Article's History: Received: 09.12.2024; Revised: 08.04.2025; Accepted: 27.05.2025

Bulletin of Medical and Biological Research

Vol. 7, No. 2
2025

DOI: 10.63341/bmbr/2.2025.21

Journal homepage: https://bmbr.com.ua/en

UDC 612.39:579.61

The impact of changes in gut microbiota on the body's ability to process gluten proteins: A mini review

Tetiana Popova*

PhD in Biological Sciences, Associate Professor
Dnipro State Medical University
49044, 9 Volodymyr Vernadsky Str., Dnipro, Ukraine
https://orcid.org/0000-0001-9627-330X

Mariia Kryvchykova

Student
Dnipro State Medical University
49044, 9 Volodymyr Vernadsky Str., Dnipro, Ukraine
https://orcid.org/0009-0002-6843-692X

Abstract. Gluten-sensitive disorders, including coeliac disease and non-coeliac gluten sensitivity, are common gastroenterological conditions characterised by impaired gastrointestinal function, systemic immune responses, and disruption of epithelial barrier integrity. This review aimed to provide a comprehensive analysis of the effects of gluten on the gut microbiota and to determine the role of the microbiome in the pathogenesis of these conditions. The analysis draws on findings from recent clinical studies, systematic reviews, and meta-analyses, as well as high-precision " next-generation sequencing techniques used to assess changes in bacterial and fungal communities of the gut microbiota at various stages of disease progression. It has been established that a gluten-free diet contributes to the partial restoration of microbial balance, in particular by reducing the number of pathogenic and opportunistic microorganisms associated with the development and persistence of chronic intestinal inflammation. At the same time, an increase in beneficial commensal microbiota – such as *Lactobacillus* and *Bifidobacterium* – has been observed. Special attention is given to the antimicrobial peptide cathelin-related antimicrobial peptide, which plays a key regulatory role in the immune response, controls the inflammatory process, and helps to maintain the homeostasis of the intestinal mucosa. The significance of the gutbrain axis has also been evaluated in the context of gluten-sensitive conditions, given that dysbiosis may influence patients' neuropsychological status, including the development of anxiety disorders, depression, and cognitive impairment. Potential therapeutic strategies are discussed, including the use of probiotics, prebiotics, postbiotics, and a diet low in fermentable oligo-, di-, monosaccharides and polyols (FODMAPs). It has been shown that diet exerts both direct and long-term effects on the composition and functional activity of the gut microbiota, which in turn modifies the clinical presentation of disease, symptom severity, and treatment outcomes. The practical value of this review lies in substantiating modern approaches to the diagnosis and treatment of glutensensitive disorders through targeted modulation of the intestinal microbiota. This opens new perspectives for personalised therapy, improvement of quality of life, prevention of complications, and restoration of patient health at a deeper – microbiome – level

Keywords: gluten intolerance; gluten-free diet; healthy nutrition; clinical nutrition; dysbiosis

INTRODUCTION

Gluten-related disorders (GRDs), such as coeliac disease (CD) and non-coeliac gluten sensitivity (NCGS), are closely linked to the composition and function of the gut microbiota. A gluten-free diet (GFD) remains the primary treatment, although it does not always fully restore microbial balance. In patients with CD, beneficial bacteria tend to decrease, while pathogenic bacteria increase – even when adhering to a GFD. Combining a GFD with other

Suggested Citation:
Popova T, Kryvchykova M. The impact of changes in gut microbiota on the body's ability to process gluten proteins: A mini review. Bull Med Biol Res. 2025;7(2):21–30. DOI: 10.63341/bmbr/2.2025.21

*Corresponding author

dietary strategies, such as a low-FODMAP diet, may alleviate symptoms more effectively. The gut microbiota plays a significant role in the development of GRDs by influencing both the immune system and the integrity of the intestinal barrier. Gluten-related disorders, including coeliac disease and non-coeliac gluten sensitivity, are increasingly recognised as important gastrointestinal and immunological conditions. Alterations in microbial composition not only affect intestinal health but also contribute to systemic inflammation and may even impact neuropsychological well-being. A deeper understanding of the interplay between gluten, diet, and the gut microbiome is essential for developing more effective, personalised treatment strategies and improving clinical outcomes.

D. Stanciu *et al*. [1] noted that GRDs occur in response to the consumption of gluten and related proteins found in wheat, barley, and rye. CD causes autoimmune damage to the intestinal mucosa, whereas NCGS does not involve an autoimmune response or structural mucosal changes. A GFD is the cornerstone of GRD therapy, although it can be difficult to maintain. Researchers have devoted considerable attention to the role of the gut microbiota in the pathogenesis of GRDs. I. Martín *et al*. [2] investigated the impact of a GFD in a group of 46 individuals with gastrointestinal complaints, migraines, and atopic dermatitis. They observed an increase in fungal diversity while the bacterial composition remained stable. A positive correlation was found between changes in fungal and bacterial diversity and shifts in species ratios after six weeks on a GFD.

G. Catassi *et al*. [3] highlighted the role of the microbiota in gluten-related conditions (CD, NCGS, wheat allergy). CD is associated with a reduction in *Lactobacillus* and *Bifidobacterium*, alongside an increase in *Bacteroides* and *E. coli*. NCGS is marked by reduced microbial diversity, an increase in *Ruminococcaceae*, and a decrease in *Bacteroidetes* and *Fusobacteria*. Notably, dysbiosis often persists despite adherence to a GFD. X. Wu *et al*. [4] reported that CD involves a compromised intestinal barrier, dysregulated immune response, and reduced gluten tolerance – all influenced by bacterial metabolites. While a GFD is the mainstay of treatment, probiotics may support the re-establishment of microbial balance. K. Naseri *et al*. [5] proposed combining a GFD with a low-FODMAP diet to relieve symptoms of irritable bowel syndrome (IBS). Microbiota imbalance is common in both IBS and gluten-sensitive conditions, further underlining the gut microbiome's pivotal role in gastrointestinal disorders. O. Gubska *et al*. [6] observed dysbiosis in CD and NCGS. In a study of 25 patients following a GFD, shifts in microbiota composition – specifically in *Bacteroidetes, Firmicutes,* and *Actinobacteria* – were correlated with the duration of dietary adherence, suggesting that diet is the primary driver of these changes. Z. Ren *et al*. [7] investigated the role of cathelicidin-related antimicrobial peptide (CRAMP) in CD. In mice, CRAMP deficiency exacerbated enteropathy, while supplementation helped to restore gut function and immune responses. Dysbiosis, characterised by an increased abundance of *Pseudomonas aeruginosa*, was found to reduce CRAMP expression, highlighting the microbiota's role in immune regulation.

This study aimed to conduct a comprehensive analysis of the impact of gluten on the composition and function of the gut microbiota and to determine the microbiome's role in the pathogenesis of gluten-related disorders. Coeliac disease and non-coeliac gluten sensitivity are common gastrointestinal conditions, marked by impaired intestinal function, immune dysregulation, and disruption of epithelial barrier integrity. To address these objectives, a detailed review of the literature was conducted using the PubMed, Medline, and Scopus databases. Publications including clinical data, experimental findings, and review articles were analysed. A systematic search strategy was employed using relevant keywords and search terms. Selection criteria included originality of data, presence of clinical or experimental results, and publication in Ukrainian or English. Studies lacking a control group in clinical trials, as well as those published only as conference abstracts or proceedings, were excluded. For the analysis of gluten's effects on gut microbiota, only sources published within the past five years (2020-2025) were considered.

THE IMPACT OF GLUTEN AND DIET ON THE GUT MICROBIOTA AND LOCAL IMMUNE MECHANISMS

Gluten-related disorders affect a substantial proportion of the population and present a complex clinical picture involving both immune and gastrointestinal dysfunction. Although a strict glutenfree diet remains the cornerstone of treatment, emerging evidence suggests that it may not be sufficient for all patients. Incorporating biotics – such as probiotics, prebiotics, synbiotics, and postbiotics – offers promising potential to restore microbial balance and enhance therapeutic outcomes. Advances in microbiome analysis are also paving the way for more personalised and effective approaches to both diagnosis and treatment.

P. Tiwari *et al*. [8] emphasised the importance of the gut microbiota in neurological disorders, particularly through the gut-brain axis. The intestinal microbiota performs several vital functions in the human body: it contributes to the metabolism of nutrients and pharmaceuticals, protects against pathogens, and modulates immune responses. The so-called gut-brain axis refers to the bidirectional relationship between the central nervous system and the gastrointestinal tract. It has been established that the gut microbiome influences various signalling pathways – neuroendocrine, immune, and neurotransmitter-mediated. Therapeutic interventions targeting the microbiota include probiotics, prebiotics, postbiotics, synbiotics, faecal microbiota transplantation, and antibiotics. Proper nutrition is considered critical for maintaining a healthy microbiota, which in turn can modulate the enteric nervous system and influence the progression of various neurological disorders. Understanding the mechanisms of interaction between the microbiota and the nervous system opens new avenues for the diagnosis and treatment of neurological diseases, particularly in the context of personalised medicine.

Q. Xie *et al*. [9] observed in their study that alterations in the gut microbiome and specific intestinal lumen factors are important markers in the development of gluten allergy. They also identified regulatory mechanisms involving distinct patterns of protein expression that contribute to the pathogenesis of this disorder. G. Caio *et al*. [10] examined the effect of a GFD on the microbiota in patients with CD and non-coeliac wheat/gluten sensitivity. They found that the diet influenced microbiota composition,

particularly the ratio between *Bacteroides* and *Bifidobacterium* species. C. Sabença *et al*. [11] conducted a review and noted that many misconceptions persist regarding the gluten-free diet. They emphasised the importance of accurately understanding and addressing such misconceptions in the dietary management of individuals with gluten-related conditions. O. Ogilvie *et al*. [12] investigated the impact of temperature and baking time on the structure of gluten proteins and the digestibility of peptides associated with coeliac disease. Their findings showed that these factors can significantly modify the nature of gluten peptides and their interaction with the digestive system.

M. Savarese *et al*. [13] reviewed the concept of "free-from" consumption, including glutenfree and lactose-free products. They identified key factors influencing consumer choices related to such products. I. Demirkesen & B. Ozkaya [14] analysed recent strategies for managing gluten-free diets and the development of compliant food products. They highlighted the importance of improving gluten-free production technologies to facilitate the lives of patients adhering to such diets. K. Arslain *et al*. [15] examined factors influencing the adoption of a GFD by individuals without CD or NCGS. They found that cultural and social influences, along with heightened health awareness, were the primary drivers. A. Jivraj *et al*. [16] reported that micronutrient deficiencies are common among adults following a gluten-free diet, regardless of its duration or adherence. They underscored the importance of micronutrient monitoring in these patients. A. Bakhshipour & R. Rafaiee [17] described cases of spontaneous latency in patients with coeliac disease after transitioning to a GFD. They investigated the diet's role in restoring intestinal function following prolonged gluten exposure. E.L. Transeth *et al*. [18] conducted a systematic review comparing the microbiome in patients with CD, NCGS, and irritable bowel syndrome. They observed notable differences in microbiota composition across the three groups.

The term "gluten-related disorders" refers to a spectrum of immune-mediated diseases triggered by gluten ingestion, primarily CD, NCGS, and wheat allergy. GRDs are associated with a broad array of clinical symptoms, affecting both gastrointestinal and extraintestinal systems, and may impact nearly any organ in genetically predisposed individuals following gluten exposure [1]. It is well established that gluten – or its components, such as gliadin (from wheat) or hordeins (from barley) – can provoke an immune response. While the elimination of gluten or even trace amounts is essential in managing GRDs, it is important not to overlook the nutritional role of grains, which are valuable sources of macro- and micronutrients and dietary fibre. Therefore, when excluding gluten-containing ingredients from the diet, it is crucial to ensure adequate nutrient intake in individuals adhering to a GFD. It has been suggested that gluten may influence molecules involved in gut permeability, such as zonulin. Moreover, when gluten is not properly hydrolysed, its peptides may be absorbed and trigger an immune-inflammatory response, leading to increased expression of Toll-like receptor 2 (TLR2), elevated levels of interferon-gamma (IFN-γ), and a higher presence of intraepithelial CD3+ T lymphocytes [2].

Although it remains unclear whether alterations in the human microbiota are a cause or a consequence of CD, these changes significantly affect intestinal function and correlate with the severity of clinical symptoms. Microorganisms play a vital role in various physiological processes, including fermentation, vitamin synthesis, pathogen inhibition, reinforcement of the gut barrier, and regulation of the immune system. In individuals adhering to a GFD, the composition of the intestinal microbiome tends to more closely resemble that of healthy individuals than of those who continue to consume gluten. Meta-analyses of GFD interventions [16] have revealed increased microbial diversity – particularly of *Bacteroides* and *Firmicutes* – in treated patients compared to those maintaining a gluten-containing diet.

At the same time, harmful taxa such as *Neisseria* and *Proteobacteria* appear less frequently in individuals following a GFD, suggesting a therapeutic benefit from dietary intervention. Nonetheless, *Bifidobacterium* levels remain consistently lower in Crohn's disease patients than in healthy controls, regardless of sample type, indicating that even long-term adherence to a GFD may not fully restore a healthy microbiota composition. *Bacteroides* species were found to be more prevalent in treated Crohn's patients than in controls – a potentially positive outcome, given their role in pathogen inhibition and in supporting the metabolic needs of other commensal organisms. *Lactobacillus* species also perform several beneficial functions in the gut, including the production of organic acids, antimicrobial activity, bile salt deconjugation, and suppression of carcinogens. Notably, *Lactobacillus* crispatus has been shown to promote anti-inflammatory responses in dendritic cells, offering therapeutic potential for inflammatory diseases such as Crohn's disease. Studies have reported significantly higher levels of *Lactobacillus* in patients on a GFD compared to untreated individuals. However, shifts in the species composition of *Lactobacillus* may go undetected if total abundance remains stable, underscoring the importance of species-level analysis in microbiome research [3].

Gliadin has been shown to activate both the innate and adaptive immune systems, thereby initiating intestinal inflammation through the induction of cytokines and chemokines. Specifically, gliadin is deamidated by tissue transglutaminase in the lamina propria of the small intestine, enabling it to bind to HLA class II DQ2/DQ8 molecules on antigen-presenting cells. This interaction activates T cells, macrophages, and dendritic cells, leading to the secretion of proinflammatory cytokines. This cascade triggers the adaptive immune response, resulting in the production of anti-endomysium, anti-gliadin, and anti-transglutaminase antibodies by B cells, thereby contributing to increased intestinal permeability. Beyond gliadin, the intestinal microbiota also plays a critical role in promoting inflammation within the intestinal mucosa of CD patients. Immune factors are well recognised as key contributors to CD, with adaptive immunity playing a central role in its pathogenesis. Research by X. Wu *et al*. [4] has demonstrated that the gut microbiota is closely linked to adaptive immunity and exerts significant regulatory influence on its two main branches – B cells and T cells. Intestinal microbes can enhance IgA production via B cell regulation and help maintain the balance between intestinal inflammation and immune tolerance by promoting the differentiation of Th17 and Treg cells. Gliadin contributes to the disruption of the intestinal barrier, facilitating

the overgrowth and translocation of pathogenic bacteria, which in turn leads to microbial imbalance. This dysbiosis further activates immune-inflammatory responses by modulating B and T cell activity. Inflammatory mediators may then exacerbate intestinal permeability by damaging epithelial cells, thereby worsening the severity of coeliac disease. Moreover, the mucosal immune response in CD may directly compromise the intestinal barrier, disrupting microbial homeostasis. The resulting dysbiosis acts as a pathogenic factor that fuels the progression of CD, thus establishing a vicious cycle of sustained inflammation.

Gluten intolerance refers to pathological conditions such as CD, wheat allergy (WA), and NCGS. Wheat allergy is a typical food allergy triggered specifically by wheat consumption rather than gluten itself and involves the activation of immune responses mediated by immunoglobulin E. The CD is an autoimmune condition that affects genetically susceptible individuals. It leads to damage of the small intestinal mucosa due to a T-cell-mediated immune response to gluten. NCGS is characterised by both gastrointestinal and extraintestinal symptoms associated with cereal consumption in individuals who do not have CD or WA. As there are no specific diagnostic tests, it is considered a diagnosis of exclusion. Importantly, NCGS does not cause intestinal damage or immune sensitisation to wheat proteins, which are characteristic features of CD and WA. According to research by K. Naseri *et al*. [5], the global prevalence of gluten-related disorders ranges from 1.1% to 1.7%, while wheat allergy occurs in approximately 0.2% to 1% of the population. Due to the absence of reliable diagnostic criteria and the limited number of population-based studies, the prevalence of NCGS is not well established, with estimates ranging from 1% to 13%. In Ukraine, no epidemiological studies have been conducted to determine the prevalence of CD or other glutenrelated disorders. A GFD is a nutritional approach that involves avoiding gluten-containing products or replacing them with gluten-free alternatives. It remains the only effective treatment for individuals diagnosed with coeliac disease. The microbiome, comprising microorganisms that reside on and within the human body, plays a vital role in maintaining health. The balance of intestinal bacteria is essential, and disruptions to this balance – known as dysbiosis – are commonly observed in various gastrointestinal disorders. These include both functional and organic digestive diseases, as well as conditions involving food sensitivities such as CD [6].

In the gastrointestinal tract, CRAMP is well recognised for its anti-infective properties. Z. Ren *et al*. [7] reported that, while its immunoregulatory roles in extra-intestinal diseases have gained attention, the involvement of CRAMP in gluten-induced small intestinal enteropathy – specifically in coeliac disease – remains largely unexplored. Using a mouse model of gluteninduced enteropathy (GIE), which mimics the small intestinal pathology of coeliac disease, they found reduced CRAMP production in the duodenal epithelium during GIE. Mice lacking CRAMP showed increased vulnerability to the development of GIE (Fig. 1).

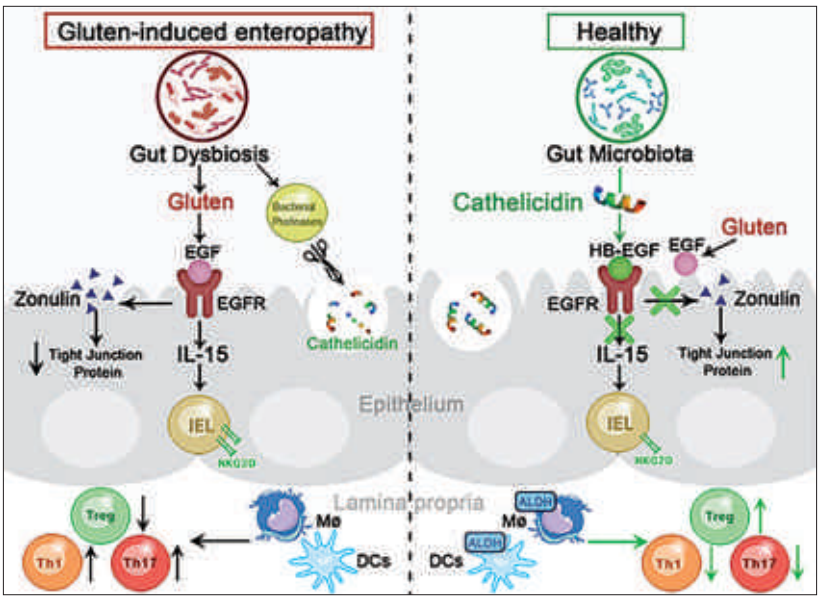

Figure 1. The protective function of cathelicidin-related antimicrobial peptide, influenced by gut microbiota in gluten-induced enteropathy

Notes: GIE-associated gut dysbiosis contributes to intestinal CRAMP degradation; CRAMP positively regulates intestinal barrier integrity and mucosal immune cell responses, offering protection against GIE; the CRAMP axis may therefore be targeted as a potential therapeutic strategy for coeliac disease

Source: [7]

Conversely, administration of exogenous CRAMP restored gliadin-induced epithelial dysfunction and enhanced regulatory immune responses within the intestinal mucosa. Furthermore, GIE-associated gut dysbiosis – marked by enrichment of *Pseudomonas aeruginosa* and its protease LasB – was found to contribute to impaired intestinal CRAMP production. These findings underscore the significance of the microbiota-CRAMP axis in

regulating intestinal barrier integrity and immune responses in GIE. Consequently, therapeutic modulation of CRAMP may offer a novel approach for the treatment of coeliac disease.

SYSTEMIC CONSEQUENCES OF DYSBIOSIS AND THE ROLE OF MICROBIOTA IN IMMUNE, NERVOUS AND NUTRITIONAL REGULATION

In this context, the gut-brain axis (GBA) has emerged as a compelling area of research, particularly in relation to the gut microbiota (GM), which has garnered increasing attention over the past five years (since 2020). The microbiome – comprising archaea, bacteria, protists, and fungi – resides in and on the human body and plays a critical role in maintaining the balance of the gastrointestinal tract microflora. Disruptions to this balance are associated with a range of pathological states, highlighting the importance of GBA-related microbiota in human health. Figure 2 provided an overview of the role of GM in neurological disorders and its modulatory impact on the GBA.

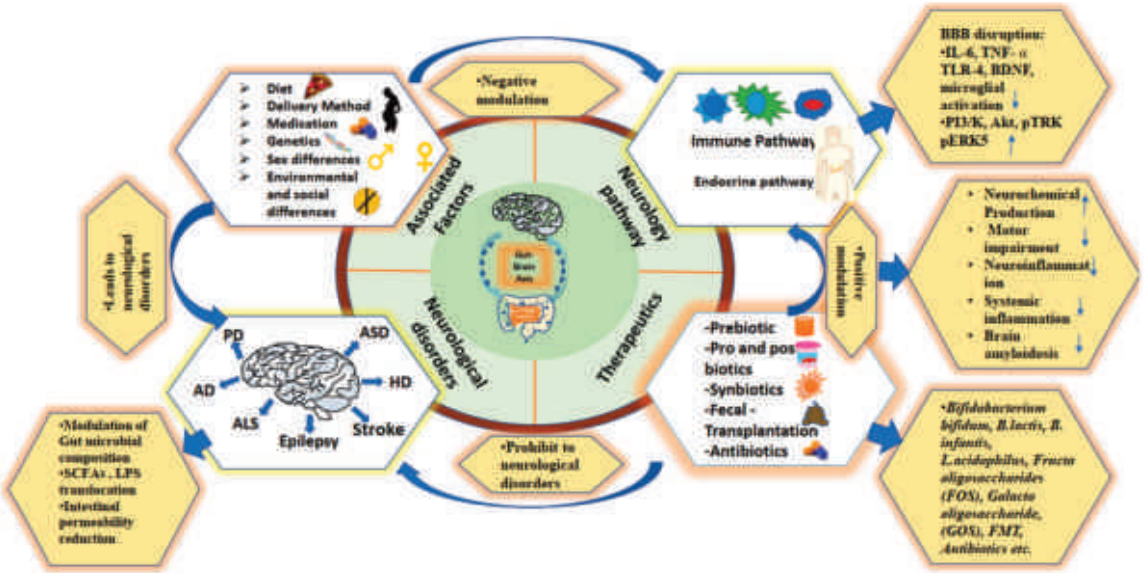

Figure 2. Overview of neurological disorders linked to the gut microbiota within the context of the gut-brain axis
Source: [8]

Several factors contribute to changes in GM composition within the GBA, which in turn influence neurological pathways and may lead to the development of various neurological disorders. These imbalances and dysfunctional microbial activities can potentially be regulated through interventions such as probiotics, prebiotics, synbiotics, postbiotics, antibiotics, and faecal microbiota transplantation (FMT). These approaches aim to modify the composition or function of the GM, thereby influencing brain function. Numerous studies [13, 18] support the view that the GM plays a crucial role in brain development and function. Both preclinical and clinical research has explored the gastrointestinal tract (GIT) microbiome within the GBA in relation to neurological conditions such as Alzheimer's disease (AD), multiple sclerosis (MS), Parkinson's disease (PD), autism spectrum disorder (ASD), epilepsy, stroke and brain injury, acute myeloid leukaemia (AML), Huntington's disease (HD), among others [8]. However, further in-depth research is required to fully elucidate the mechanisms by which the GM contributes to disease pathogenesis and its potential application in diagnostics and therapy.

The composition of the GM and its metabolites can disrupt the host's immune and endocrine systems, thereby influencing brain function and cerebral blood flow. To establish causal relationships, additional prospective and interventional studies are necessary. A considerable number of existing findings are derived from animal models, which may not always be applicable to human physiology. Moreover, human studies are often complicated by numerous confounding factors, including diet, demographics, socioeconomic status, sample collection protocols, clinical history, and genetic sequencing methods. Nevertheless, practical challenges remain in implementing microbial-based therapies, such as determining optimal dosages, treatment durations, and timing of interventions. It is also essential to identify the most appropriate patient populations, considering variables such as disease stage and age, in order to develop tailored therapeutic strategies. Furthermore, the effects of dietary components and microbe-derived metabolites on host physiology and overall health must be systematically evaluated [18].

Previous research by a group of scientists [9] on yoga, meditation, and yoga-based lifestyle interventions has shown that these practices can modulate stress-related biomarkers – including cortisol, interleukin-6, brain-derived neurotrophic factor, and reactive oxygen species – within six to eight weeks following intervention in patients with glaucoma and retinoblastoma. These interventions were associated with reduced oxidative stress and improvements in overall quality of life. While some evidence supports the beneficial neurological effects of yoga, its specific influence on GM composition and the abundance of beneficial microbial species within the GBA remains unclear. Another area requiring further investigation is the interaction between the GM and pharmacological treatments, as many patients

are subject to polypharmacy. Understanding GM-drug interactions is crucial for developing safe and effective microbiota-targeted therapies. In conclusion, the gut microbiota represents a critical interface between human health and neurological disease [8].

Anatomically, the gut maintains a complex and bidirectional communication with the central nervous system (CNS), a relationship commonly referred to as the gut-brain axis. This dynamic cross-talk plays a critical role in both health and disease. Sensory visceral signals originating in the gut are transmitted to the CNS primarily via the vagus nerve, influencing not only reflex responses but also cognitive and emotional processes such as mood regulation. In turn, the brain sends signals to modulate various gut functions, including motility, secretion, and immune responses (Fig. 3).

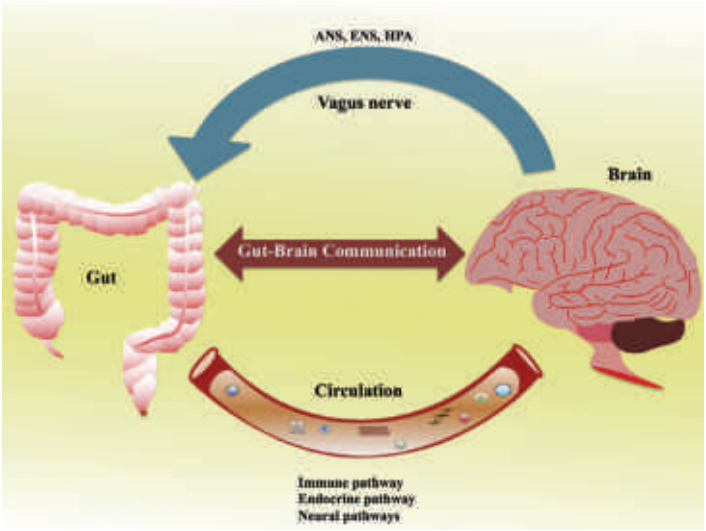

Figure 3. A schematic diagram illustrating the two-way communication between the gut and the brain
Source: [19]

This communication involves both afferent neurons, which transmit signals from the gut to the CNS, and efferent neurons, which send responses from the CNS back to the gut. These signals travel through multiple interconnected pathways, including the autonomic nervous system (ANS), the enteric nervous system (ENS), the hypothalamic-pituitary-adrenal (HPA) axis, the sympatho-adrenal axis, and descending monoaminergic pathways. Each of these systems is intricately interwoven and modulated by neurohumoral and inter-relational factors. Of particular importance, the ENS – often referred to as the "second brain" – is a complex network of neurons responsible for the intrinsic control of gastrointestinal function. It comprises two primary ganglionated plexuses: the myenteric plexus, which primarily regulates gut motility (e.g. peristalsis), and the submucosal plexus, which oversees secretory and absorptive processes within the gastrointestinal tract [19].

As of 2025, there is insufficient conclusive evidence regarding the extent to which gluten intake contributes to gastrointestinal symptoms in individuals who do not have coeliac disease. Patients on a gluten-containing (GC) diet often experience a significant exacerbation of symptoms such as fatigue and abdominal discomfort; however, the underlying mechanisms remain unclear. Notably, the effects of gluten have also been examined in individuals with IBS, particularly those with diarrhoea-predominant symptoms. Findings by O. Ogilvie *et al*. [12] suggest that gluten consumption increases stool frequency, an effect more pronounced in individuals carrying the HLA-DQ2 or HLA-DQ8 genotypes. The mechanisms by which gluten triggers symptoms in noncoeliac gluten sensitivity differ from those in coeliac disease and are not yet fully understood as of 2025. Current evidence [12] did not conclusively demonstrate abnormalities in adaptive immunity or increased intestinal permeability in NCGS. Despite this, NCGS is associated with signs of intestinal inflammation, such as elevated levels of interferon-gamma (IFN-γ) and a higher count of intraepithelial lymphocytes – findings that suggest enhanced immune activity within the gut lining. These observations imply that adaptive immunity may contribute to NCGS, while the involvement of innate immunity is also indicated, particularly through the possible activation of toll-like receptors (such as TLR-1 and TLR-2) implicated in its pathogenesis. Despite these insights, the condition remains controversial.

E.L. Transeth *et al*. [18] argued that NCGS is not a distinct clinical entity but rather a subset of IBS, given that roughly one-third of IBS patients report gluten sensitivity. They proposed that fermentable oligo-, di-, mono-saccharides and polyols (FODMAPs) are the true source of gastrointestinal symptoms in these cases. Nonetheless, NCGS is increasingly recognised as a separate clinical condition that shares symptomatic overlap with both IBS and CD but lacks the intestinal mucosal damage characteristic of CD [5]. Furthermore, distinguishing between food sensitivity and food intolerance is crucial for accurate diagnosis and treatment. Food intolerance typically involves gastrointestinal symptoms arising from the fermentation of poorly metabolised carbohydrates by the colonic microbiota, while food sensitivity refers to an immune-mediated reaction to dietary antigens that can cause both gastrointestinal and extraintestinal symptoms. Given these

distinctions, IBS and NCGS should be considered as separate disorders with overlapping clinical features, which complicate diagnosis and management [16].

Nutrition plays a critical role in maintaining gut health, which in turn is closely linked to immune and neurological function. In particular, there is growing interest in the findings of D.N. Koutzoumis *et al*. [20] regarding the role of the gut microbiota in the pathogenesis of neurodegenerative diseases such as Parkinson's disease (PD), using a rodent model. Their evidence indicates that gut dysbiosis may precede motor symptoms and contribute to neuroinflammation and dopaminergic neuron loss. In this study, using a 6-hydroxydopamine (6-OHDA) rodent model of PD, chronic treatment with non-absorbable antibiotics was shown to attenuate dopaminergic neuron degeneration and reduce neuroinflammatory markers in the striatum, accompanied by improved motor performance. These findings highlight a potential involvement of the gut microbiota in the pathophysiology of PD.

In individuals with coeliac disease, ingestion of gluten triggers a variable range of symptoms accompanied by inflammation of the small intestine. This immune-mediated response is characterised by villous atrophy and infiltration of inflammatory cells in the epithelial layer and lamina propria, which significantly impairs the functional capacity of the intestine. The resulting mucosal damage [21] often leads to malabsorption of essential nutrients, including iron, folate, vitamin B12, and zinc – contributing to the frequent observation of nutrient deficiencies at the time of CD diagnosis. As of 2024-2025, the only effective treatment for CD is lifelong adherence to a strict GFD, which generally permits mucosal healing of the small intestine within one to two years. However, even minimal exposure to gluten – intentional or inadvertent – can sustain intestinal inflammation and continue to impair nutrient absorption. Nutrient deficiencies in CD may also stem from the inherent limitations of the GFD itself. Processed gluten-free products have been shown by A. Jivraj *et al*. [16] to be lower in micronutrients such as iron and folate, with inconsistent fortification practices across the market. Consequently, individuals adhering to a GFD are at a greater risk of consuming a less nutrient-dense diet compared to those following a gluten-containing diet. A. Bakhshipour & R. Rafaiee [17] highlighted an increased risk of micronutrient deficiencies – particularly vitamins D and K, and iron – among individuals with coeliac disease, even those adhering to a gluten-free diet. However, the extent of these deficiencies and the roles of GFD duration, adherence, and persistent symptoms remain unclear. It is also uncertain whether such nutritional gaps are unique to CD patients or similarly affect non-CD individuals who follow a GFD.

In the digestive tract, gluten is broken down into gluten immunogenic peptides (GIPs), which cause coeliac disease. These peptides are resistant to complete digestion in the intestine and can interact with the immune system of coeliac patients, triggering an autoimmune reaction. Previously, there was no reliable way to objectively monitor gluten intake. However, a relatively new technique, developed by D. Stanciu *et al*. [1], enables the direct detection of GIP – specifically, gliadin epitopes equivalent to a 33-mer peptide – in urine and faeces after gluten consumption. This method uses monoclonal antibodies and is a non-invasive, highly sensitive, quantitative, and objective way to assess compliance with a gluten-free diet. The sensitivity of the test allows for the detection of even the smallest amounts of gluten – as little as 50 mg. However, the link between a positive GIP test result and the presence of villous atrophy has not yet been established, so it is not currently possible to assess intestinal damage using this marker. It should be noted that even among patients who claim to strictly adhere to dietary guidelines, unintentional dietary errors are common.

In a controlled study, M. Myhrstad *et al*. [22] also turned their attention to improving the nutritional quality of diets in specific populations, such as individuals with coeliac disease, who must strictly adhere to a gluten-free diet. This dietary restriction often results in reduced fibre intake, as many gluten-free products are low in dietary fibre and of poor sensory quality. A randomised controlled trial explored participants' experiences with fibre-rich gluten-free bread developed for the study, compared to commercially available gluten-free bread. Participants reported avoiding gluten-free bread prior to the study due to its unpleasant taste and texture, but expressed a preference for the fibre-rich wholegrain bread provided during the intervention. They emphasised the importance of satiety, texture, and palatability in gluten-free products, indicating a demand for higher-quality, fibre-rich alternatives. E.M. Domsa *et al*. [23] and L. Garnweidner-Holme *et al*. [24] underscored the central role of the gut microbiota as a mediator between dietary input and brain health. While antibiotic-induced modulation of the microbiota appears neuroprotective in PD models, dietary enrichment with fermentable fibre may offer a nonpharmacological avenue to promote a healthy microbiome.

Although the availability of gluten-free products has increased in recent years, individuals with CD continue to face multiple challenges in maintaining this diet. A study from Norway [25], using interpretative phenomenological analysis, highlighted the lived experiences of people with CD and revealed barriers to successfully following a gluten-free diet at the individual, interpersonal, community, and policy levels. Participants reported initial difficulties in acquiring knowledge about the GFD and expressed doubts about its nutritional adequacy. Social aspects – such as the fear of contamination and feeling different during shared meals – negatively affected their quality of life. At the community level, participants emphasised the limited availability and poor sensory quality of gluten-free products, while at the policy level, affordability emerged as a pressing concern. These findings underscore the need for comprehensive support for individuals with CD – from immediate post-diagnosis education to structural changes in food policy and product development.

Amid these challenges, pseudocereals such as quinoa, amaranth, and buckwheat have emerged as promising gluten-free alternatives due to their favourable nutritional profiles and natural absence of gluten, according to S. Graziano *et al*. [26]. These crops are rich in essential amino acids, fibre, and micronutrients, making them suitable for enhancing the dietary quality of glutenfree products. However, their broader adoption in the food industry faces significant constraints. The presence of anti-nutritional compounds and bitter-tasting substances can limit

palatability and necessitate processing methods that may be costly or environmentally burdensome. Additionally, agronomic limitations restrict large-scale cultivation to specific regions – often in developing countries where the risk of overexploitation and socio-economic inequity is high. The integration of biotechnological tools and sustainable breeding programmes is essential for enhancing the desirable traits of pseudocereals while protecting the livelihoods of smallholder farmers who maintain these crops' genetic diversity [27]. Taken together, these perspectives emphasised a dual imperative: improving the quality and accessibility of gluten-free products for individuals with CD, and advancing the responsible, sustainable development of alternative glutenfree crops such as pseudocereals. Efforts across the food industry, agriculture, policy, and public health must converge to ensure progress on both fronts.

CONCLUSIONS

It was found that gluten-sensitive disorders, such as coeliac disease and non-coeliac gluten sensitivity, significantly affect the state of the intestinal microbiota, causing an imbalance known as dysbiosis. This imbalance is characterised by a decrease in the number of beneficial bacteria – particularly *Lactobacillus* and *Bifidobacterium* – and an increase in opportunistic microorganisms, such as *Bacteroides* and *Escherichia coli*. The gluten-free diet, which is the primary method of treatment, contributes to the partial normalisation of this microbial balance, reducing pathogenic forms and increasing beneficial bacteria. However, even with adherence to the diet, complete restoration of a healthy microbiota does not always occur. Particular attention is given to the antimicrobial peptide CRAMP, which plays a key role in regulating the immune response, controlling inflammation, and maintaining the homeostasis of the intestinal mucosa. Reduced production of CRAMP in the duodenum is associated with gluten-induced enteropathy, and its exogenous administration has been shown to promote the restoration of epithelial function and enhancement of regulatory immune responses. It has also been found that the dysbiosis accompanying this pathology is characterised by an increase in *Pseudomonas aeruginosa*, which inhibits CRAMP synthesis. In addition, the importance of the gut-brain axis has been confirmed, as the intestinal microbiota performs key functions, including nutrient metabolism, protection against pathogens, and modulation of the immune response. Dysbiosis can influence the neuropsychiatric status of patients, including the development of anxiety disorders, depression, and cognitive impairment. Potential therapeutic strategies – such as the use of probiotics, prebiotics, postbiotics, and low-FODMAP diets – have been reviewed for their ability to modulate the composition and functional activity of the intestinal microbiota. Thus, the findings highlighted a complex interaction between gluten, the intestinal microbiota, and the immune system, emphasising the need for an integrated approach to the diagnosis and treatment of gluten-sensitive disorders. Future research should focus on the development of individualised therapeutic strategies through targeted modulation of the intestinal microbiota, as well as the refinement of diagnostic methods – such as the detection of gluten immunogenic peptides in faeces and urine – to enable objective monitoring of adherence to a gluten-free diet and the timely identification of latent disorders.

ACKNOWLEDGEMENTS

None.

FUNDING

None.

CONFLICT OF INTEREST

None.

REFERENCES

[1] Stanciu D, Staykov H, Dragomanova S, Tancheva L, Pop RS, Ielciu I, et al. Gluten unraveled: Latest insights on terminology, diagnosis, pathophysiology, dietary strategies, and intestinal microbiota modulations – a decade in review. Nutrients. 2024;16(21):3636. DOI: 10.3390/nu16213636

[2] Martín ISM, Oliva SL, Vilar EG, Niño GMS, Penadés BF, Lora AT, et al. Effects of gluten on gut microbiota in patients with gastrointestinal disorders, migraine, and dermatitis. Nutrients. 2024;16(8):1228. DOI: 10.3390/nu16081228

[3] Catassi G, Lener E, Grattagliano MM, Motuz S, Zavarella MA, Bibbò S, et al. The role of microbiome in the development of gluten-related disorders. Best Pract Res Clin Gastroenterol. 2024;72:101951. DOI: 10.1016/j.bpg.2024.101951

[4] Wu X, Qian L, Liu K, Wu J, Shan Z. Gastrointestinal microbiome and gluten in celiac disease. Ann Med. 2021;53(1):1797–805. DOI: 10.1080/07853890.2021.1990392

[5] Naseri K, Dabiri H, Rostami-Nejad M, Yadegar A, Houri H, Olfatifar M, et al. Influence of low FODMAP-gluten free diet on gut microbiota alterations and symptom severity in Iranian patients with irritable bowel syndrome. BMC Gastroenterol. 2021;21:292. DOI: 10.1186/s12876-021-01868-5

[6] Gubska OY, Kuzminets AA, Denesyuk OR, Koliada OK, Moseyko VV, Dolko OA. Features of the intestinal microbiome in patients with gluten-sensitive diseases who are on a gluten-free diet. Gastroenterology. 2023;57(2):96–100. DOI: 10.22141/2308-2097.57.2.2023.538

[7] Ren Z, Pan LL, Huang Y, Chen H, Liu Y, Liu H, et al. Gut microbiota-CRAMP axis shapes intestinal barrier function and immune responses in dietary gluten-induced enteropathy. EMBO Mol Med. 2021;13:e14059. DOI: 10.15252/emmm.202114059

[8] Tiwari P, Dwivedi R, Bansal M, Tripathi M, Dada R. Role of gut microbiota in neurological disorders and its therapeutic significance. J Clin Med. 2023;12(4):1650. DOI: 10.3390/jcm12041650

[9] Xie Q, Liu C, Fu W, Chen C, Luo D, Xue W. Combination of gut microbial features and the proteomic pattern revealed changes in specific intestinal luminal factors and mechanisms of their regulation of gluten allergy. J Agric Food Chem. 2023;71(33):12558–73. DOI: 10.1021/acs.jafc.3c02861

[10] Caio G, Lungaro L, Segata N, Guarino M, Zoli G, Volta U, et al. Effect of gluten-free diet on gut microbiota composition in patients with celiac disease and non-celiac gluten/wheat sensitivity. Nutrients. 2020;12(6):1832. DOI: 10.3390/nu12061832
[11] Sabença C, Ribeiro M, De Sousa T, Poeta P, Bagulho AS, Igrejas G. Wheat/gluten-related disorders and gluten-free diet misconceptions: A review. Foods. 2021;10(8):1765. DOI: 10.3390/foods10081765
[12] Ogilvie O, Roberts S, Sutton K, Gerrard J, Larsen N, Domigan L. The effect of baking time and temperature on gluten protein structure and celiac peptide digestibility. Food Res Int. 2021;140:109988. DOI: 10.1016/j.foodres.2020.109988
[13] Savarese M, Wismer W, Graffigna G. Conceptualizing "free-from" food consumption determinants: A systematic integrative literature review focused on gluten and lactose. Food Qual Prefer. 2021;90:104170. DOI: 10.1016/j.foodqual.2020.104170
[14] Demirkesen I, Ozkaya B. Recent strategies for tackling the problems in gluten-free diet and products. Crit Rev Food Sci Nutr. 2022;62(3):571–97. DOI: 10.1080/10408398.2020.1823814
[15] Arslain K, Gustafson CR, Baishya P, Rose DJ. Determinants of gluten-free diet adoption among individuals without celiac disease or non-celiac gluten sensitivity. Appetite. 2021;156:104958. DOI: 10.1016/j.appet.2020.104958
[16] Jivraj A, Hutchinson JM, Ching E, Marwaha A, Verdu EF, Armstrong D, et al. Micronutrient deficiencies are frequent in adult patients with and without celiac disease on a gluten-free diet, regardless of duration and adherence to the diet. Nutrition. 2022;103–104:111809. DOI: 10.1016/j.nut.2022.111809
[17] Bakhshipour A, Rafaiee R. Spontaneous latency in adult patients with celiac disease on a normal diet after gluten-free diet: Case series. Middle East J Dig Dis. 2022;14(3):354–8. DOI: 10.34172/mejdd.2022.295
[18] Transeth EL, Dale HF, Lied GA. Comparison of gut microbiota profile in celiac disease, non-celiac gluten sensitivity and irritable bowel syndrome: A systematic review. Turkish J Gastroenterol. 2020;31:735–45. DOI: 10.5152/tjg.2020.19551
[19] Suganya K, Koo BS. Gut-brain axis: Role of gut microbiota on neurological disorders and how probiotics/prebiotics beneficially modulate microbial and immune pathways to improve brain functions. Int J Mol Sci. 2020;21(20):7551. DOI: 10.3390/ijms21207551
[20] Koutzoumis DN, Vergara M, Pino J, Buddendorff J, Khoshbouei H, Mandel RJ, et al. Alterations of the gut microbiota with antibiotics protects dopamine neuron loss and improve motor deficits in a pharmacological rodent model of Parkinson's disease. Exp Neurol. 2020;325:113159. DOI: 10.1016/j.expneurol.2019.113159
[21] Hassan HF, Mourad L, Khatib N, Assi R, Akil S, El Khati S, et al. Perceptions towards gluten free products among consumers: A narrative review. Appl Food Res. 2024;4(2):100441. DOI: 10.1016/j.afres.2024.100441
[22] Myhrstad MCW, Slydahl M, Hellmann M, Garnweidner-Holme L, Lundin KEA, Henriksen C, et al. Nutritional quality and costs of gluten-free products: A case-control study of food products on the Norwegian marked. Food Nutr Res. 2021;65:6121. DOI: 10.29219/fnr.v65.6121
[23] Domsa EM, Berindan-Neagoe I, Para I, Munteanu L, Matei D, Andreica V. Celiac disease: A multi-faceted medical condition. J Physiol Pharmacol. 2020;71(1):3–14. DOI: 10.26402/jpp.2020.1.01
[24] Garnweidner-Holme L, Hellmann M, Henriksen C, Austad E, Watters SI, Gaundal L, et al. Experiences with gluten-free bread: A qualitative study amongst people with coeliac disease participating in a randomised controlled trial. Foods. 2023;12(23):4338. DOI: 10.3390/foods12234338
[25] Garnweidner-Holme L, Sende K, Hellmann M, Henriksen C, Lundin KEA, Myhrstad MCW, et al. Experiences of managing a gluten-free diet on multiple levels of society: A qualitative study. BMC Nutr. 2020;6:65. DOI: 10.1186/s40795-020-00390-3
[26] Graziano S, Agrimonti C, Marmiroli N, Gullì M. Utilisation and limitations of pseudocereals (quinoa, amaranth, and buckwheat) in food production: A review. Trends Food Sci Technol. 2022;125:154–65. DOI: 10.1016/j.tifs.2022.04.007
[27] Braun V, Clarke V. To saturate or not to saturate? Questioning data saturation as a useful concept for thematic analysis and sample-size rationales. Qual Res Sport Exerc Health. 2021;13(2):201–16. DOI: 10.1080/2159676X.2019.1704846

Вплив змін в кишковій мікробіоті на здатність організму переробляти білки глютену: міні огляд

Тетяна Попова
Кандидат біологічних наук, доцент
Дніпровський державний медичний університет
49044, вул. Володимира Вернадського, 9, м. Дніпро, Україна
https://orcid.org/0000-0001-9627-330X

Марія Кривчикова
Студент
Дніпровський державний медичний університет
49044, вул. Володимира Вернадського, 9, м. Дніпро, Україна
https://orcid.org/0009-0002-6843-692X

Анотація. Глютен-чутливі розлади, зокрема целіакія та нецеліакійна чутливість до глютену, є поширеними гастроентерологічними станами, що супроводжуються порушенням функціонування кишкового тракту, системної імунної відповіді та бар'єрної функції епітелію. Метою даної роботи стало всебічне вивчення впливу глютену на стан кишкової мікробіоти та визначення ролі мікробіому в патогенезі зазначених захворювань. У процесі аналізу використано результати сучасних клінічних досліджень, систематичних оглядів, метааналізів, а також високоточні методики секвенування нового покоління для оцінки змін у бактеріальному та грибковому складі кишкової мікрофлори на різних стадіях захворювання. Встановлено, що безглютенова дієта сприяє частковій нормалізації мікробного балансу, зокрема зменшує кількість патогенних та умовно-патогенних мікроорганізмів, пов'язаних із розвитком і підтриманням хронічного запального процесу в кишечнику. Натомість відзначається зростання представників корисної коменсальної мікрофлори, таких як *Lactobacillus* і *Bifidobacterium*. Особливу увагу приділено антимікробному пептиду Cathelin-related antimicrobial peptide, який виконує важливу регуляторну функцію в імунній відповіді, контролює розвиток запалення та забезпечує гомеостаз слизової оболонки кишківника. Також оцінено значення осі кишечник-мозок у контексті глютен-чутливих станів, з огляду на те, що дисбіоз може впливати на нейропсихічний статус пацієнтів, включаючи розвиток тривожних розладів, депресії та когнітивних порушень. Розглянуто потенційні терапевтичні стратегії, включаючи застосування пробіотиків, пребіотиків, постбіотиків, а також дієти з низьким вмістом ферментованих оліго-, ді-, моносахаридів і поліолів (FODMAP). Показано, що харчування чинить безпосередній і тривалий вплив на склад та функціональну активність кишкової мікробіоти, що, своєю чергою, модифікує клінічну картину захворювання, вираженість симптомів і ефективність терапії. Практична цінність огляду полягає в обґрунтуванні сучасних підходів до діагностики та лікування глютен-чутливих розладів шляхом цілеспрямованої модуляції кишкової мікробіоти. Це відкриває нові перспективи для індивідуалізованої терапії, поліпшення якості життя, запобігання ускладненням та відновлення здоров'я пацієнтів на більш глибокому – мікробіомному – рівні

Ключові слова: непереносимість глютену; безглютенова дієта; здорове харчування; клінічне харчування; дисбактеріоз