Letter to the Editor

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Microbiome in motion: revolutionizing musculoskeletal recovery

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Dear Editor,

Emerging evidence highlights the intestinal microbiome as a central regulator of systemic inflammation, immune responses, and metabolic pathways. While its role in metabolic and neurological disorders is established, its integration into musculoskeletal rehabilitation paradigms remains unexplored. We propose that targeted modulation of the microbiome—via diet, probiotics, and prebiotics—can accelerate recovery following musculoskeletal injuries and surgeries by mitigating inflammation, enhancing metabolism, and improving tissue regeneration.

Systemic inflammation and recovery

Dysbiosis, or microbial imbalance, promotes chronic low-grade inflammation, delaying the healing of musculoskeletal tissues. A dysbiotic microbiome disrupts the production of anti-inflammatory molecules, instead favoring the release of proinflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), which are known to impair the regeneration of bone, cartilage, and muscle tissue[1].

Probiotic strains such as *Lactobacillus* and *Bifidobacterium* have demonstrated significant anti-inflammatory effects by reducing systemic cytokine levels. For example, *Lactobacillus rhamnosus GG* has been shown to attenuate IL-6 production and enhance regulatory T-cell activity, promoting an anti-inflammatory state conducive to healing[2]. Coupled with anti-inflammatory diets rich in omega-3 fatty acids, polyphenols, and dietary fiber, microbiome modulation can create an optimal environment for musculoskeletal repair[3]. Omega-3 fatty acids, found in foods like fatty fish and flaxseeds, exhibit direct anti-inflammatory effects by suppressing proinflammatory eicosanoid production.

In addition, dietary polyphenols from sources such as green tea and berries interact with the gut microbiota to increase the production of beneficial metabolites like short-chain fatty acids (SCFAs)[4]. These metabolites not only have anti-inflammatory properties but also enhance mucosal barrier integrity, which prevents the translocation of bacterial endotoxins and further systemic inflammation.

Muscle metabolism and regeneration

The microbiome plays a pivotal role in muscle metabolism and regeneration, primarily through the production of SCFAs such as butyrate, acetate, and propionate. Butyrate, in particular, improves insulin sensitivity and enhances mitochondrial function in muscle cells, both of which are critical for energy metabolism during recovery[5]. However, dysbiosis compromises SCFA production, resulting in inefficient energy utilization and slower recovery from musculoskeletal injuries.

Specific probiotics and prebiotics could counteract these deficits[6]. For instance, supplementation with *Akkermansia muciniphila*, a gut bacterium associated with metabolic health, has been shown to increase butyrate production, improving energy delivery to regenerating tissues[7]. Similarly, prebiotics such as inulin and fructo-oligosaccharides (FOS) stimulate the growth of SCFA-producing bacteria, thereby enhancing metabolic efficiency during tissue repair.

Moreover, the microbiome influences muscle protein synthesis, a key process in rehabilitation following injuries or surgeries[3]. Certain microbial metabolites, including SCFAs and secondary bile acids, activate pathways such as the mammalian target of rapamycin (mTOR), which regulates protein synthesis and muscle hypertrophy. By promoting these anabolic pathways, targeted microbiome modulation could significantly enhance recovery trajectories.

Pain and neuroinflammation

The gut-brain axis, a bidirectional communication network between the gut and central nervous system (CNS), links intestinal dysbiosis to neuroinflammation and pain perception. Dysbiosis promotes the production of proinflammatory cytokines and endotoxins, which can cross the blood-brain barrier and exacerbate neuroinflammatory processes. These changes contribute to central sensitization, a mechanism underlying chronic pain conditions[8].

Interventions targeting the microbiome may alleviate these effects[9]. For instance, probiotic strains like *Bifidobacterium longum* and *Lactobacillus helveticus* have been shown to modulate neurotransmitter production, including gamma-aminobutyric acid (GABA) and serotonin, which are critical for pain regulation and mood. By reducing neuroinflammatory mediators and restoring neurotransmitter balance, these probiotics may improve pain perception and rehabilitation outcomes.

In addition, preclinical studies have demonstrated that SCFAs can modulate microglial activation in the CNS, reducing

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neuroinflammation and associated pain[10]. These findings suggest that enhancing SCFA production through dietary or probiotic interventions could offer a novel strategy for managing pain in musculoskeletal rehabilitation.

Clinical implications

Incorporating microbiome analysis into rehabilitation protocols represents a significant advancement in precision medicine. Techniques such as 16S rRNA sequencing allow for the identification of individual microbial profiles, enabling personalized interventions tailored to the specific needs of patients. For example, post-arthroplasty patients could benefit from microbiome-targeted therapies to reduce systemic inflammation and postoperative pain, while athletes recovering from muscle injuries might accelerate regeneration through fermented, anti-inflammatory diets[11].

Such approaches complement traditional physiotherapy by addressing underlying systemic factors that influence recovery. For instance, a rehabilitation program incorporating anti-inflammatory diets, probiotic supplementation, and prebiotic-rich foods could enhance outcomes for patients with chronic musculoskeletal conditions, such as osteoarthritis or tendinopathies[12,13].

Future directions

Despite the promising evidence, integrating microbiome modulation into clinical practice requires further research. Large-scale randomized controlled trials are needed to establish the efficacy of specific probiotics, prebiotics, and dietary interventions in musculoskeletal rehabilitation. In addition, exploring the role of the microbiome in conditions such as tendinopathy, ligament injuries, and bone fractures could expand its applications.

Emerging technologies, such as machine learning and metagenomics, could facilitate the development of predictive models linking microbial profiles to rehabilitation outcomes. These advancements would enable the design of more effective, personalized interventions that optimize recovery trajectories.

Conclusions

Integrating microbiome modulation into musculoskeletal rehabilitation represents a novel, evidence-based strategy to improve clinical outcomes. By reducing systemic inflammation, enhancing metabolism, and addressing neuroinflammation, microbiome-targeted therapies could shorten recovery times and improve quality of life. Given its potential, this paradigm warrants further clinical investigation and adoption in rehabilitation settings. As our understanding of the microbiome continues to evolve, its integration into holistic rehabilitation frameworks could redefine standards of care in musculoskeletal medicine.

CRediT author statement

Roberto Tedeschi: Conceptualization, Methodology, Data analysis, Writing – Original draft, Writing – Review & Editing.

Declaration of competing interest

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Ethics statement

Not required.

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Declaration of generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

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