 32553). Unique Journal Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).

Punkty Ministerialne z 2019 – aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych). © The Authors 2026.

OPEN ACCESS · CC BY-NC-SA 4.0 This article is published with open access under the License Open Journal Systems of Nicolaus Copernicus University in Toruń, Poland, and is distributed under the terms of the Creative Commons Attribution Non-commercial Share Alike License (<http://creativecommons.org/licenses/by-nc-sa/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the work is properly cited. The authors declare no conflict of interest regarding the publication of this paper.

Gut–Immune–Muscle Axis as a Framework Linking Exercise Stress, Intestinal Dysfunction, and Overtraining Syndrome in Athletes: A Narrative Review

Konstancja Owczarenko

ORCID: <https://orcid.org/0009-0009-2232-7753>

Lower Silesian Centre of Oncology, Pulmonology and Hematology, plac Ludwika Hirszfelda
12, 53-413 Wrocław, Poland

e-mail: konstancja.owczarenko@gmail.com

Kacper Szada-Borzyszkowski

ORCID: <https://orcid.org/0009-0006-4967-215X>

Lower Silesian Center of Oncology, Pulmonology and Hematology, plac Ludwika Hirszfelda
12, 53-413 Wrocław, Poland

e-mail: kacperrrada@gmail.com

Corresponding author: Konstancja Owczarenko, konstancja.owczarenko@gmail.com

Abstract

Elite athletic performance requires high training loads, but insufficient recovery in the context of accumulated stress may contribute to the development of overtraining syndrome (OTS). Current models associate OTS with neuroendocrine, immune, and inflammatory disturbances; however, these frameworks do not fully explain why individual athletes demonstrate different susceptibilities to impaired recovery.

The gastrointestinal tract represents a dynamic interface connecting physical stress, immune responses, and metabolic changes with skeletal muscle adaptation. At the centre of this interaction is the gut–immune–muscle axis, a framework that describes the continuous dialogue between intestinal microbes, epithelial barrier integrity, and skeletal muscle function.

Microbe-derived metabolites may act as important signalling molecules that contribute to metabolic regulation during exercise adaptation. However, when high training demands are considered, this finely balanced system may become disrupted. Reduced intestinal barrier integrity can then contribute to systemic inflammatory responses, providing a potential link between gastrointestinal stress, immune activation, and impaired recovery.

Increased intestinal permeability may facilitate the translocation of microbial-derived components, thereby activating systemic inflammatory signalling. During strenuous exercise, physiological stress on the gastrointestinal tract may further compromise epithelial barrier integrity, potentially amplifying these immune responses, thereby interfering with skeletal muscle remodelling and recovery processes.

In this review, the gut–immune–muscle axis is proposed as a framework connecting intestinal dysfunction, immune alterations, and exercise maladaptation. Gut-related mechanisms are unlikely to represent a direct cause of OTS; rather, they may function as important biological modifiers that influence an athlete's capacity to tolerate and recover from excessive training stress.

Keywords: Gut-muscle axis; Gut microbiota; Overtraining syndrome; Sports performance

Introduction

Sustaining elite athletic performance hinges on a delicate equilibrium between physical exertion and rest. While structured exercise drives positive adaptations—such as enhanced muscle

function, metabolic efficiency, and immune regulation—an unresolved imbalance triggers a downward spiral. When training outpaces recovery, athletes risk developing overtraining syndrome (OTS). This state is marked by chronic performance drops, exhaustion, mood shifts, and sleep disruptions that persist even after shedding the training workload [1–3].

Diagnosing overtraining syndrome (OTS) remains a major challenge in sports medicine, as no single validated biomarker is currently available. Existing models emphasize the combined contribution of excessive training load, insufficient recovery, neuroendocrine alterations, and immune dysregulation. However, these frameworks do not fully account for why individual athletes display markedly different responses to comparable workloads, with some developing prolonged maladaptation while others successfully adapt and recover [1, 4, 5].

Early perspectives on OTS pathogenesis focused primarily on disruptions within hormonal and immune regulatory systems. These concepts contributed to the development of the cytokine hypothesis, which proposed that repeated exposure to excessive training stress may promote persistent inflammatory signalling and impair recovery processes. Although research has demonstrated associations between overtraining states and altered immune responses, the complexity of OTS suggests that endocrine and immune mechanisms represent only one part of a broader physiological network. This has encouraged exploration of additional regulatory pathways that may influence individual susceptibility to maladaptation [6–8].

The gut does far more than just process food; it is a major regulatory organ linking physical stress to host metabolism and immunity. This connection relies heavily on the intestinal microbiota. Through specialized metabolites, these microbes communicate directly with host tissues and may influence processes involved in exercise adaptation. Yet, this ecosystem is highly vulnerable. Chronic training loads, coupled with poor nutrition and failed recovery, may disrupt this balance, contributing to microbial imbalance and impaired intestinal function [9–11].

The gut–muscle axis facilitates a continuous, bidirectional dialogue between intestinal microbes and skeletal tissue. Bacterial metabolites—notably short-chain fatty acids and bile acid derivatives—can influence mitochondrial function, energy metabolism, and processes involved in muscle remodelling. Moreover, the dynamic cross-talk between microbial signals and muscle-derived myokines highlights that athletic adaptation is a systemic process involving communication across multiple organs [12–14].

Systemic inflammatory responses during strenuous exercise may be influenced by intestinal barrier disruption. Heavy and prolonged training can reduce gastrointestinal blood flow, contributing to epithelial stress and increased intestinal permeability [15, 16]. When barrier integrity is compromised, microbial-derived components such as lipopolysaccharide (LPS) may translocate into circulation, contributing to innate immune activation and inflammatory signalling [17].

Acute inflammation is an essential component of muscle repair and exercise adaptation. However, when recovery is insufficient, prolonged immune activation may contribute to chronic low-grade inflammation. The gut-immune-muscle axis provides an additional perspective on this interaction by highlighting how intestinal barrier alterations and microbial-derived signals may influence systemic immune regulation. Exercise-induced disruption of intestinal barrier function may represent one pathway linking gastrointestinal stress with inflammatory responses during periods of high physiological demand [18]. Persistent alterations in immune regulation may, in turn, contribute to impaired recovery and maladaptation associated with excessive training stress [19].

The gut-immune-muscle axis introduced here serves as a holistic model tying together microbial shifts, barrier disruption, and immune responses with their downstream effects on skeletal tissue during extreme training. Crucially, we do not argue that intestinal failure alone causes OTS. Instead, our framework positions the gastrointestinal tract as a key biological modifier that may help explain why some athletes develop overtraining-related maladaptation, while others continue to adapt and recover despite similar training demands.

This review follows a mechanistic progression from microbial regulation to exercise maladaptation. First, the role of the gut microbiota as a dynamic regulator of metabolic and immune processes during exercise adaptation is discussed. Subsequently, exercise-induced alterations in intestinal barrier function are examined as a potential interface between gastrointestinal stress and systemic responses. The following sections explore how microbial-derived signals and immune activation may influence skeletal muscle adaptation through the gut-immune-muscle axis. Finally, the preceding biological mechanisms are integrated within the conceptual framework of the gut-immune-muscle axis to examine their potential contribution to exercise maladaptation and overtraining syndrome.

The Athletic Gut Microbiota: Composition, Diversity, and Functional Adaptation

The gut microbiota is a living ecosystem that actively tunes host metabolism and immunity. For athletes, this microbial community is shaped by several shifting forces: training volume, exercise intensity, diet, and recovery status. This means the athletic microbiome works both ways. It is not just a consequence of physical training. Instead, it operates as a major biological engine driving adaptation to chronic exercise stress. [9, 20].

Comparative studies show that regular exercise yields greater microbial diversity and distinct functional shifts compared to sedentary baselines. This heightened diversity acts as a buffer, ensuring ecosystem stability and functional resilience while driving the synthesis of compounds vital for host adaptation. Evidence from elite cohorts confirms these deep-seated differences in taxonomy and metabolic pathways, pointing to a specialized, exercise-associated microbiome with functional characteristics that may support adaptation to high energy demands and repeated physical stress [10, 21].

Diet acts as a primary conductor of the exercise–microbiota interaction. The availability of dietary fibre, carbohydrates, and protein, alongside overall energy balance, directly dictates microbial metabolism and the resulting metabolite pool. Consequently, performance-focused nutritional strategies shape bacterial function in elite cohorts. On the flip side, chronic energy deficiencies, restrictive eating habits, or neglected recovery nutrition dismantle this microbial equilibrium, eroding intestinal resilience [9, 11].

Microbial production of bioactive metabolites represents a foundational mechanism governing exercise adaptation. Chief among these are short-chain fatty acids (SCFAs)—specifically acetate, propionate, and butyrate—synthesized via the fermentation of nondigestible carbohydrates. Rather than merely supporting the gut, SCFAs actively preserve barrier integrity, modulate immune signalling, and fuel host energy pathways. In skeletal tissue, these molecules cross into circulation to regulate mitochondrial biogenesis, substrate utilization, insulin sensitivity, and localized inflammation, effectively forging a molecular bridge between the microbiome and muscle plasticity [12, 14].

Beyond short-chain fatty acids, the microbiota-mediated biotransformation of bile acids represents another crucial signalling axis. Gut microorganisms biochemically convert primary bile acids into secondary metabolites, which serve as potent ligands for host receptors. Through these precise interactions, modified bile acids directly modulate systemic energy metabolism,

mitochondrial biogenesis, and the signalling cascades that govern skeletal muscle responses to training stress [22].

Systematic communication within this network relies on deeply interconnected immune, metabolic, and endocrine pathways. During physical exertion, contracting skeletal tissue releases myokines that orchestrate metabolic shifts, resolve inflammation, and drive tissue remodelling. Concurrently, circulating microbial signals fine-tune systemic immunity and host energy metabolism. This intense, two-way dialogue reinforces the paradigm that athletic adaptation is a systemic property born from integrated multi-organ cross-talk, rather than an isolated tissue response [13, 23].

The paradigm in microbiome research is rapidly moving past individual bacterial taxa to decode the actual functional machinery of microbial populations. Meta-omic evaluations of elite cohorts highlight distinct metabolic networks associated with physical stress, most notably the metabolic clearance of systemic lactate by targeted gut microorganisms. These functional signatures may provide greater insight than static taxonomic data, offering a clearer understanding of the biological cross-talk governing exercise adaptation and post-effort recovery [24].

Crucially, the interaction between physical activity and the gut microbiota is strictly dose-dependent. While moderate, well-regulated training fortifies microbial stability, functional capacity, and immune balance, extreme conditioning outpaces this adaptive threshold. When heavy training volumes clash with poor recovery, the system shifts toward microbial dysbiosis, functional degradation, and a disruption of intestinal homeostasis [20, 21].

Viewing the gut–immune–muscle axis as a cohesive system means that microbial shifts cannot be treated as an isolated trigger for performance drops or overtraining syndrome. Rather, these bacterial changes are just one facet of a larger physiological network that encompasses gut barrier efficiency, immune surveillance, metabolic pathways, and muscular remodelling. Consequently, the shift from beneficial microbial adaptation toward dysbiosis may represent a critical transition point, potentially affecting an athlete's recovery capacity when exposed to unrelenting training stress.

In summary, the gastrointestinal microbiome functions as a plastic, highly integrated element of training adaptation. While maintaining microbial homeostasis underpins long-term biological resilience and recovery, structural shifts toward dysbiosis may compromise these

protective mechanisms. These alterations may increase susceptibility to chronic physiological stress and contribute to the development of overtraining-related symptoms.

Exercise-Induced Intestinal Barrier Dysfunction: From Physiological Adaptation to Maladaptive Responses

The intestinal barrier forms the interface between the gut lumen and the host, where it regulates interactions between the gut microbiota, immune system, and metabolic processes. In athletes, maintaining intestinal barrier integrity is especially important because repeated exposure to intensive training, prolonged endurance exercise, environmental stress, and nutritional challenges may disturb gastrointestinal homeostasis. Although regular moderate exercise is generally associated with beneficial adaptations, prolonged or excessive exercise may impair barrier function, increase intestinal permeability, and contribute to systemic inflammatory responses [18, 25].

Exercise-induced gastrointestinal dysfunction is common among endurance athletes, particularly during prolonged and high-intensity exercise. Frequently reported symptoms include nausea, abdominal discomfort, diarrhoea, and impaired nutrient absorption. These manifestations reflect a combination of physiological changes, including reduced gastrointestinal blood flow, epithelial injury, increased intestinal permeability, and activation of immune pathways [18, 26].

Redistribution of blood flow is considered a key mechanism underlying exercise-induced intestinal dysfunction. During strenuous exercise, increased oxygen demand by active skeletal muscles and thermoregulatory processes reduce splanchnic perfusion, resulting in intestinal hypoperfusion. Exercise-induced splanchnic hypoperfusion has been associated with measurable small intestinal injury, with the extent of injury correlating with transient increases in intestinal permeability, indicating temporary impairment of gut barrier function [16].

Exercise intensity and duration are key factors influencing intestinal barrier function. While moderate exercise may promote beneficial adaptations within the gastrointestinal tract, prolonged high-intensity exercise can overwhelm these adaptive responses and impair epithelial integrity. Studies in endurance athletes have shown that greater exercise intensity is associated with more pronounced changes in intestinal permeability, suggesting a relationship between exercise load and the development of gastrointestinal dysfunction [15].

Intestinal barrier integrity depends on the coordinated function of epithelial cells and tight junction proteins, which regulate selective transport across the intestinal wall. Excessive exercise stress may impair intestinal barrier function, increasing permeability and facilitating the translocation of luminal molecules and microbial components into the circulation. This phenomenon, commonly referred to as increased intestinal permeability or “leaky gut,” represents a potential link between local intestinal disturbances and systemic immune activation [18, 25].

Environmental conditions may further influence the susceptibility of athletes to intestinal dysfunction. Heat stress, dehydration, and prolonged exercise performed under challenging conditions increase cardiovascular strain and may exacerbate reductions in gastrointestinal blood flow. Recent studies suggest that exercising in hot environments can affect markers of intestinal integrity, indicating that environmental stress may contribute to greater vulnerability of the gut barrier in athletes [27, 28].

Increased intestinal permeability may facilitate the passage of microbial-derived molecules, including lipopolysaccharide (LPS), beyond the intestinal barrier, potentially activating innate immune pathways and inflammatory responses [17]. Studies in endurance athletes have demonstrated associations between prolonged exercise, intestinal stress, transient endotoxemia, and increased inflammatory cytokine responses. These findings suggest that excessive physiological stress during endurance exercise may contribute to systemic inflammatory activation [18, 29].

Intestinal barrier dysfunction should not necessarily be interpreted as a pathological response in all circumstances. A transient increase in intestinal permeability following strenuous exercise may reflect a physiological adaptation involved in immune monitoring and communication between the gut and other tissues. However, repeated episodes of barrier disruption combined with inadequate recovery may contribute to long-term disturbances in intestinal homeostasis and a greater inflammatory load [18, 25].

The interaction between intestinal barrier function and the gut microbiota is reciprocal. Microbial-derived metabolites, particularly short-chain fatty acids such as butyrate, contribute to the maintenance of epithelial integrity and modulation of immune responses. In contrast, disturbances in the gut microbiota caused by excessive training load, inadequate nutritional intake, or insufficient recovery may impair barrier function, potentially reinforcing the relationship between dysbiosis and intestinal dysfunction [11, 12].

Within the gut–immune–muscle axis framework, intestinal barrier dysfunction may represent a potential link between excessive exercise stress and systemic physiological disturbances. Increased intestinal permeability may facilitate microbial translocation and immune activation, contributing to inflammatory responses that could influence skeletal muscle metabolism, remodelling processes, and recovery capacity [14, 30].

Therefore, intestinal integrity may serve as an important marker reflecting the balance between physiological adaptation and excessive exercise stress. Although current evidence does not support the view that intestinal barrier dysfunction alone is sufficient to cause overtraining syndrome, alterations in barrier function may represent one contributing factor within a broader network involving the gut microbiota, immune responses, metabolism, and skeletal muscle adaptation.

Gut–Immune–Muscle Axis: Microbial Translocation, Immune Activation, and Skeletal Muscle Adaptation

The intestinal barrier serves as a critical interface between the gut microbiota and the host immune system, forming an essential component of the gut–immune–muscle axis. Under physiological conditions, this barrier enables controlled communication between microbial communities and immune pathways, supporting metabolic homeostasis and tissue adaptation. However, excessive exercise stress may disrupt this balance by increasing intestinal permeability and enhancing the passage of microbial-derived molecules beyond the intestinal environment. These processes may contribute to systemic inflammatory signalling and provide a mechanistic link between intestinal dysfunction and altered skeletal muscle responses following strenuous exercise [17, 18].

A potential consequence of impaired intestinal barrier function is microbial translocation, during which bacterial components may interact with host immune pathways. Lipopolysaccharide (LPS), derived from Gram-negative bacteria, can activate innate immune signalling through pattern recognition receptors, including Toll-like receptor 4 (TLR4). Activation of these pathways promotes inflammatory mediator production and represents one mechanism through which intestinal disturbances may influence systemic immune responses [17, 31, 32].

Studies investigating strenuous endurance exercise have demonstrated transient endotoxemia, increased inflammatory cytokine responses, and activation of acute-phase pathways following prolonged physiological stress. Early research showed that exhaustive exercise may increase

circulating endotoxin concentrations, while subsequent studies reported associations between gastrointestinal symptoms, endotoxemia, and systemic inflammatory activation in endurance athletes [29, 33, 34].

The extent of microbial translocation is influenced by multiple interacting factors, including exercise intensity and duration, environmental conditions, hydration status, nutritional availability, and individual susceptibility. Repeated exposure to high training loads may therefore promote recurrent episodes of intestinal stress, potentially contributing to a greater inflammatory burden when recovery is inadequate [18, 27].

Innate immune activation following exercise is not inherently harmful. Acute inflammatory signalling represents an important component of skeletal muscle repair, remodelling, and adaptation. Exercise-induced increases in inflammatory mediators such as interleukin-6 (IL-6) are part of the normal physiological response to muscle stress and may contribute to tissue recovery and adaptation processes [35, 36].

However, persistent activation of inflammatory pathways may contribute to maladaptation. Repeated exposure to excessive physiological stress can shift immune responses from adaptive regulation toward chronic low-grade activation. Such alterations may negatively influence recovery capacity, energy metabolism, and exercise tolerance, particularly when high training loads are combined with insufficient recovery [1, 6, 19].

Therefore, intestinal dysfunction may represent one of the factors influencing skeletal muscle physiology during periods of excessive exercise stress. Systemic inflammatory mediators may affect muscle protein metabolism, mitochondrial function, oxidative balance, and tissue remodelling processes. Consequently, alterations in intestinal function may contribute to impaired skeletal muscle adaptation when physiological stress exceeds recovery capacity [14, 30].

The relationship between the gut and skeletal muscle is considered bidirectional. Exercise-induced myokines contribute to immune and metabolic regulation, whereas microbial-derived signals may influence inflammatory pathways, energy metabolism, and tissue function. Disruption of this communication network may impair the ability of skeletal muscle to adapt effectively to repeated exercise stimuli [13, 23].

From the perspective of overtraining syndrome, gut-related inflammatory processes may represent one factor contributing to differences in individual responses to similar external

training loads. Variations in microbiota composition, intestinal resilience, nutritional status, and immune regulation may influence the balance between successful adaptation and maladaptive responses to repeated exercise stress. Importantly, current evidence does not support the view that microbial translocation or intestinal inflammation alone is sufficient to cause OTS. Instead, these processes should be considered as potential components of a broader physiological network involving training stress, recovery capacity, neuroendocrine regulation, immune responses, and skeletal muscle adaptation. Within this framework, the gut–immune–muscle axis may represent an additional pathway contributing to impaired recovery and increased susceptibility to overtraining-related symptoms [1, 5].

In summary, gut-derived inflammatory signalling may represent an important mechanistic link between exercise-induced intestinal dysfunction and systemic physiological responses. The balance between transient adaptive inflammation and prolonged immune activation may influence whether exercise promotes beneficial adaptation or contributes to maladaptive responses associated with overtraining syndrome.

The Gut–Immune–Muscle Axis in Overtraining Syndrome: From Biological Mechanisms to Maladaptation

Overtraining syndrome (OTS) represents a complex condition associated with persistent fatigue, impaired performance capacity, and prolonged disturbances in recovery despite adequate rest. Although excessive training stress is considered an important factor contributing to OTS development, current evidence indicates that no single mechanism or biomarker is sufficient to explain its occurrence. Instead, OTS is likely the result of interactions between multiple physiological systems, including neuroendocrine regulation, immune responses, metabolic processes, and skeletal muscle adaptation [1, 2, 5].

Within this multifactorial framework, the gut–immune–muscle axis may represent an additional pathway involved in the transition from successful adaptation toward maladaptation. Exercise-induced alterations in intestinal barrier function, microbial activity, and immune regulation may influence systemic responses to repeated physiological stress. However, these processes should be considered as potential modifying factors rather than independent causes of OTS [17, 18].

Athletes exposed to high training loads may experience repeated disturbances in intestinal homeostasis, particularly when intensive exercise is combined with insufficient recovery, nutritional limitations, or environmental stress. Although transient changes in intestinal permeability and immune activity may form part of normal exercise adaptation, repeated

disruption of these processes may contribute to an imbalance between physiological stress and recovery capacity. Such alterations may increase susceptibility to maladaptive responses when excessive training stress exceeds recovery capacity [1, 37].

The gut microbiota may further influence individual responses to exercise stress through regulation of epithelial integrity, immune homeostasis, and production of microbial metabolites. Short-chain fatty acids and bile acid derivatives have been proposed as important mediators of communication between the gut and peripheral tissues, including skeletal muscle. Changes in microbial composition or function associated with training load, dietary factors, or inadequate recovery may therefore modify metabolic and inflammatory responses relevant to exercise adaptation [12, 14, 22].

An important implication of the gut–immune–muscle axis model is its potential to explain why athletes exposed to similar external training loads may experience different outcomes. Individual differences in microbiota composition, intestinal resilience, nutritional status, immune regulation, and recovery strategies may influence whether physiological stress results in successful adaptation or contributes to maladaptation [9, 11].

At the level of skeletal muscle, prolonged inflammatory activation and altered metabolic signalling may affect processes involved in recovery, remodelling, and adaptation. However, the available evidence does not currently demonstrate a direct causal relationship between gut dysfunction and OTS development. Most studies have investigated intestinal responses, inflammation, or microbiome alterations separately, and longitudinal evidence directly connecting these mechanisms with clinically defined OTS remains limited [5, 38].

Therefore, the gut–immune–muscle axis should be viewed as a complementary model that expands current understanding of overtraining-related maladaptation. Rather than representing a single cause of OTS, gut-derived mechanisms may act as part of a broader biological network in which training stress, recovery capacity, immune regulation, nutrition, and skeletal muscle responses interact to determine individual adaptation outcomes.

Future research should focus on longitudinal studies that integrate microbiome analysis, intestinal permeability markers, inflammatory profiles, metabolic measurements, and performance monitoring throughout training cycles. Such studies may help identify whether gut-related indicators can contribute to earlier recognition of impaired recovery and support more individualized strategies for athlete management.

In conclusion, the gut–immune–muscle axis provides a promising perspective for understanding the complexity of OTS. By integrating gastrointestinal, immune, metabolic, and muscular responses, this model may help explain the transition from effective adaptation to maladaptation while highlighting the need for further research before gut-related mechanisms can be considered for routine monitoring of athlete health and performance.

Conclusions and Limitations

The gut–immune–muscle axis provides an emerging integrative framework for understanding the complex biological mechanisms involved in exercise adaptation, impaired recovery, and overtraining syndrome (OTS). Although traditional models of OTS emphasize excessive training stress, neuroendocrine disturbances, immune dysfunction, and inflammatory imbalance, these mechanisms do not fully explain individual variability in athletes' responses to similar training demands [1, 2].

Current evidence suggests that the gastrointestinal tract and gut microbiota may represent important regulatory components linking exercise stress with systemic physiological responses. Exercise-induced alterations in intestinal barrier function may facilitate microbial translocation and activate innate immune pathways, contributing to inflammatory signalling and impaired recovery processes [17, 18].

Microbiota-derived metabolites, including short-chain fatty acids and bile acid derivatives, may influence skeletal muscle metabolism, mitochondrial function, immune regulation, and tissue adaptation. Therefore, microbial function and intestinal integrity may represent potential modifiers of the balance between beneficial adaptation and maladaptive responses during periods of excessive physiological stress [12, 14, 22].

The proposed gut–immune–muscle axis model does not suggest that microbiota disruption or intestinal dysfunction independently causes OTS. Instead, it identifies gut-related mechanisms as components of a broader biological network involving training load, recovery capacity, nutrition, immune regulation, and skeletal muscle adaptation. This perspective may help explain differences in individual susceptibility to overtraining-related maladaptation.

Future research should prioritize longitudinal studies that integrate microbiome analysis, intestinal permeability markers, inflammatory profiles, and performance monitoring. Such approaches may contribute to the identification of early indicators of impaired recovery and support individualized strategies for maintaining athlete health and performance.

Several limitations should be considered when interpreting the proposed model. First, direct evidence linking gut microbiota alterations and intestinal barrier dysfunction specifically to overtraining syndrome remains limited. Most available studies investigate exercise-induced gastrointestinal responses, inflammation, or microbiome changes separately rather than within a unified longitudinal framework.

Second, the human gut microbiome is highly variable and influenced by multiple factors, including dietary habits, genetic background, training history, environmental exposure, medication use, and lifestyle factors. Therefore, distinguishing exercise-specific effects from broader determinants of microbial variation remains challenging [9, 11].

Third, current evidence is largely based on observational studies, acute exercise interventions, or mechanistic research models. Although these studies provide biological plausibility, causal relationships between gut dysfunction, immune activation, and OTS development remain to be established.

Finally, microbiome-based biomarkers and potential interventions require further validation before routine application in athlete monitoring. Future investigations should focus on standardized methodologies, repeated measurements over training cycles, and integration of microbial, immune, metabolic, and performance-related outcomes.

Despite these limitations, the gut–immune–muscle axis represents a valuable framework for expanding current understanding of overtraining-related maladaptation. By integrating gastrointestinal, immune, and muscular responses, this model may help identify new research priorities focused on recovery monitoring, prevention strategies, and individualized approaches to athlete management.

Disclosure

Author's contribution

Conceptualization, K.S.-B. and K.O.; methodology, K.S.-B. and K.O.; software, K.S.-B. and K.O.; check, K.S.-B. and K.O.; formal analysis, K.S.-B.; investigation, K.S.-B.; resources, K.O.; data curation, K.S.-B.; writing - rough preparation, K.S.-B and K.O.; writing - review and editing, K.S.-B and K.O.; visualization, K.S.-B and K.O.; supervision, K.O.; project administration, K.O.

All authors have read and agreed with the published version of the manuscript

Funding statement

No funding was received for this study by the authors

Institutional Review and Board statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Conflict of Interest Statement

Authors declare no conflict of interest.

References

1. Meeusen, R., Duclos, M., Foster, C., Fry, A., Gleeson, M., Nieman, D., Raglin, J., Rietjens, G., Steinacker, J., Urhausen, A.: Prevention, Diagnosis, and Treatment of the Overtraining Syndrome. *Med. Sci. Sports Exerc.* 45, 186–205 (2013). <https://doi.org/10.1249/MSS.0b013e318279a10a>
2. Kreher, J.: Diagnosis and prevention of overtraining syndrome: an opinion on education strategies. *Open Access J. Sports Med.* Volume 7, 115–122 (2016). <https://doi.org/10.2147/OAJSM.S91657>
3. Budgett, R.: Fatigue and underperformance in athletes: the overtraining syndrome. *Br. J. Sports Med.* 32, 107–110 (1998). <https://doi.org/10.1136/bjism.32.2.107>
4. Kellmann, M., Bertollo, M., Bosquet, L., Brink, M., Coutts, A.J., Duffield, R., Erlacher, D., Halson, S.L., Hecksteden, A., Heidari, J., Kallus, K.W., Meeusen, R., Mujika, I., Robazza, C., Skorski, S., Venter, R., Beckmann, J.: Recovery and Performance in Sport: Consensus Statement. *Int. J. Sports Physiol. Perform.* 13, 240–245 (2018). <https://doi.org/10.1123/ijsp.2017-0759>

5. Weakley, J., Halson, S.L., Mujika, I.: Overtraining Syndrome Symptoms and Diagnosis in Athletes: Where Is the Research? A Systematic Review. *Int. J. Sports Physiol. Perform.* 17, 675–681 (2022). <https://doi.org/10.1123/ijsp.2021-0448>
6. SMITH, L.L.: Cytokine hypothesis of overtraining: a physiological adaptation to excessive stress? *Med. Sci. Sports Exerc.* 32, 317 (2000). <https://doi.org/10.1097/00005768-200002000-00011>
7. Gleeson, M.: Immune function in sport and exercise. *J. Appl. Physiol.* 103, 693–699 (2007). <https://doi.org/10.1152/japplphysiol.00008.2007>
8. Cadegiani, F.A., Kater, C.E.: Hormonal aspects of overtraining syndrome: a systematic review. *BMC Sports Sci. Med. Rehabil.* 9, 14 (2017). <https://doi.org/10.1186/s13102-017-0079-8>
9. Mailing, L.J., Allen, J.M., Buford, T.W., Fields, C.J., Woods, J.A.: Exercise and the Gut Microbiome: A Review of the Evidence, Potential Mechanisms, and Implications for Human Health. *Exerc. Sport Sci. Rev.* 47, 75–85 (2019). <https://doi.org/10.1249/JES.0000000000000183>
10. Barton, W., Penney, N.C., Cronin, O., Garcia-Perez, I., Molloy, M.G., Holmes, E., Shanahan, F., Cotter, P.D., O’Sullivan, O.: The microbiome of professional athletes differs from that of more sedentary subjects in composition and particularly at the functional metabolic level. *Gut.* 67, 625–633 (2018). <https://doi.org/10.1136/gutjnl-2016-313627>
11. Hughes, R.L., Holscher, H.D.: Fueling Gut Microbes: A Review of the Interaction between Diet, Exercise, and the Gut Microbiota in Athletes. *Advances in Nutrition.* 12, 2190–2215 (2021). <https://doi.org/10.1093/advances/nmab077>
12. Frampton, J., Murphy, K.G., Frost, G., Chambers, E.S.: Short-chain fatty acids as potential regulators of skeletal muscle metabolism and function. *Nat. Metab.* 2, 840–848 (2020). <https://doi.org/10.1038/s42255-020-0188-7>
13. Przewłocka, K., Folwarski, M., Kaźmierczak-Siedlecka, K., Skonieczna-Żydecka, K., Kaczor, J.J.: Gut-Muscle Axis Exists and May Affect Skeletal Muscle Adaptation to Training. *Nutrients.* 12, 1451 (2020). <https://doi.org/10.3390/nu12051451>

14. Gizard, F., Fernandez, A., De Vadder, F.: Interactions between gut microbiota and skeletal muscle. *Nutr. Metab. Insights.* 13, (2020). <https://doi.org/10.1177/1178638820980490>
15. Pals, K.L., Chang, R.-T., Ryan, A.J., Gisolfi, C. V.: Effect of running intensity on intestinal permeability. *J. Appl. Physiol.* 82, 571–576 (1997). <https://doi.org/10.1152/jappl.1997.82.2.571>
16. van Wijck, K., Lenaerts, K., van Loon, L.J.C., Peters, W.H.M., Buurman, W.A., Dejong, C.H.C.: Exercise-Induced Splanchnic Hypoperfusion Results in Gut Dysfunction in Healthy Men. *PLoS One.* 6, e22366 (2011). <https://doi.org/10.1371/journal.pone.0022366>
17. Thaïss, C.A., Zmora, N., Levy, M., Elinav, E.: The microbiome and innate immunity. *Nature.* 535, 65–74 (2016). <https://doi.org/10.1038/nature18847>
18. Costa, R.J.S., Snipe, R.M.J., Kitic, C.M., Gibson, P.R.: Systematic review: exercise-induced gastrointestinal syndrome—implications for health and intestinal disease. *Aliment. Pharmacol. Ther.* 46, 246–265 (2017). <https://doi.org/10.1111/apt.14157>
19. Walsh, N.P., Gleeson, M., Shephard, R.J., Gleeson, M., Woods, J.A., Bishop, N.C., Fleshner, M., Green, C., Pedersen, B.K., Hoffman-Goetz, L., Rogers, C.J., Northoff, H., Abbasi, A., Simon, P.: Position statement. Part one: Immune function and exercise. *Exerc. Immunol. Rev.* 17, 6–63 (2011)
20. Mohr, A.E., Jäger, R., Carpenter, K.C., Kerksick, C.M., Purpura, M., Townsend, J.R., West, N.P., Black, K., Gleeson, M., Pyne, D.B., Wells, S.D., Arent, S.M., Kreider, R.B., Campbell, B.I., Bannock, L., Scheiman, J., Wissent, C.J., Pane, M., Kalman, D.S., Pugh, J.N., Ortega-Santos, C.P., ter Haar, J.A., Arciero, P.J., Antonio, J.: The athletic gut microbiota. *J. Int. Soc. Sports Nutr.* 17, (2020). <https://doi.org/10.1186/s12970-020-00353-w>
21. Clarke, S.F., Murphy, E.F., O’Sullivan, O., Lucey, A.J., Humphreys, M., Hogan, A., Hayes, P., O’Reilly, M., Jeffery, I.B., Wood-Martin, R., Kerins, D.M., Quigley, E., Ross, R.P., O’Toole, P.W., Molloy, M.G., Falvey, E., Shanahan, F., Cotter, P.D.: Exercise and associated dietary extremes impact on gut microbial diversity. *Gut.* 63, 1913–1920 (2014). <https://doi.org/10.1136/gutjnl-2013-306541>

22. Mancin, L., Wu, G.D., Paoli, A.: Gut microbiota–bile acid–skeletal muscle axis. *Trends Microbiol.* 31, 254–269 (2023). <https://doi.org/10.1016/j.tim.2022.10.003>
23. Saponaro, F., Bertolini, A., Baragatti, R., Galfo, L., Chiellini, G., Saba, A., D’Urso, G.: Myokines and Microbiota: New Perspectives in the Endocrine Muscle–Gut Axis. *Nutrients.* 16, 4032 (2024). <https://doi.org/10.3390/nu16234032>
24. Scheiman, J., Luber, J.M., Chavkin, T.A., MacDonald, T., Tung, A., Pham, L.-D., Wibowo, M.C., Wurth, R.C., Punthambaker, S., Tierney, B.T., Yang, Z., Hattab, M.W., Avila-Pacheco, J., Clish, C.B., Lessard, S., Church, G.M., Kostic, A.D.: Meta-omics analysis of elite athletes identifies a performance-enhancing microbe that functions via lactate metabolism. *Nat. Med.* 25, 1104–1109 (2019). <https://doi.org/10.1038/s41591-019-0485-4>
25. Lamprecht, M., Frauwallner, A.: Exercise, intestinal barrier dysfunction and probiotic supplementation. *Med. Sport Sci.* 59, 47–56 (2012). <https://doi.org/10.1159/000342169>
26. PETERS, H.P.F., DE VRIES, W.R., VANBERGE-HENEGOUWEN, G.P., AKKERMANS, L.M.A.: Potential benefits and hazards of physical activity and exercise on the gastrointestinal tract. *Gut.* 48, 435–439 (2001). <https://doi.org/10.1136/gut.48.3.435>
27. Cinca-Morros, S., Álvarez-Herms, J.: The Importance of Maintaining and Improving a Healthy Gut Microbiota in Athletes as a Preventive Strategy to Improve Heat Tolerance and Acclimatization. *Microorganisms.* 12, 1160 (2024). <https://doi.org/10.3390/microorganisms12061160>
28. Beiter, T., Erz, G., Würden, A., Nieß, A.M.: Impact of moderate environmental heat stress during running exercise on circulating markers of gastrointestinal integrity in endurance athletes. *Physiol. Rep.* 13, (2025). <https://doi.org/10.14814/phy2.70305>
29. Camus, G., Nys, M., Poortmans, J.-R., Venneman, I., Monfils, T., Deby-Dupont, G., Juchm□s-Ferir, A., Deby, C., Lamy, M., Duchateau, J.: Endotoxaemia, production of tumour necrosis factor? and polymorphonuclear neutrophil activation following strenuous exercise in humans. *Eur. J. Appl. Physiol.* 79, 62–68 (1998). <https://doi.org/10.1007/s004210050474>

30. Lefevre, C., Bindels, L.B.: Role of the Gut Microbiome in Skeletal Muscle Physiology and Pathophysiology. *Curr. Osteoporos. Rep.* 20, 422–432 (2022). <https://doi.org/10.1007/s11914-022-00752-9>
31. Kamada, N., Seo, S.-U., Chen, G.Y., Núñez, G.: Role of the gut microbiota in immunity and inflammatory disease. *Nat. Rev. Immunol.* 13, 321–335 (2013). <https://doi.org/10.1038/nri3430>
32. Ducharme, J.B., McKenna, Z.J., Deyhle, M.R.: Exercise mitigates the Toll of muscle atrophy: a narrative review of the effects of exercise on Toll-like receptor-4 in leukocytes and skeletal muscle. *American Journal of Physiology-Cell Physiology.* 322, C581–C589 (2022). <https://doi.org/10.1152/ajpcell.00005.2022>
33. JEUKENDRUP, A.E., VET-JOOP, K., STURK, A., STEGEN, J.H.J.C., SENDEN, J., SARIS, W.H.M., WAGENMAKERS, A.J.M.: Relationship between gastro-intestinal complaints and endotoxaemia, cytokine release and the acute-phase reaction during and after a long-distance triathlon in highly trained men. *Clin. Sci.* 98, 47–55 (2000). <https://doi.org/10.1042/cs0980047>
34. Jeukendrup, A.E., Vet-Joop, K., Sturk, A., Stegen, J.H., Senden, J., Saris, W.H., Wagenmakers, A.J.: Relationship between gastro-intestinal complaints and endotoxaemia, cytokine release and the acute-phase reaction during and after a long-distance triathlon in highly trained men. *Clin. Sci. (Lond).* 98, 47–55 (2000)
35. Bruunsgaard, H., Galbo, H., Halkjaer-Kristensen, J., Johansen, T.L., MacLean, D.A., Pedersen, B.K.: Exercise-induced increase in serum interleukin-6 in humans is related to muscle damage. *J. Physiol.* 499, 833–841 (1997). <https://doi.org/10.1113/jphysiol.1997.sp021972>
36. Peake, J.M., Neubauer, O., Walsh, N.P., Simpson, R.J.: Recovery of the immune system after exercise. *J. Appl. Physiol.* 122, 1077–1087 (2017). <https://doi.org/10.1152/jappphysiol.00622.2016>

37. Schwellnus, M., Soligard, T., Alonso, J.-M., Bahr, R., Clarsen, B., Dijkstra, H.P., Gabbett, T.J., Gleeson, M., Hägglund, M., Hutchinson, M.R., Janse Van Rensburg, C., Meeusen, R., Orchard, J.W., Pluim, B.M., Raftery, M., Budgett, R., Engebretsen, L.: How much is too much? (Part 2) International Olympic Committee consensus statement on load in sport and risk of illness. *Br. J. Sports Med.* 50, 1043–1052 (2016). <https://doi.org/10.1136/bjsports-2016-096572>
38. Carrard, J., Rigort, A.-C., Appenzeller-Herzog, C., Colledge, F., Königstein, K., Hinrichs, T., Schmidt-Trucksäss, A.: Diagnosing Overtraining Syndrome: A Scoping Review. *Sports Health: A Multidisciplinary Approach.* 14, 665–673 (2022). <https://doi.org/10.1177/19417381211044739>