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Review

The Gut Microbiome in Post-Traumatic Stress Disorder: Mechanisms, Evidence, and Future Directions

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Abstract

Objective: Post-traumatic stress disorder (PTSD) affects about 4% of people worldwide, the gut microbiome has drawn interest as a possible factor in PTSD, though the evidence is still growing. This review brings together what is known about gut microbiota changes in PTSD, explores the pathways that may connect gut dysbiosis to the disorder, and examine whether microbiome-targeted treatments show promise. **Methods:** A literature review was conducted by searching several platforms for studies published between January 2015 and May 2026, supplemented by manual screening of reference lists and inclusion of earlier foundational references where relevant. **Results:** Fewer than a dozen studies have directly examined gut microbiota in PTSD, and findings vary. The most consistent pattern is a reduction in hort-chain fatty acids-producing bacteria, especially Lachnospiraceae. Faecal microbiota transplantation studies in rodents show that stress-altered microbiota can transfer anxiety-like behaviors and weaken fear extinction. Four mechanistic pathways were identified: hypothalamic-pituitary-adrenal axis dysregulation, lipopolysaccharide-driven systemic inflammation, shifts in tryptophan metabolism toward the kynurenine pathway, and impaired vagal signaling. Together these may form a self-reinforcing feedback loop. Two pilot trials have tested microbiome-targeted interventions alongside psychotherapy, both promising but not yet sufficient to guide clinical practice. Comple PTSD has been almost entirely overlooked in gut–brain research. **Conclusions:** Gut dysbiosis is a plausible contributor to PTSD, but this has not been tested directly in the disorder. Nearly all human evidence is cross-sectional, and mechanistic data come mainly from animal models. Key priorities include longitudinal studies with trauma-exposed controls, control for psychotropic medication, and research that distinguishes complex PTSD from single-incident PTSD.

Key words: Post-traumatic stress disorder (PSTD); gut microbiome; microbiota-gut-brain axis; hypothalamic-pituitary-adrenal (HPA) axis; short-chain fatty acid (SCFA).

1. Introduction

Post-traumatic stress disorder (PTSD) is a serious mental health condition that can develop after exposure to traumatic events involving actual or threatened death, serious injury, or sexual violence. According to American Psychiatric Association, the core symptoms of PTSD fall into four clusters: unwanted re-experiencing of the traumatic event, avoidance of reminders, negative shifts in thinking and mood, and a state of heightened arousal that keeps the body on alert. PTSD affects huge number of individuals worldwide associated with significant personal, social, and healthcare costs. It has been estimated that around 3.9% of the general population will experience PTSD during their lifetime, with the prevalence increasing to 5.6% among trauma-exposed individuals (1). Rates have been reported to exceed 15% in groups which affected by armed conflict or sexual violence (2).

The impact of PTSD extends far beyond psychological distress. The disorder can negatively impact a person's ability to work, difficult to maintain close relationships, and not able to function effectively in everyday life. PTSD has also been linked to a range of physical health problems, including cardiovascular disease, metabolic syndrome, and gastrointestinal disorders (3). Individuals with PTSD face the high risk of suicide. In a population-based study involving more than three million people, men with PTSD had almost four times the risk of suicide, while women had nearly seven times the risk compared with the general population (4). Despite decades of research and growing recognition of its impact, the biological mechanisms underlying PTSD remain limited understood.

Several effective treatments are currently available for PTSD. Trauma-focused psychotherapies, including Cognitive Processing Therapy (CPT), Eye Movement Desensitization and Reprocessing, and Prolonged Exposure are considered first-line approaches (5). Pharmacological options are more limited, with sertraline and paroxetine as the only medications approved specifically for PTSD (6). However, these treatments do not work for everyone. Meta-analyses show that a meaningful share of patients still meet diagnostic criteria after completing a full course of therapy or pharmacotherapy (7). Treatment dropout is also common, around 18% of patients discontinue trauma-focused psychotherapy before completion, with even higher rates reported in some settings (8). These numbers highlight the need to identify new biological mechanisms, such as the gut microbiome as potential therapeutic targets.

The microbiota-gut-brain axis is an important framework for understanding the biological links between the gut and the brain (9). Growing evidence from both animal and human studies suggests that disruptions in the gut microbiota, often referred to as gut dysbiosis, are associated with several psychiatric disorders, including major depressive disorder and anxiety disorders (10). More recently, studies have begun to examine the role of gut microbiota in PTSD. For example, He, et al. (11) conducted a two-sample Mendelian randomization study that identified potential causal associations between several gut microbial taxa and PTSD, suggesting that gut–brain axis dysfunction may be relevant to the disorder.

This review has four aims: First, it summarizes current evidence on gut microbiota changes in PTSD. Second, it explores how gut dysbiosis may be involved in PTSD-related processes, including intestinal barrier dysfunction, inflammation, changes in neurotransmitter metabolism and altered vagal signaling. Although direct evidence from PTSD studies is limited, findings from related psychiatric conditions and animal studies are considered to help explain possible mechanisms. Third, it surveys microbiome-targeted strategies: probiotics, prebiotics, and dietary interventions. Last, it maps out what is missing from the current literature and suggests some possible research directions.

2. Search Strategy

A preliminary literature search was conducted in Psychological Information Database, Google Scholar, PubMed, Sage Journals, Elsevier, Frontiers, Nature and Taylor & Francis. The search mainly focused on studies published between January 2015 and May 2026, although earlier key studies were also included when they were considered foundational or highly relevant to the topic. Search terms including "PTSD", "post-traumatic stress disorder", "gut microbiota", "gut microbiome", "microbiota-gut-brain axis", "dysbiosis", "probiotics", and "hypothalamic-pituitary-adrenal (HPA) axis". Additional relevant studies were identified by manually checking the reference lists of key review articles.

3. PTSD: Neurobiological Profile and the Rationale for a Gut-Brain Perspective

PTSD is associated with long-term changes across several biological systems, many of which are

closely connected to gut function. One of the most widely studied is the HPA axis. Under normal conditions, stress activates the HPA axis, leading to the release of cortisol which then helps regulate and shut down the stress response through negative feedback. In PTSD, this feedback loop appears disrupted. Many individuals show lower basal cortisol levels but increased glucocorticoid sensitivity, along with increased corticotropin-releasing hormone in cerebrospinal fluid (12).

PTSD is also associated with changes in brain regions involved in fear and emotion regulation. Reduced hippocampal volume and dysfunction of the prefrontal cortex may impair fear extinction and weaken top-down control of the amygdala (13). In the meantime, the amygdala tends to be hyperreactive, producing threat responses even to neutral stimuli (14).

The autonomic nervous system is also consistently affected. Schneider and Schwerdtfeger (15) reported that PTSD patients had lower heart rate variability than controls at rest and during stress, with reductions in high frequency heart rate variability and root mean square of successive differences pointing to weaker parasympathetic activity. Resting heart rate was higher as well. Reduced vagal tone is relevant here for a specific reason: the vagus nerve is one of the primary anatomical connections between the gut and the brain (16). Whether reduced vagal tone directly impairs microbiome-related signaling in PTSD is not yet known (17).

Together, these findings show that PTSD is not confined to the brain. The endocrine and autonomic disruptions in PTSD also affect the body, and the gastrointestinal system is among those affected. PTSD is strongly associated with functional gut disorders. A systematic review found that PTSD was linked to worse GI symptom severity and higher risk of disease exacerbation (18). A meta-analysis reported that PTSD approximately tripled the risk of irritable bowel syndrome (19), and studies in veteran and war-exposed populations further support the long-term gastrointestinal impact of trauma exposure (20). These findings suggest that gastrointestinal disturbances are common in PTSD and may reflect alterations in gut–brain communication. However, studies directly examining gut microbiota composition in PTSD remain limited: some have small samples, and most are cross-sectional, making it difficult to establish causal relationships (21).

These findings support the idea that biological changes involved in PTSD may interact in both directions with the gut microbiome. The HPA axis and cortisol can directly affect gut barrier function and motility. Reduced vagal tone may disrupt important pathways of gut–brain communication. At the same time, unhealthy gut microbiota could change how neurotransmitters are produced and may also affect HPA axis activity. More importantly, these effects are unlikely to run in just one direction. Stress can disturb the gut while a disturbed gut can feed back into the stress response, creating loops that sustain themselves over time.None of these mechanisms has been firmly proven in PTSD. But the overlap between PTSD biology and gut–brain biology is strong; this supports further study of the gut microbiome as a possible factor in PTSD and as a potential treatment target.

4. Human Evidence: Gut Microbiota Alterations in PTSD

Direct human evidence linking gut microbiota to PTSD is still quite limited. Most of the available studies have only been published in the last few years, and many rely on small samples and different methodologies. A meta-analysis by Petakh, et al. (22) included six studies on gut microbiota composition in PTSD. When the data were pooled, there was no significant difference in the Shannon Diversity Index between PTSD and control groups (SMD = 0.27, 95% CI −0.62 to 0.609, p = 0.110). For bacterial abundance, two studies found reduced Lachnospiraceae in PTSD groups, but other findings did not really align. Overall, current evidence does not strongly support reduced alpha diversity as a stable feature of PTSD. A more recent systematic review by Winder, et al. (21) screened 130 records, but only three studies actually met the inclusion criteria. These studies all reported some taxonomic differences between PTSD and control groups, although the results were very heterogeneous and not easy to compare across studies.

If place the PTSD literature within a broader psychiatric context, highlights how little attention this disorder has received compared to other conditions. Nikolova, et al. (10) analyzed 59 case-control studies across different psychiatric disorders, which found a cross-disorder pattern of gut dysbiosis. They found lower levels of butyrate-producing, anti-inflammatory bacteria, together with higher levels of pro-inflammatory bacteria in depression, bipolar disorder, schizophrenia, and anxiety disorders. PTSD was included, but only represented by a single study in the whole dataset. This gap shows that gut microbiome research in PTSD has not kept pace with research on other psychiatric disorders.

Even with the small number of studies, some early findings are starting to appear. Hemmings, et al. (23) compared gut microbiota in 18 individuals with PTSD and 12 trauma-exposed controls, overall microbial diversity did not differ significantly between groups. However, random forest analysis identified three phyla: Actinobacteria, Lentisphaerae, and Verrucomicrobia as important in distinguishing PTSD status. Lower total abundance of these three phyla was significantly associated with higher CAPS-5 scores ($r = -0.387$, $p = 0.035$). An additional observation was that individuals who had experienced childhood trauma also showed lower levels of Actinobacteria and Verrucomicrobia, regardless of their adult PTSD status. This is a finding that points to early-life adversity as an independent driver of microbiota disruption.

Beyond PTSD diagnosis itself, early-life trauma may have lasting associations with adult gut microbiota composition. (24) showed in a large population-based cohort that childhood living conditions and environmental exposures have long-term effects on the adult gut microbiome. Some studies have linked early-life trauma to higher levels of Anaerostipes, and chronic stress in rodents also increases Anaerostipes abundance (25). The role of this bacterium remains unclear, however, as it has been associated with both beneficial and inflammatory effects in different contexts. These findings raise an important question for future research: individuals with CPTSD which a disorder characterized by prolonged, repeated interpersonal trauma, often beginning in childhood, may show more persistent microbiota alterations. This has not yet been directly studied. The limited evidence on CPTSD may partly reflect that it is a relatively new diagnosis in ICD-11 and was not consistently defined in earlier studies. The complexity of its diagnostic criteria and the lack of standardized assessment tools have further limited research in this area (26).

5. Limitations

The human evidence has some limitations, as all existing studies are cross-sectional, making it difficult to determine whether microbiota changes precede PTSD, develop alongside it or result from it. Besides, the majority of PTSD patients in clinical studies are taking psychotropic medications, and many of these drugs have direct antimicrobial properties (27). This means observed differences between PTSD and control groups may partly reflect drug effects rather than disease biology, yet few studies have controlled for medication status. Lastly, no study has separated participants by trauma type or CPTSD status, even though trauma duration and developmental timing may independently shape the gut microbiome.

6. Gut Microbiota and PTSD: Potential Mechanisms

PTSD is associated with dysregulation across several physiological systems, including stress hormone regulation, immune function, neurotransmitter systems and autonomic signaling. There is also growing evidence that these systems may interact with the gut microbiome. This section looks at four possible pathways through which gut dysbiosis may contribute to PTSD-related processes, and then ends with an integrative framework that brings these mechanisms together.

6.1 Endocrine and HPA Axis Dysregulation

The HPA axis as the body's main stress hormone system which is centrally involved in PTSD (28). What happens to HPA axis after trauma is not always straightforward. A fairly consistent finding is that many people with PTSD show low cortisol at rest, but at the same time their tissues appear more sensitive to cortisol. It is as if the whole feedback system has been reset. Increasing evidence suggests that the relationship between the HPA axis and the gut microbiome is bidirectional, with each influencing the function of the other (29).

Sudo, et al. (30) found that germ-free mice showed much stronger adrenocorticotropic hormone and corticosterone responses to restraint stress. This response could be partly reversed by colonization with Bifidobacterium infantis or SPF faecal material, but only when it was given during early development. More recently, Tofani, et al. (31) reported that reducing gut microbes through antibiotics or germ-free conditions disrupted the normal daily rhythm of plasma corticosterone. The peaks of glucocorticoids were shifted to times of day when they would not usually occur. These findings suggest that the gut microbiome is involved in its timing and daily organization. This timing aspect of HPA regulation has not received much attention in PTSD research, even though cortisol rhythms are known to be disturbed in this population (32).

The reverse pathway may also be important. High cortisol can increase intestinal permeability by disrupting epithelial tight junctions. Experimental studies suggest that short-chain fatty acids (SCFAs) help maintain intestinal barrier under stress, and they

may also influence HPA axis activity through immune and neuroendocrine pathways (33). However, evidence in humans is still limited, and it remains unclear whether SCFA supplementation can reduce cortisol responses.

6.2 Immune and Inflammatory Pathways

Increasing evidence suggests that PTSD is linked to chronic low-grade inflammation. The gut microbiome may be involved in this process, and it may also be affected by it. Under normal conditions, the intestinal epithelium acts as a barrier that prevents bacterial products from entering the bloodstream (34). When this barrier becomes more permeable, bacterial components such as lipopolysaccharide (LPS) can enter circulation. This condition is often described as metabolic endotoxemia. In individuals with PTSD, higher levels of serum LPS and LPS-binding protein have been reported which suggest possible gut barrier dysfunction (35). Once LPS is in the blood, it binds to Toll-like receptor 4 on immune cells. This activates a well-known signaling pathway through Myeloid differentiation primary response 88 and Nuclear factor kappa-light-chain-enhancer of activated B cells, which then increases the production of pro-inflammatory cytokines, especially Tumor Necrosis Factor alpha and Interleukin-6 (36).

Animal studies suggest that stress-related changes in the gut microbiome may affect inflammatory processes. For example, faecal microbiota transplantation from stressed rodents to naïve animals has been linked with increased inflammatory signaling (37) and altered serotonin metabolism (38).

From the gut, these inflammatory signals can reach the central nervous system through several pathways, and may activate the brain's resident immune cell microglia. When microglia become overactivated, this has been linked to changes in fear processing, which is relevant to PTSD (39). In addition, a reduction in butyrate-producing bacteria may weaken anti-inflammatory signaling. Some experimental studies show that giving SCFAs can restore microglial maturation and function in germ-free mice, suggesting that gut microbes help maintain normal neuroimmune balance (40). These findings support a potential role for gut microbiota in neuroinflammatory processes relevant to the disorder.

6.3 Metabolic and Neurotransmitter Pathways

Several neurotransmitter systems implicated in PTSD, particularly serotonin may be influenced by gut microbial activity through the metabolism of dietary substrates (41). Tryptophan is the sole precursor of serotonin, and the gut microbiome plays an important role in determining its metabolic fate. Under normal conditions, only a small proportion of dietary tryptophan is converted into serotonin, whereas most enters the kynurenine pathway. During inflammatory states, pro-inflammatory cytokines, particularly interferon-gamma, can activate indoleamine-2,3-dioxygenase, the rate-limiting enzyme of the kynurenine pathway (42). This shifts tryptophan metabolism away from serotonin synthesis and towards kynurenine metabolites, including quinolinic acid, which has neurotoxic properties via N-methyl-D-aspartate receptor overactivation and oxidative stress (43). An increased kynurenine-to-tryptophan ratio is widely used as an indicator of enhanced indoleamine-2,3-dioxygenase activity and inflammatory burden (44). Given the elevated inflammatory state often observed in PTSD, alterations in this pathway may potentially contribute to mood dysregulation and hyperarousal (45), although direct evidence remains limited.

Another possible mechanism involves Gamma-aminobutyric acid (GABA), which is the main inhibitory neurotransmitter in the central nervous system. Some bacterial groups including Lactobacillus and Bifidobacterium are able to produce GABA (46). At the same time, lower levels of Bifidobacterium have been reported in anxiety-related disorders (47). Beyond amino acid-derived neurotransmitters, the gut microbiome also produces SCFAs, particularly butyrate which act through distinct epigenetic mechanisms to influence brain function. Butyrate is produced by taxa including Faecalibacterium prausnitzii and Roseburia intestinalis, may influence neuroplasticity through inhibition of histone deacetylases and regulation of brain-derived neurotrophic factor (BDNF) (48). In animal models of PTSD, reduced hippocampal BDNF has been associated with impaired fear extinction (49). Therefore, reductions in some butyrate-producing bacteria reported in PTSD studies may have downstream implications for emotional regulation and neuroplasticity.

6.4 Neural Communication via the Vagus Nerve

The vagus nerve represents one of the important communication pathways between the gut and the brain. Approximately 80% of vagal fibers are afferent, transmitting signals from the

gastrointestinal tract to the nucleus tractus solitarius and subsequently to limbic, and cortical regions involved in emotional processing and threat detection (50). Several evidence suggest that vagal signaling may be relevant to PTSD. Clinically, PTSD is consistently associated with reduced heart rate variability which is commonly used indirect marker of vagal tone, indicated impaired parasympathetic regulation (51).

Experimental studies further support the vagus nerve is significant in microbiota-brain communication. In mice, administration of Lactobacillus rhamnosus JB-1 reduced anxiety-like behaviors and stress-induced corticosterone responses. However, these effects disappeared following vagotomy, suggesting that intact vagal signaling may be necessary for certain microbial influences on behavior (52).

The vagus nerve may also be relevant to fear extinction which is often impaired in PTSD. In animal models, vagus nerve stimulation has been shown to improve extinction learning and reduce PTSD-like behaviors (53). While it remains unclear whether microbiome-targeted interventions can achieve similar effects, these findings suggest that vagal pathways may represent a biologically plausible mechanism linking gut microbial activity to PTSD-related symptoms.

6.5 Integrative Model: A Putative Feedback Loop

When considered individually, each of the pathways described above provides only a partial explanation of how gut dysbiosis may relate to PTSD. Together, these findings suggest a possible self-reinforcing feedback loop between stress-related biological systems and the gut microbiome over time.

One potential pathway is as below: trauma exposure activates the HPA axis, leading to cortisol release (54). Cortisol may increase intestinal permeability, allowing bacterial products such as LPS to enter the bloodstream. In turn, this may trigger inflammatory responses and raise levels of pro-inflammatory cytokines. These cytokines can reach the brain through the bloodstream and via nerves. Once there, they may activate microglia. There is also evidence that these signals can reduce BDNF expression and push tryptophan metabolism toward the kynurenine pathway, away from serotonin.

Alongside these immune changes, chronic stress appears to shift the composition of gut microbes. Reductions in some butyrate-producing and GABA-producing taxa may weaken anti-inflammatory protection, change metabolite production, and disrupt gut–brain communication. Through a combination of inflammatory, neuroendocrine, metabolic, and neural mechanisms, these gut microbial changes may help maintain symptoms such as hyperarousal, impaired fear extinction, and emotional dysregulation. It should be noted that in chronic PTSD, basal cortisol levels are often low rather than high, reflecting enhanced HPA axis negative feedback. Whether cortisol-driven gut barrier disruption occurs mainly in the acute phase or persists in chronic PTSD remains an open question.

Importantly, this model (see Figure 1) remains hypothetical and has not been directly tested in PTSD. Still, it may help explain why PTSD treatments do not work equally well for all patients, if multiple systems are interconnected, targeting just one may not be enough to break the wider cycle. Future research could examine whether people exposed to prolonged or repeated trauma, including those meeting criteria for complex PTSD, show more persistent changes across these interconnected systems.

7. Therapeutic Implications: Microbiome-Targeting Strategies

The mechanistic evidence reviewed in previous sections raises a practical question: can targeting the gut microbiome improve outcomes in PTSD? At present, the answer is tentatively promising but the clinical evidence is still early-stage, and it would be premature to draw firm conclusions. This section reviews what is currently known about probiotics, dietary interventions, and their potential integration with existing PTSD therapies (figure 2).

7.1 Probiotics and Psychobiotics

Two recent clinical studies provided ideas for microbiome-targeted treatment in PTSD. Brenner, et al. (55) designed to test Lactobacillus rhamnosus GG in US military veterans with PTSD. The study used a randomized, double-blind, placebo-controlled design, with plasma high-sensitivity C-reactive protein as the primary outcome. This was intended to test whether Lactobacillus rhamnosus GG could reduce neuroinflammation, which is a process thought to contribute to PTSD symptom persistence. The trial planned to enroll 118 participants, making it one of the larger microbiome intervention studies in PTSD, but the published paper describes the

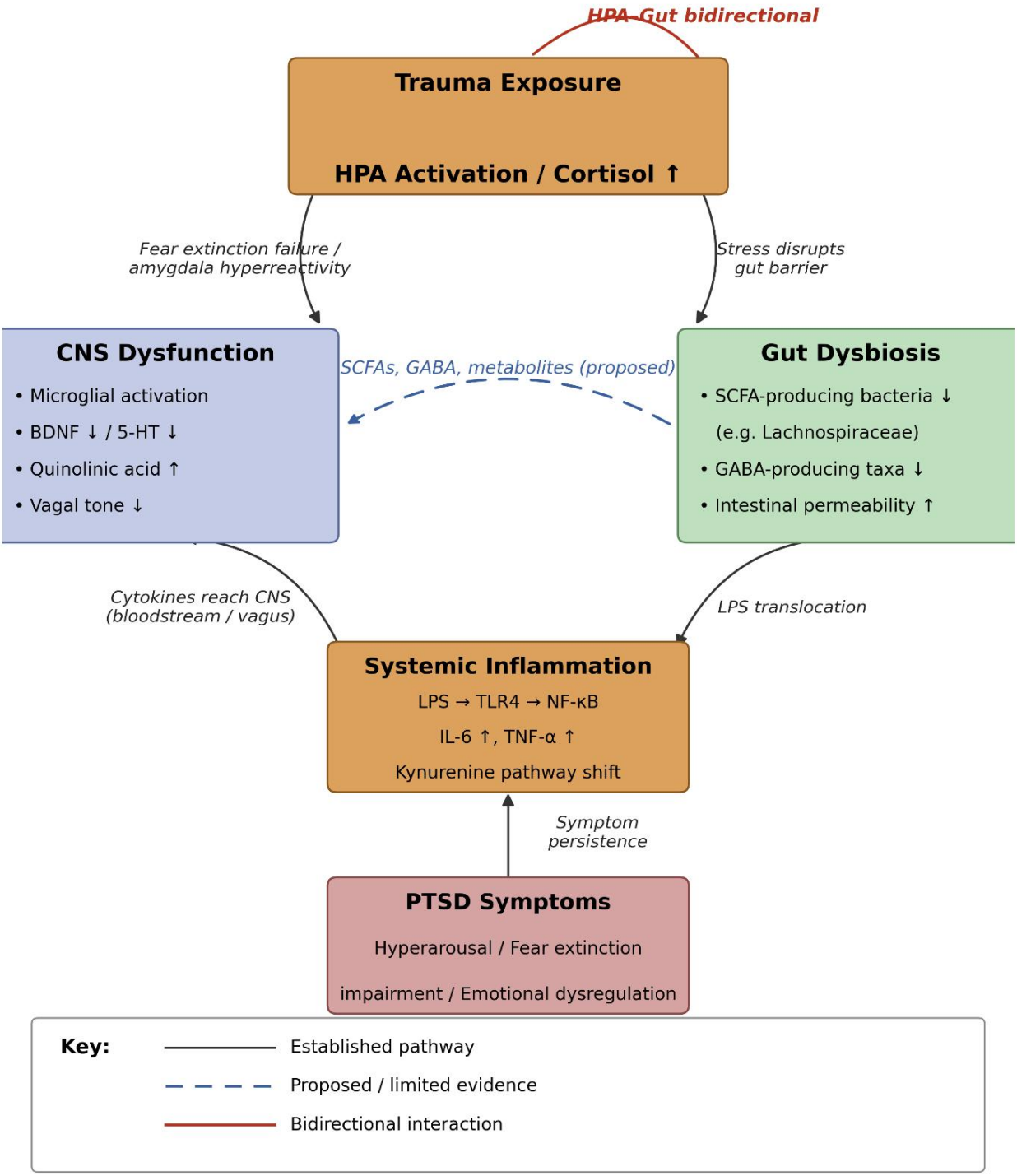


Figure 1. Proposed self-reinforcing gut–brain feedback loop in PTSD. Solid arrows indicate established pathways with supporting evidence from human and animal studies. Dashed arrows indicate proposed links for which direct evidence in PTSD remains limited or absent. The model illustrates how trauma-induced HPA axis activation may increase intestinal permeability, facilitating LPS translocation and systemic inflammation, which in turn may promote neuroinflammation, microglial activation, and amygdala hyperreactivity, processes associated with impaired fear extinction and symptom persistence. Concurrently, chronic stress may alter gut microbiota composition, including reductions in SCFA-producing and GABA-producing taxa, further weakening anti-inflammatory buffering and gut–brain communication. This model has not been directly tested in PTSD.

rationale and methods only; peer-reviewed results are not yet available at the time of writing.

Voigt, et al. (56) tested a different approach combining psychotherapy with a microbiome-targeted intervention. In this pilot trial, 70 veterans received CPT, with about half also taking a daily prebiotic fiber supplement for 12 weeks. The study found that PTSD symptom severity was associated with a lower abundance of propionate-producing bacteria. As a group, the prebiotic did not show a significant benefit over placebo beyond CPT, and both groups improved over time. Even so, the trial provides early evidence that prebiotics can modify gut microbiota composition in PTSD, and suggests that SCFA-related pathways, such as propionate production may be of interest in this disorder.

In conclusion, these studies are encouraging but limited. Both were small, and neither was powered to detect changes in PTSD symptom severity as a primary endpoint. The broader psychobiotics literature offers some support: in a general adult population with moderate psychological distress, a high-prebiotic diet improved anxiety and stress scores compared to placebo (57). However, this study did not involve PTSD participants. The field still lacks adequately powered trials with PTSD as the primary diagnosis and PTSD symptom reduction as the primary endpoint.

7.2 Dietary Interventions

Diet is a modifiable upstream factor that shapes gut microbiota composition, and several lines of evidence suggest it may be relevant to PTSD outcomes. In a cross-sectional study of 191 women, Ke, et al. (58) found that lower adherence to a Mediterranean diet was associated with more severe PTSD symptoms. This relationship appeared to be partly mediated by gut microbiome composition, such as Eubacterium eligens was positively associated with Mediterranean diet components and inversely associated with PTSD symptoms.

Omega-3 polyunsaturated fatty acids deserve particular attention in trauma-exposed populations. In a study of pregnant women, those with high adverse childhood experience scores who consumed more dietary omega-3s showed a dampened interleukin-6 response to acute stress compared with high-adverse childhood experience women with lower omega-3 intake. This suggests a possible protective effect in individuals with early-life trauma, which is a group at elevated risk for PTSD. Mechanistically, omega-3 polyunsaturated fatty acids have been shown to promote SCFA-producing taxa, including Bifidobacterium and Lactobacillus which may contribute to their anti-inflammatory effects (59). Dietary fiber acts as a prebiotic substrate for SCFA production. Given the consistent finding of reduced butyrate-producing bacteria in PTSD populations, increasing fiber intake is a straightforward and low-risk approach, one that is compatible with existing treatments and requires no prescription.

7.3 Integration with Existing PTSD Therapies

Microbiome-targeting interventions are unlikely to replace trauma-focused psychotherapy. The more realistic goal is adjunctive use, in order to help to create a neurobiological environment in which existing therapies can work more effectively.

Fear extinction learning is thought to be a core mechanism of exposure-based treatments such as Prolonged Exposure (60). This process depends on synaptic plasticity in the amygdala and hippocampus, which in turn relies on adequate BDNF expression . As reviewed in previous section, dysbiosis is associated with reduced SCFA production, which is linked to decreased BDNF. This suggests a plausible biological pathway by which restoring gut microbiota health through dietary fiber, prebiotics, or targeted probiotics. It could enhance the extinction learning that PE is designed to facilitate. Voigt, et al. (80) tested this logic directly, pairing a prebiotic with CPT to see whether microbiota modulation could augment therapy response.

This integrative approach may be especially relevant for people with complex trauma histories. Those with CPTSD whose disorder stems from prolonged, repeated trauma, often beginning in childhood, may show more persistent alterations in stress-related biological systems than those with single-incident PTSD. However, no study has directly compared gut microbiota or HPA axis function between PTSD and CPTSD, so this remains a hypothesis. Standard 12 to 16 sessions trauma therapies were not designed for this population, and dropout from trauma-focused treatments is substantial. A recent meta-analysis reported a pooled rate of 16% (13). A longer-duration microbiome intervention integrated with phase-based approaches that begin with stabilization before trauma processing, might be more appropriate for this group.

7.4 Critical Appraisal

It is unclear whether microbiome interventions are most beneficial in the acute aftermath of trauma, when HPA activation and gut permeability changes

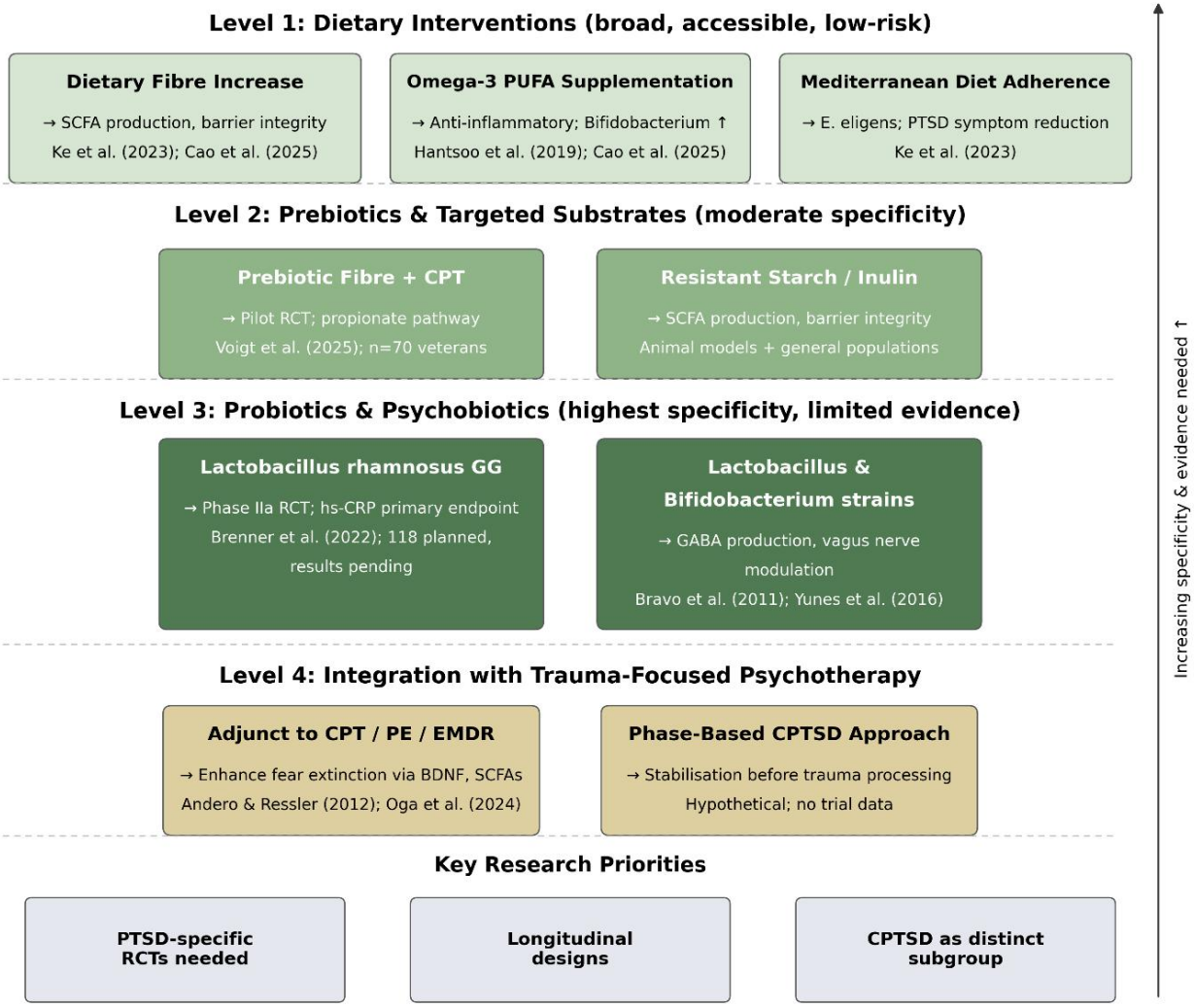


Figure 2. Microbiome-targeting therapeutic strategies for PTSD, organised by level of biological integration and strength of supporting evidence. Level 1 (Dietary Interventions): dietary fibre, omega-3 PUFA, and Mediterranean diet, broad, accessible, low-risk strategies with observational and mechanistic support but no PTSD-specific randomised controlled trial (RCT) data. Level 2 (Prebiotics): targeted fibre substrates to promote SCFA production, with one pilot RCT providing preliminary evidence in a PTSD population. Level 3 (Probiotics and Psychobiotics): strain-specific interventions including Lactobacillus rhamnosus GG, with one Phase IIa trial designed but results not yet published. Level 4 (Integration with Psychotherapy): adjunctive use of microbiome-targeted strategies alongside CPT, PE, or Eye Movement Desensitization and Reprocessing to enhance fear extinction. They all currently theoretical with no completed efficacy trials. Proposed CPTSD-specific interventions are included as a hypothetical direction. Darker shading indicates stronger direct evidence; lighter shading indicates more theoretical or indirect evidence.

are most pronounced or in chronic PTSD, where dysbiosis may be more entrenched. These may require different intervention strategies altogether, and current trials do not address this distinction.

8. Research Gaps and Future Directions

8.1 Longitudinal designs

Nearly all existing studies are cross-sectional, making it impossible to determine whether gut microbiota changes precede PTSD development or result from the disorder. Prospective cohort studies that track microbiota composition from the acute post-trauma period through the emergence (or absence) of PTSD symptoms are urgently needed.

8.2 Causal evidence in humans

While FMT studies in rodents provide proof-of-concept that stress-altered microbiota can transfer anxiety-like phenotypes, equivalent evidence in humans is absent. Randomized designs that manipulate the microbiome and measure downstream effects on PTSD-related processes are needed to move beyond association.

8.3 Multi-omics integration

Relying on 16S rRNA sequencing alone cannot capture functional changes in microbial metabolism. Future work should combine metagenomics with metabolomics to identify the specific microbial genes and metabolite pathways that are altered in PTSD.

8.4 Medication control

Psychotropic medications are known to alter gut microbiota composition. Studies should either recruit drug-naïve or monotherapy PTSD patients or systematically control for medication exposure as a covariate.

8.5 Sex differences

PTSD is more prevalent in women, and gut microbiota composition differs by sex. Some preliminary findings suggest that microbiome-targeted interventions may show sex-dependent effects, yet no study has been specifically designed to examine this.

8.6 PTSD-specific microbiome-targeted RCTs

No completed RCT has been designed with PTSD symptom reduction as a primary endpoint and adequate statistical power. Future trials should include both clinical and microbiome-related endpoints, with follow-up periods long enough to assess durability of effects.

In summary, complex PTSD represents an important gap in the current literature. To our knowledge, no study has directly compared gut microbiota composition between PTSD and CPTSD, and no clinical study has examined CPTSD as a separate subgroup. This is important because CPTSD is characterized by disturbances in self-organization, including difficulties with emotion regulation, negative self-concept and problems in relationships. These symptoms may provide useful and clinically relevant outcomes for future microbiome research. However, it remains unknown whether disturbances in self-organization symptoms are associated with specific microbial or metabolic profiles. Further research is needed to explore this possibility.

9. Conclusion

The picture from this review is more about promising signals than clear conclusions. Changes in the gut microbiota, especially lower levels of SCFA-producing bacteria, have been reported often enough in PTSD to be taken seriously. The pathways linking the gut and brain including inflammation, tryptophan metabolism, neural signaling, and the HPA axis, have also give a reasonable biological explanation for why these changes may matter. What is still missing is firm and reliable direct evidence: More longitudinal studies are needed which follow people from trauma exposure to later outcomes, larger trials that test whether changing the microbiome can improve PTSD symptoms, and research that separates different types of trauma and includes complex PTSD. Without this, the impact of gut microbiome in PTSD is still an interesting idea, but not yet a confirmed treatment target.

Declarations

1. ***Consent to publication***
   We declare that all authors agreed to publish the manuscript in this journal based on the signed Copyright Transfer Agreement and followed publication ethics.
2. ***Ethical approval and consent of participants***
   None.
3. ***Disclosure of conflict of interests***
   We declare that no conflict of interest exists in this work.
4. ***Funding***
   None.
5. ***Availability of data and material***
   Not applicable.
6. ***Authors' Contributions***
   Xiaoding Xie is the sole author and performed all aspects of the study, including conceptualization, literature search, evidence synthesis, and manuscript preparation.
7. **Acknowledgement**
   None.

8. Authors' biography

None.

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