


Exercise-induced intestinal barrier dysfunction: a potential contributor to athlete mental health

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ABSTRACT

Athlete mental health has become a growing concern across endurance, aesthetic and weight-sensitive sports. While psychosocial factors play major roles, emerging evidence suggests biological pathways related to gastrointestinal function may contribute. Intense exercise induces transient intestinal barrier dysfunction through splanchnic hypoperfusion, hyperthermia and tight-junction disruption, increasing permeability and microbial product exposure. These changes resemble biomarker patterns in psychiatric populations, where elevated zonulin, lipopolysaccharide and intestinal fatty-acid binding protein are associated with anxiety, depression and neuroinflammation.

This viewpoint proposes a bidirectional model linking exercise-induced gut barrier stress and mood disturbance. Gut-derived signals including vagal afferent activation and cytokine-mediated tryptophan-kynurenine shifts may influence mood-regulating brain regions, while psychological stress reciprocally impairs gut integrity via corticotropin-releasing hormone and sympathetic activation. Female athletes may face heightened vulnerability through hypoestrogenic states and psychosocial pressures.

While exercise physiology and psychiatric literatures remain separate, their convergence highlights an under-recognised dimension of athlete health warranting clinical awareness and Relative Energy Deficiency in Sport integration. Research priorities include longitudinal athlete studies and multi-omics approaches to determine whether gut barrier dysfunction is a contributor, modifier or parallel correlate of athlete mental health.

INTRODUCTION

Athletes experience meaningful rates of depression, anxiety and burnout, with prevalence varying by sport, competitive level and study methodology. The IOC's consensus statements emphasise that while some athlete groups show psychiatric condition prevalence comparable to the general population, others, particularly endurance sport, aesthetic sport and weight-class athletes, demonstrate elevated psychological vulnerability.¹ Alongside psychosocial contributors like performance pressure, travel demands and injury, increasing interest focuses on the

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Intense or prolonged exercise can acutely increase intestinal permeability through splanchnic hypoperfusion and heat stress.
- ⇒ Gut barrier dysfunction and dysbiosis have been associated with depressive and anxiety symptoms in non-athlete populations.
- ⇒ Athlete mental health is influenced by both biological stressors and psychosocial pressures, with Relative Energy Deficiency in Sport (RED-S) providing one established integrative model.

WHAT THIS STUDY ADDS

- ⇒ Proposes a bidirectional gut-brain stress model linking exercise-induced barrier dysfunction with mood disturbance in athletes.
- ⇒ Integrates exercise physiology, neuroimmune signalling, vagal pathways and sex-specific hormonal factors into a unified conceptual framework.
- ⇒ Acknowledges that while mechanistically plausible, no longitudinal studies have yet demonstrated that gut barrier dysfunction predicts future mood disturbances in athletes, representing a critical research gap.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Identifies key research priorities, including longitudinal athlete studies, sex-specific analyses and multi-omics approaches.
- ⇒ Encourages clinicians to consider gut-brain interactions particularly in high-load, heat-exposed or RED-S-susceptible athletes while avoiding premature biomarker use.
- ⇒ Suggests a broader, integrative perspective on athlete mental health that may inform future screening, education and interdisciplinary care models.

biological pathways linking training stress to mental health.

Exercise-induced intestinal barrier dysfunction is characterised by transient increases in epithelial permeability, systemic exposure to microbial products and low-grade inflammation during intense or prolonged exertion.^{2 3} Although traditionally studied in gastrointestinal conditions, such

perturbations may plausibly influence neuroimmune signalling and mood.^{4,5}

This viewpoint, integrating evidence across exercise physiology, gastroenterology and psychiatry, proposes a hypothesis-driven, bi-directional model linking gut barrier stress and athlete mental health. Without claiming that gut permeability causes depression in athletes, we outline a framework to guide future research and clinical awareness.

Gut barrier stress in endurance training

Acute physiological stressors

Intense or prolonged exercise redistributes blood away from the gastrointestinal tract, with splanchnic hypoperfusion during ~70% maximal capacity exercise.³ This ischaemic stress reduces oxygen delivery to epithelial cells and contributes to epithelial injury and increased permeability. Heat stress further amplifies these effects: core temperatures approaching or exceeding 39°C are consistently associated with increased epithelial permeability in humans, and experimental hyperthermia (41–42°C) produces marked epithelial damage in vivo.^{6,7}

Heat stress also induces expression of heat shock proteins (HSPs), particularly HSP70, which play a cytoprotective role in maintaining epithelial integrity under thermal and oxidative stress.^{8,9} While HSP induction may represent an adaptive response to repeated exercise, experimental models suggest that insufficient HSP signalling is associated with impaired barrier function and amplified inflammatory responses.^{10,11}

Biomarker evidence of epithelial injury

Several biomarkers confirm acute barrier disruption during endurance exercise. Intestinal fatty-acid binding protein (I-FABP), a marker of enterocyte damage, increases twofold to threefold following marathon running.¹² Zonulin, a regulator of tight-junction permeability, also increases following prolonged exertion, with particularly pronounced elevations observed in heat stress.^{13,14} These physiological changes parallel findings in psychiatric cohorts: individuals with anxiety or depression exhibit elevated zonulin, I-FABP and circulating lipopolysaccharide (LPS) and dysbiosis with enrichment of LPS-biosynthesis pathways.^{4,5}

Recovery kinetics and the transition toward chronicity

In most athletes, exercise-induced permeability elevations are transient and return toward baseline with recovery. However, repeated high-load sessions, especially when combined with heat stress, dehydration or low energy availability, may exacerbate barrier perturbations. Human evidence is limited but preclinical models demonstrate that repeated episodes of hypoperfusion, heat stress or epithelial injury can sustain permeability and prolong inflammatory signalling^{2,6,7} exposing the barrier to stressors relevant to neuroimmune signalling.

When adaptation becomes maladaptation

Exercise, mood and the U-shaped curve

Epidemiological analyses consistently describe a U-shaped relationship between exercise volume and mental health: moderate activity shows the lowest mental-health burden whereas both lower and extremely high weekly volumes are associated with worse outcomes.¹⁵ This pattern is not evidence of gut-mediated mechanisms but provides context within which barrier dysfunction could plausibly contribute.

Integration with the Relative Energy Deficiency in Sport framework

Relative Energy Deficiency in Sport (RED-S) offers additional insight into vulnerability to gut-barrier stress. Low energy availability limits nutrients for gastrointestinal maintenance and recovery with gastrointestinal (GI) disturbance being a recognised feature of RED-S. The 2023 IOC consensus identifies irritability, sleep disturbance, impaired concentration and depressive symptoms as psychiatric manifestations. Gut-barrier integrity is absent from current diagnostic and return-to-play considerations. Given RED-S may impair GI integrity, incorporating GI symptoms and biomarkers into RED-S assessment warrants exploration.¹

Defining maladaptation cautiously

Maladaptation should not be framed as a discrete threshold. Repeated epithelial stress, dysbiosis and low-grade inflammation may interact in certain athletes to influence neuroimmune signalling. Chronic low-grade inflammation, typically reflected by elevated interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF- α) or c-reactive protein (CRP), is consistently associated with depressive symptoms and cytokine-induced alterations in monoamine and glutamate pathways.^{16,17} This model is biologically plausible but remains unproven in athletes.

A bi-directional gut-brain stress loop

Gut \rightarrow brain pathways

Translocation of microbial products such as LPS can activate innate immune receptors, initiating cytokine cascades that affect the brain via humoral and neural pathways.¹⁸ Elevated zonulin, LPS and I-FABP have been reported in anxiety and depressive disorders. Patients with recent suicidal behaviour show markedly elevated I-FABP and altered zonulin patterns consistent with impaired gut integrity.^{4,5} Vagal afferents with mechanosensitive and chemosensitive endings detect intestinal inflammation, microbial metabolites and serotonin released from enterochromaffin cells.¹⁹

Afferent signals project to the nucleus tractus solitarius and locus coeruleus and modulate limbic regions involved in mood regulation. Importantly, vagal afferents can respond to local intestinal inflammatory signals independent of systemic cytokine elevations, suggesting a mechanism through which subclinical barrier disturbances could influence mood.²⁰

Inflammatory cytokines activate indoleamine 2,3-dioxygenase, diverting tryptophan metabolism toward kynurenine and generating neuroactive metabolites that promote neuroinflammation, impair glutamate clearance and reduce serotonin availability.¹⁷ Disrupted intestinal serotonin homeostasis may thus contribute to both peripheral barrier dysfunction and central mood disturbances, though the relative contributions of gut-derived versus centrally synthesised serotonin to psychiatric symptoms remain debated.²¹

Brain → gut pathways

Stress itself can impair the intestinal barrier. Acute psychological stress activates the hypothalamus-pituitary-adrenal axis and peripheral corticotropin releasing hormone (CRH) reproduces this permeability increase in a mast-cell-dependent manner.²²

Sympathetic activation may similarly alter tight-junction proteins and compromise mucosal perfusion.²³

Thus, barrier dysfunction is bi-directional: gut injury may influence mood but mood and stress can also worsen gut integrity, creating a feedback loop potentially amplified under high training stress [figure 1](#).

Convergent evidence

Athletes exhibit acute load-dependent barrier dysfunction and systemic inflammatory responses. Psychiatric cohorts show elevated permeability biomarkers and dysbiosis. While these literatures are separate, their convergence strengthens the plausibility of a gut-brain link. Still, no longitudinal athlete study has linked barrier dysfunction to future mood disturbance, an important gap.

Sex-specific and psychosocial considerations

Female athletes experience a higher burden of depressive symptoms and eating-related psychopathology. These differences are multifactorial, reflecting psychosocial contributors such as harassment, inequitable resources and perfectionism, as well as biological vulnerabilities including low energy availability and RED-S.^{1,24}

Hormonal influence on gut permeability and microbiota

Oestrogen supports epithelial barrier integrity, shapes microbial composition through the estrobolome and influences inflammatory tone, with marked changes during menopause.²⁵

Hypoestrogenic states such as RED-S or functional hypothalamic amenorrhoea may heighten susceptibility to barrier disturbances. Progesterone modulates gastrointestinal motility and immune tone. These hormonal cycles may create windows of altered vulnerability to gut-brain disturbances in female athletes, although direct evidence in sport populations is lacking.²⁵

Psychosocial integration

Sex differences in athlete mental health are not reducible to hormonal biology. Harassment, inequitable resources and gendered performance expectations are independent stressors that interact with and amplify biological

vulnerabilities, and any model that omits them is incomplete.²⁴

Clinical implications for athlete health

Screening considerations

Clinicians should consider gut-brain interactions when athletes present with:

- ▶ Persistent GI complaints during high training volumes.
- ▶ Unexplained mood changes.
- ▶ Menstrual irregularities or RED-S features.
- ▶ Marked heat-intolerance or GI distress with strenuous exercise.

Symptom logs and RED-S screening tools remain the primary approach. Biomarkers (I-FABP, zonulin) are research-only and should not be used diagnostically.

Adequate recovery after high-intensity or heat-stress sessions is essential; minimising back-to-back gut stressors, along with cooling and hydration strategies, may reduce thermal epithelial injury.

Nutritional strategies

Maintaining carbohydrate availability during long sessions helps limit epithelial injury.²

Probiotic supplementation shows mixed and preliminary evidence for reducing permeability under physiological or heat stress, and bovine colostrum has demonstrated variable effects across exercise-heat models.^{2,26}

Anti-inflammatory dietary patterns, including Mediterranean-style diets, may offer supportive benefit through effects on systemic inflammation and gut microbiota composition.^{26,27}

All interventions should be framed as adjunctive to established mental-health care.

Future directions

Priorities for research include longitudinal studies tracking gut biomarkers, training load and mood, sex-specific analyses with hormonal measures, athlete phenotyping (eg, ultra-distance, heat-exposed sports, low energy availability), trials assessing gut-targeted interventions, investigation of neuromodulation approaches such as vagal nerve stimulation and multi-omics approaches integrating microbiome, metabolomics, cytokines and performance data.

LIMITATIONS

This viewpoint synthesises evidence across exercise physiology, neuroimmunology and psychiatric research, but much of the support derives from parallel literature studies rather than athlete-specific longitudinal data. Direct causal relationships between barrier dysfunction and mood disturbance in athletes remain undemonstrated, biomarker data in sport populations are limited and several mechanistic inferences are extrapolated from non-athlete or preclinical models. As such, the framework should be interpreted as hypothesis-generating.

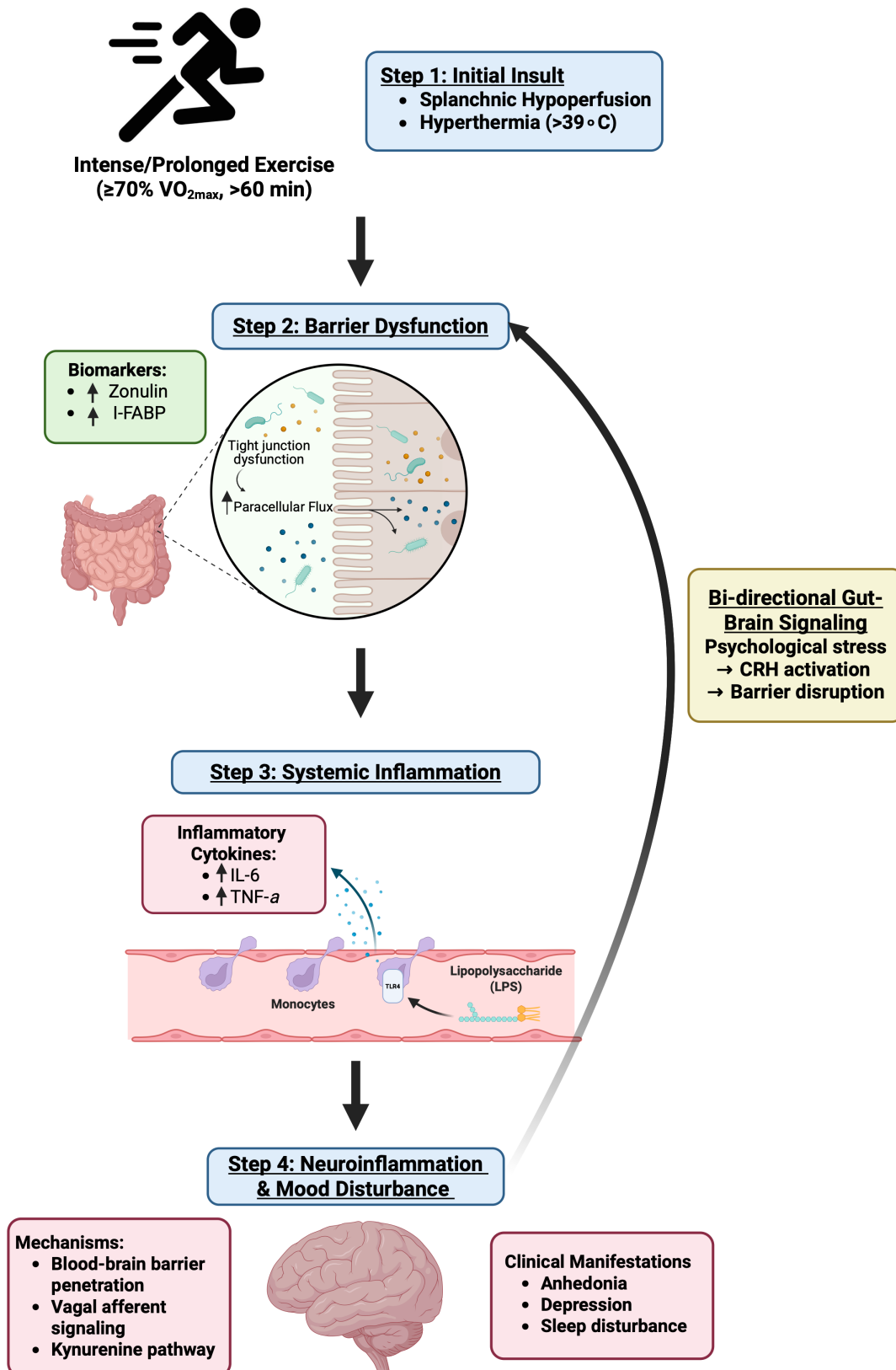


Figure 1 A proposed bi-directional mechanistic pathway linking intense exercise to mood disturbance via the gut-brain axis. Intense or prolonged exercise induces splanchnic hypoperfusion and hyperthermia (Step 1), leading to intestinal barrier dysfunction and increased paracellular permeability (Step 2). These changes can trigger systemic inflammatory responses (Step 3) and contribute to neuroinflammation and mood disturbances (Step 4), such as anhedonia, depression and sleep disruption. Psychological stress and CRH mediated pathways may, in turn, further impair barrier integrity, highlighting a bi-directional gut-brain. IL-6, Interleukin-6; TNF- α , Tumour necrosis factor-alpha; CRH, corticotropin releasing hormone; I-FABP, intestinal fatty-acid binding protein.

CONCLUSION

Exercise-induced intestinal barrier dysfunction is a biologically plausible contributor to mood disturbance in athletes, functioning within a bi-directional gut-brain stress loop. While current evidence is indirect and largely extrapolated from separate literatures, the conceptual framework aligns with known training physiology, neuroimmune mechanisms and sex-specific factors. Recognising gut health as one dimension of athlete well-being may enrich clinical assessments and inspire interdisciplinary research. This viewpoint aims to stimulate inquiry, not assert causality, towards a more integrated understanding of athlete mental health.

Contributors ADC conceived the idea for the manuscript, led the literature synthesis, developed the conceptual framework, drafted the manuscript and coordinated revisions. OVW and MCC contributed to the conceptual development, provided critical intellectual input, reviewed and edited the manuscript for scientific accuracy and clarity and contributed to interpretation of the sports psychiatry and athlete mental health context. Portions of the editorial drafting process were assisted by ChatGPT (OpenAI), which was used for language refinement, subheading suggestions and clarification of phrasing. All content was reviewed, edited and approved by the authors, who take full responsibility for its accuracy and integrity.

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