

Obsessive-Compulsive Disorder and the Gut Microbiota: The Microbiota–Gut–Brain Axis and Therapeutic Approaches

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Abstract

Obsessive-compulsive disorder (OCD) is a psychiatric disorder characterized by obsessions and compulsions that significantly impair functioning, affecting approximately 1–3% of individuals during their lifetime. The persistence of clinically significant symptoms in a sizable percentage of patients necessitates the development of novel treatment strategies despite existing pharmacological and psychotherapy methods. According to recent research, the pathophysiology of OCD may be significantly influenced by the gut-brain-microbiome axis, which characterizes the bidirectional communication between the gut microbiota and the central nervous system. This review examines the relationship between OCD and gut microbiota through the lens of short-chain fatty acids (SCFAs), neurotransmitter modulation, inflammatory pathways, and microbiota-derived metabolites. Through the hypothalamus-pituitary-adrenal (HPA) axis and the vagus nerve, neuroimmune and neurohumoral pathways mediate the reciprocal relationship between gut microbiota and OCD. According to research, OCD may be associated with dysbiosis, reduced microbial diversity, poor formation of SCFAs, and abnormalities in neurotransmitter systems like serotonin, dopamine, glutamate, and GABA. It is also reported that a Western-style diet, which is low in fiber, may contribute to this process by negatively affecting microbiota composition. It has been suggested that microbiota-based interventions, such as probiotics, prebiotics, synbiotics, and micronutrient supplements, may have potential regulatory effects on OCD symptoms. In conclusion, approaches targeting the gut microbiota appear promising for developing new complementary and supportive strategies in the treatment of OCD.

Keywords: Obsessive-compulsive disorder, Gut microbiota, Microbiota-gut-brain axis, Probiotics, Dietary patterns.

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1. Introduction

Obsessive-compulsive disorder (OCD) is a debilitating condition characterized by distressing, time-consuming, controlling obsessions and compulsions, affecting one to three out of every hundred people during their lifetime (Brock et al., 2024; Mahjani et al., 2021). The term egodystonic (inconsistent with the person's ideal self-image) for obsessions was first used in Diagnostic and Statistical Manual of Mental Disorders (DSM)-III to emphasize the distinction between psychotic thoughts and obsessions (Faraji et al., 2023). With the updates made to the DSM-5 and ICD-11 classification systems, OCD is positioned as a core component of the obsessive-compulsive and related disorders spectrum, which also includes body dysmorphic disorder, hoarding disorder, trichotillomania (hair pulling),

excoriation disorder (skin picking), and other related conditions (Fineberg et al., 2020).

Selective serotonin reuptake inhibitors (SSRIs), cognitive behavioral therapy, and exposure and response prevention are evidence-based first-line therapies for OCD. In patients with limited or no response, clomipramine, antipsychotics, and glutamate-modifying agents may be used in addition to these treatments. However, clinically significant symptoms persist in approximately half of patients despite current treatments (Wolf et al., 2025).

The World Health Organization lists OCD as one of the top ten most incapacitating conditions globally, with a lifetime prevalence of 0.8–3%. As such, OCD poses a serious threat to global health (Eghdami et al., 2025). The lifetime prevalence of OCD was found to be 4.1% in a study that was carried out between 2005 and 2019 utilizing data from ten countries and the DSM-IV diagnostic criteria. The 12-month prevalence was

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3%, which is nearly as high. Lifetime prevalence varies greatly between countries, ranging from as low as 0.4% to as high as 5.5%. The situation is very similar for the 12-month prevalence; it varies between 0.3% and 4.5% across countries. Additionally, when comparing high-income and lower-middle-income countries, the prevalence was found to be lower in high-income countries (Stein et al., 2025).

The most common subtypes of OCD in all societies are contamination and doubt obsessions and cleaning and control compulsions. These are followed by other subtypes of obsessions and compulsions, such as checking compulsions, sexual obsessions, religious obsessions, symmetry/ordering obsessions, obsessions about harm (to self or others), illness obsessions, hoarding compulsions which vary from country to country, and even within the same country, depending on the geographical region (Faraji et al., 2023). Individuals with contamination obsessions, in particular, live with the constant fear and stress of being contaminated by invisible microorganisms, dirt, or grime. Approximately 60% of individuals diagnosed with OCD have contamination obsessions. They feel compelled to avoid all environments they perceive as contaminated (schools, hospitals, hotels, etc.), and if they do not avoid them, they worry about being exposed to substances that are difficult to avoid, such as dust, germs, urine, feces, and semen (Faraji et al., 2023). Individuals experiencing contamination obsession also face difficulties in their daily habits. This is especially evident during food preparation. Due to fear of contamination and concerns about wasting time, individuals may turn to packaged foods, which are perceived as more practical and controlled, and generally low in fiber and nutritional value. This dietary pattern has the potential to negatively impact the gut microbiota (Chen et al., 2023; Chen et al., 2021; Grassi & Pampaloni, 2024). The gut microbiota is a complex ecosystem consisting of trillions of microorganisms found in the gastrointestinal system (Al Bander et al., 2020). Because of its genetic diversity and metabolic capacity, the gut microbiota is referred to as the "second brain" and "second genome" of the human body (He et al., 2025). In recent years, there has been increased interest in the effects of the microbiota on brain function and behavior via the brain-gut-microbiome axis (Eghdami et al., 2025). The gut microbiota communicates bidirectionally with the brain via neuroimmune, neuroendocrine, and neural pathways, and these interactions can modulate brain development and function (Dai et al., 2025).

In patients with OCD, specific dietary habits that can affect microbiota composition are observed. In particular, low dietary fiber intake and restrictive eating behaviors due to fear of contamination can reduce dietary diversity and negatively impact the support of beneficial gut bacteria that produce short-chain fatty acids (SCFAs). The fact that the effects of diet on the gut microbiota can appear quickly and

persist for a long time suggests that this relationship is an important environmental factor to consider in the pathophysiology of OCD (Johnson et al., 2019; Nguyen et al., 2021).

A better understanding of the relationship between gut microbiota and OCD is known to contribute to elucidating the pathophysiology of the disease, as well as developing new microbiota-targeting treatment strategies such as probiotics, prebiotics, synbiotics, fecal microbiota transplantation, and nutrition-based approaches (Grassi & Pampaloni, 2024). Therefore, a comprehensive evaluation of the existing evidence is needed. The aim of this review is to comprehensively examine the relationship between gut microbiota and OCD, the possible underlying mechanisms, and microbiota-based intervention studies conducted to date, in light of current literature.

2. Method

This narrative review examines the relationship between obsessive-compulsive disorder, gut microbiota, and diet-based treatment approaches. Relevant literature was comprehensively searched using the PubMed, Google Scholar, ScienceDirect, and Elsevier databases. The keywords "obsessive-compulsive disorder", "gut microbiota", "gut-microbiota-brain axis", "probiotics", "dietary pattern", "ketogenic diet", "nutrition", and "vitamins" were used during the search process which was conducted between November 2025 and June 2026. The publications included in the review consist of systematic reviews and meta-analyses, human and animal studies.

3. Gut Microbiota: The Microbiota-Brain Axis

The early 1900s laid the foundation for microbiota research, revealing that numerous microorganisms—including bacteria, yeasts, and viruses—coexist in various parts of the human body, such as the gut, skin, lungs, and oral cavity. Furthermore, the human microbiota, also known as the "hidden organ," provides 150 times more genetic information than the entire human genome (Hou et al., 2022).

By improving the host's capacity for digestion, shielding the intestinal epithelial barrier from harm, and limiting pathogen invasion, the gut microbiota plays a critical role in preserving human health. Bacteria dominate the diverse microbial ecosystem of the human gut, representing over 99% of the total content (Zhao et al., 2023). In terms of overall bacterial content, the bacterial phyla *Bacteroidota* and *Bacillota* are dominant in the human gut, representing approximately 90% of the total bacterial abundance in many individuals, while *Pseudomonadota* is dominant in a small number of people (McCallum & Tropini, 2024). Damage to this

gut ecosystem is called dysbiosis. Increased intestinal permeability and the movement of bacterial lipopolysaccharides (LPS) can result from dysbiosis. This can cause systemic inflammation, which can then spread to the Central Nervous System (CNS) through compromised blood-brain barrier integrity. These gut disturbances can potentially pose a risk to the host's health due to numerous intestinal diseases such as intestinal candidiasis, Crohn's Disease, ulcerative colitis, pseudomembranous enteritis, and inflammatory bowel disease, as well as food allergies and intolerances or colorectal cancer, and various neurological, respiratory, metabolic, hepatic, and cardiovascular disorders (Eghdami et al., 2025; Góralczyk-Bińkowska et al., 2022; Wong & Yu, 2023). The microbiota profoundly influences both systemic physiology and mental health. Disruptions in the composition of the gut microbiota (dysbiosis) can alter the production and availability of SCFAs. Consequently, dysbiosis can affect brain function and intestinal barrier integrity, potentially triggering conditions such as anxiety and even obsessive-compulsive disorder (Bendriess et al., 2023).

Diet is considered one of the most influential environmental factors shaping the composition of the gut microbiota. Specifically, the fat, carbohydrate, protein, and fiber content of the diet, as well as the dietary pattern, significantly shapes the diversity of the gut microbiota and the distribution of dominant bacterial communities (Flynn et al., 2023). Dietary modifications can quickly change the composition of the microbiota, impacting the synthesis of microbial metabolites, the function of the gut barrier, and neurophysiological processes through the gut-brain axis. Therefore, nutrition is considered one of the most important modifiable determinants of the microbiota (David et al., 2014; Sonnenburg & Bäckhed, 2016).

3.1. Interaction Between OCD and Gut Health

OCD is the second most prevalent psychiatric comorbidity among patients with functional bowel disorders, accounting for about 20% of cases. Similarly, the prevalence of gastrointestinal disorders in patients with OCD ranges from 15% to 35% (Abdelnaim et al., 2025).

The time-consuming nature of obsessions and compulsions can also affect individuals' food preferences and alternatives. To avoid specific symptoms such as the risk of contamination or the danger of harming others using a knife, patients with OCD may prefer ready-to-eat foods with lower fiber content or microwaveable options (Chen et al., 2023). In contrast, it has been reported that a fiber-rich Mediterranean diet may reduce depressive symptoms and improve overall mental health (Parletta et al., 2019; Psaltopoulou et al., 2013). Furthermore, increased dietary fiber is converted by the gut microbiota into SCFAs particularly butyrate and these metabolites are associated

with anti-inflammatory and neuroprotective effects (Chen et al., 2023).

Compulsions such as excessive washing and cleaning can affect microbiota diversity by reducing individuals' contact with environmental microbial diversity. Individuals with OCD may develop dietary restrictions and changes due to avoidance of post-defecation habits or fear of contamination. While these behaviors can reduce the frequency of bowel movements, increased anxiety can affect bowel motility, leading to diarrhea in some individuals. Furthermore, excessive straining in an attempt to achieve a feeling of "complete emptying" can increase the risk of hemorrhoids and rectal prolapse. Excessive and inappropriate use of laxatives may also be observed in these individuals, negatively impacting the gut microbiota composition. In addition, individuals with OCD may restrict fluid intake. This can increase the risk of chronic kidney failure, cause constipation, and subsequently affect the composition of the gut microbiome (Grassi & Pampaloni, 2024).

4. Microbiota And OCD: Bidirectional Communication

There is complex, bidirectional communication between OCD and the gut microbiota along the brain-gut-microbiome axis. This bidirectional communication is mediated by specific microbial products—including SCFAs, cytokines, and neurotransmitters—via the hypothalamic-pituitary-adrenal (HPA) axis and vagus nerve pathways (Figure 1). Through complex neurohumoral pathways, signals originating from the brain can alter the sensorimotor and secretory functions of the gut, while visceral afferent signals from the gastrointestinal tract can modulate brain function (Dalile et al., 2019).

The metabolic pathway involves the release of microbiota-derived products into the systemic circulation; these products—which include SCFAs, neurotransmitters, hormones, and inflammatory factors—arise from the metabolic activity of microorganisms and regulate central nervous system function either directly or indirectly (Cryan et al., 2019; Sharon et al., 2016). Dopamine, acetylcholine, γ -aminobutyric acid, norepinephrine, serotonin, and corticotropin-releasing hormone are among the neurotransmitter precursors and hormones that have been demonstrated to be produced by a variety of gut bacteria. In addition to producing peripheral serotonin, gut microorganisms can also influence central serotonin transmission by modulating plasma tryptophan production (Bendriess et al., 2023). Signals from the gut to the central nervous system are transmitted via the vagus nerve. When gut bacteria modulate the production of neurotransmitters such as γ -aminobutyric acid, serotonin, dopamine,

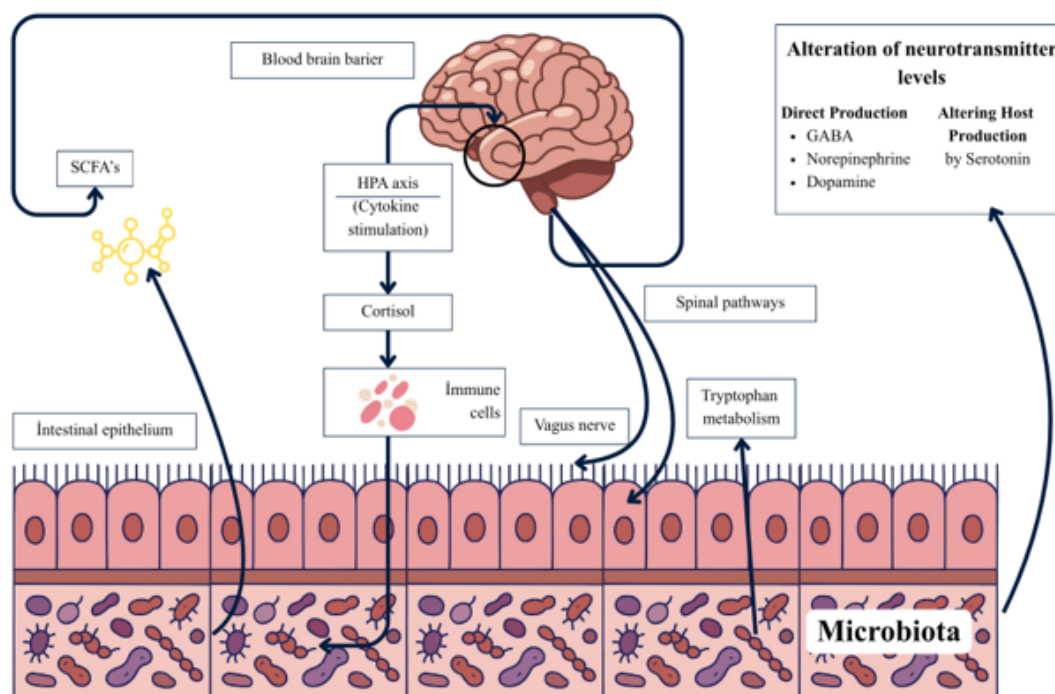


Figure 1. Diagrammatic illustration of the bidirectional communication that occurs between the immune system, endocrine system, central nervous system, enteric nervous system, and spinal cord pathways and the microbiota-gut-brain axis.

Source: Adapted from Banerjee et al. (2021)

norepinephrine, glutamate, and acetylcholine, these can bind to primary afferents of the enteric nervous system and the vagus nerve, influencing brain function and behavior (Breit et al., 2018).

OCD-related behaviors, such as excessive cleaning, restricted eating, and fluid intake, reduce microbial diversity; this disrupted gut balance triggers OCD symptoms, creating a reciprocal cycle. This reveals a bidirectional interaction between the gut and the brain, mutually influencing each other (Grassi & Pampaloni, 2024).

In a study by Turna et al. involving 21 patients with OCD and 22 healthy controls, analysis of stool and blood samples revealed that, compared with controls, the OCD group exhibited reduced α -diversity and lower abundances of the three butyrate-producing genera *Oscillospira*, *Odoribacter*, and *Anaerostipes*, alongside elevated CRP levels, with no significant differences in IL-6 or TNF- α (Turna et al., 2020). Butyrate deficiency compromises both intestinal barrier integrity and microglial homeostasis (Eghdami et al., 2025).

In a study by Domènech et al., 16S rRNA gene-based metagenomic sequencing of 32 patients with OCD and 32 healthy controls showed that OCD patients had a trend toward reduced bacterial α -diversity, accompanied by an increased abundance of the genus *Alistipes* (*Rikenellaceae*) and decreased abundances of *Agathobacter* and *Coprococcus*, particularly within the *Prevotellaceae* and

Lachnospiraceae families (Domènech et al., 2022). In a study by Zhang et al., stool samples from patients with OCD were transplanted into mice free of specific pathogens. Full-length 16S rRNA sequencing was used to examine the fecal microbiota. Mice that underwent fecal transplantation showed neuronal degeneration in certain brain regions and inflammation in the colon. An increase in succinic acid levels was observed in the transplanted mice. This increased succinic acid level inhibits neural activity in the brain and causes inflammation in the colon, thereby increasing intestinal permeability (Zhang et al., 2024). In summary, OCD is characterized by a dysbiotic profile, marked by decreased α -diversity of the gut microbiota and a reduction in butyrate-producing bacteria. These changes are thought to contribute to the pathophysiology of OCD by influencing neuroinflammatory processes through impaired gut barrier integrity and increased systemic inflammation. However, it is not yet definitively clear whether microbiota changes are a cause or a consequence of OCD, and further research is needed in this area.

4.1. Gut-Brain Axis Mechanisms in the Pathophysiology of OCD

The gut–brain axis operates through multiple interconnected pathways that directly relate to established OCD pathophysiology. Mechanistically, gut microbiota produce

SCFAs that maintain intestinal barrier integrity and possess potent anti-neuroinflammatory properties. Specific bacterial strains synthesize or metabolize key neurotransmitters involved in OCD. The vagus nerve facilitates direct neural communication between the gut and the brain, transmitting signals capable of regulating the HPA axis and influencing microglial activation (Eghdami et al., 2025).

4.1.1. The Role and Barrier Function of SCFAs

The synthesis of SCFAs through microbial breakdown of fiber in the large intestine is the primary function by which the gut microbiota contributes to host health. Key SCFAs, including acetate, propionate, and butyrate, play a role in maintaining intestinal barrier integrity, neurotransmitter production, and immuno-inflammatory regulation (Bruun et al., 2024). Specifically, butyrate contributes to maintaining intestinal barrier integrity by increasing the expression of tight junction proteins such as zonula occludens-1, claudin-5, and occludin, and suppresses zonulin-mediated permeability increase. A reduction in butyrate levels can lead to increased intestinal permeability and a state of dysfunction by causing an increase in epithelial permeability (Bendriess et al., 2023). In a microbiome study conducted in patients with psychiatric disorders and a healthy control group, butyrate-synthesizing bacteria were found to be at lower levels in the group with psychiatric disorders (Chen et al., 2021).

SCFAs are microbial metabolites that play a critical role in regulating gut metabolism and are important mediators of gut-brain axis interaction. In dysbiosis, decreased SCFAs production leads to impaired intestinal barrier function and increased intestinal permeability, resulting in systemic inflammation and potential neuroinflammatory processes (Bendriess et al., 2023).

Increased intestinal permeability, particularly allowing LPS from gram-negative bacteria to pass into the systemic circulation, triggers the release of pro-inflammatory cytokines and contributes to low-grade chronic inflammation. Intestinal barrier integrity can be affected by various factors such as psychological stress, oxidative stress, and pro-inflammatory cytokines, leading to neuroinflammation (Zengil & Laloğlu, 2024). In conclusion, it has been shown that alterations in the gut microbiota can influence the gut–brain axis through SCFAs production and barrier function, and that these mechanisms may be associated with the onset or exacerbation of psychiatric symptoms (Huang et al., 2019; Kılıç et al., 2020; Shen et al., 2018).

4.1.2. Microbiota-Derived Neurotransmitter Modulation

Specific bacterial species can modulate neurological processes by playing a role in the synthesis and metabolism of key neurotransmitters associated with OCD. The balance

of neurotransmitters such as serotonin, dopamine, glutamate, and γ -aminobutyric acid (GABA), which influence the development of compulsive behaviors in OCD, is shaped by microbiota composition. Enterococcus and Bacillus species contribute to dopamine production, while Lactobacillus species can synthesize GABA. Several different classes also affect serotonin metabolism via the tryptophan-kynurenine pathway (Eghdami et al., 2025).

It has been demonstrated that in OCD patients, dysregulation of the serotonergic system responsible for obsessive behavior results from malfunction of the orbitofrontal cortex, which is involved in emotion processing and decision-making. Enterochromaffin cells (EC) and neurons of the Enteric Nervous System (ENS) synthesize serotonin, while Escherichia Coli and various species of Lactococcus, Lactobacillus, Streptococcus, Morganella, Klebsiella, Hafnia, Bacteroides, Bifidobacterium, Propionibacterium, Eubacterium, Roseburia, and Prevotella can influence serotonin production and metabolism in the gut (Kamble & Dandekar, 2023). SCFAs are able to regulate the levels of tyrosine hydroxylase and tryptophan hydroxylase 1, a rate-limiting enzyme involved in serotonin production (Bendriess et al., 2023).

Dopamine plays a role in habit formation and reward-based learning, and its imbalance is known to trigger OCD (Mota et al., 2026). Bacteroides uniformis increases dopamine transporter (DAT) expression, while Prevotella copri decreases it. Lactobacillus Plantarum PS128 increases DAT expression, while some Ruminococcaceae species have been shown to decrease D2 receptor activity. Additionally, Ruminococcus species have been reported to be associated with decreased activity of tyrosine hydroxylase, a rate-limiting enzyme involved in dopamine production. Various microorganisms from the genera Prevotella, Bacteroides, Lactobacillus, Bifidobacterium, Clostridium, Enterococcus, and Ruminococcus can modulate receptors, transporters, and specific targets of dopaminergic pathways (Kamble & Dandekar, 2023).

The gut microbiota can produce GABA by processing the amino acid glutamate. Lactobacillus brevis and Bifidobacterium dentium can increase GABA levels by breaking down monosodium glutamate. These neurotransmitters can regulate neural signaling in the ENS and also alter brain function by affecting epithelial cells (Kamble & Dandekar, 2023).

4.1.3. Pathways by Which the Gut Microbiota Modulates the CNS

The vagus nerve, which controls the HPA axis and modulates microglial activity, facilitates direct neurological communication between the gut and the brain. This transmission works in conjunction with neuroinflammatory processes, neurotransmitter imbalances, the role of

microbial metabolites as histone deacetylase inhibitors, and epigenetic alterations. All these mechanisms are clustered in OCD-specific neural networks encompassing cortico-striato-thalamo-cortical circuits (Eghdami et al., 2025).

The HPA axis, immune system modulation, and stress management are all significantly impacted by the gut microbiota. Stress is known to alter the composition of the gut microbial population in social experimental models. Activation of the HPA axis following OCD increases cortisol production, which in turn affects immune cells, leading to increased levels of pro-inflammatory cytokines. Elevated systemic cytokine levels cause increased gut permeability and disruption of the gut microbiota. The gut microbiota can also modulate CNS function by producing neuroactive compounds such as GABA, norepinephrine, dopamine, and serotonin, tryptophan, and microbial metabolites such as SCFAs (Kamble & Dandekar, 2023).

4.2. OCD and Neurotransmitters

4.2.1. Serotonin

Serotonin plays a critical role in inhibiting compulsions and supporting the individual's adaptation to changing environmental conditions. Accordingly, imbalances in the serotonergic system are known to significantly contribute to the emergence of repetitive behaviors specific to OCD (Yin et al., 2024). When examined at the receptor level, functional changes in Serotonin 1B and 1D receptors, in particular, appear to play a role in increasing the severity of OCD symptoms (Gargano et al., 2023). In the context of neuroinflammatory pathways, it has been observed that tryptophan, a precursor of serotonin, is generally decreased in individuals with OCD, while levels of kynurenine and quinolinic acid, degradation products of tryptophan, are usually increased in the same individuals (Eghdami et al., 2025). Because of this loss of function and imbalance in serotonergic tone, SSRIs, which increase serotonin levels in the synaptic cleft by blocking serotonin reuptake in the brain, are considered first-line pharmacological agents in the treatment of OCD (Singh et al., 2023).

4.2.2. Dopamine

Dopamine is a crucial neurotransmitter involved in various brain functions, including learning, reward, motor control, emotion, and executive function. The basal ganglia, particularly the striatum, are integral to habit formation and reward-based learning. In OCD, dysregulated dopaminergic signaling can disrupt these processes, contributing to the development and maintenance of compulsive behavior despite its negative impact on an individual's daily functioning (Mota et al., 2026).

The molecular basis of OCD lies in the unbalanced interaction of different receptor subtypes (D1, D2, and D3) to which dopamine binds. Literature shows that quinpirole, an

agonist of D2 and D3 receptors, triggers repetitive behaviors associated with OCD in rodent models. Similarly, excessive stimulation of D1 receptors, another subtype, has been observed in OCD patients. Experimental studies have shown that when the activity of D1 receptors is pharmacologically inhibited, OCD-like behaviors decrease significantly. In light of this data, it is considered that the irrational and dysfunctional nature of repetitive behaviors in OCD is directly related to the increase in dopamine occurring in the right nucleus accumbens, the brain's reward center (Gargano et al., 2023; Singh et al., 2023).

4.2.3. Glutamate

Glutamate is a key excitatory neurotransmitter in the adult central nervous system and also plays a critical role as a precursor molecule in the biosynthesis of GABA, glutamine, and glutathione, which exhibits antioxidant properties. Altered glutamate levels affect OCD; higher levels of glutamate in cerebrospinal fluid have been shown in individuals with OCD (Karthik et al., 2020). In a study comparing individuals with OCD and healthy controls, neurochemical analysis of the anterior cingulate cortex (ACC) and supplementary motor area revealed that the OCD group exhibited increased glutamate levels and a higher glutamate/GABA ratio, along with decreased GABA levels in the ACC (Biria et al., 2023).

4.2.4. γ -aminobutyric acid (GABA)

The primary inhibitory neurotransmitter of the central nervous system, GABA is essential for both neuronal inhibition in the adult brain and developmental processes (cell migration, proliferation, differentiation, and synaptic maturation). Evidence suggests decreased GABAergic activity in individuals with OCD (Eghdami et al., 2025; Singh et al., 2023).

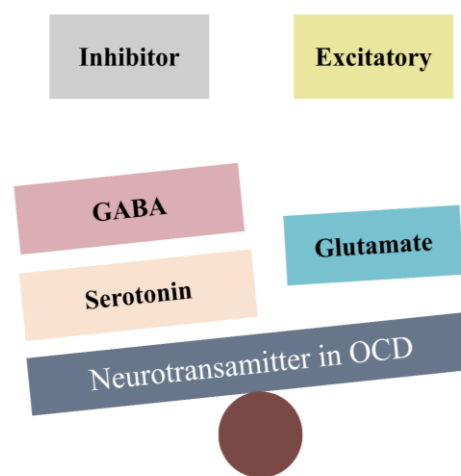


Figure 2. OCD and Neurotransmitters.
Adapted from (Singh et al., 2023)

5. Microbiota-Based Interventions in OCD

5.1. Probiotics and Synbiotics

Probiotics are live bacteria that help the host's health when ingested in appropriate amounts. These microorganisms ferment prebiotic substrates such as dietary fiber and resistant starch, contributing to the production of various postbiotic metabolites, primarily SCFAs. Synbiotics refer to combinations where probiotics and prebiotics are used together. Dietary fiber and resistant starch play a significant role in postbiotic production by supporting fermentation processes in the gut microbiota (Bendriess et al., 2023).

Probiotics such as *Lactobacillus*, *Bifidobacterium*, or *Akkermansia* contribute to the production of SCFA by fermenting dietary fiber, exhibiting beneficial effects for the host (Bendriess et al., 2023). In a study conducted by Sanikhani et al. on adult male rats, the probiotic *Lactobacillus casei* Shirota was administered at a specific daily dose for 4 weeks, and it was reported that this probiotic administration showed effects similar to fluoxetine, a SSRI, in reducing repetitive and compulsive behaviors similar to OCD (Sanikhani et al., 2020). In a study conducted by Szklany et al. (2020) on male mice, it was observed that supplementing the mice with indigestible oligosaccharides (prebiotics) from birth led to changes in the serotonergic system, resulting in a decrease in anxiety and repetitive behaviors. Furthermore, it was reported that this intervention increased levels of SCFAs, particularly butyrate, while decreasing levels of valeric, isobutyric, and isovaleric acids (Szklany et al., 2020). Another study in an autism model found that probiotic strains and probiotic-based complex therapy significantly improved microbial diversity, recurrent behavior, and TNF- α , BDNF, and 5-HT concentrations (Sunand et al., 2021).

5.2. Dietary Patterns

Although the field of nutritional psychiatry, which examines the impact of nutrition on mental health, has rapidly developed in recent years, OCD is not adequately represented in research in this area compared to other psychiatric disorders. To date, the number of longitudinal and randomized controlled trials evaluating the effect of dietary interventions on OCD symptoms is quite limited (Dawson et al., 2025). Although it is well known that individuals with depression, bipolar disorder, and psychotic disorders often have poor dietary quality, to date, few published studies have investigated the overall dietary quality of individuals with OCD (Marx et al., 2021; Teasdale et al., 2019; Nguyen et al., 202). Also, the low dietary fiber content of Western-style diets leads to dysbiosis in the gut microbiota, emerging as a key factor in the etiology of many modern diseases and disorders (Bendriess et al., 2023).

A recent review highlights that metabolic alterations such as insulin resistance, glucose metabolism disorders, and

mitochondrial dysfunction may play a role in the pathophysiology of OCD. In addition, chronic low-grade inflammation, oxidative stress (dysregulation in the HPA axis), and changes in the gut microbiota are among the mechanisms that may contribute to the development and maintenance of the disease. The fact that these biological processes can be largely influenced by diet suggests that diet-based interventions could be considered a complementary approach in the treatment of OCD (Dawson et al., 2025).

In this context, the Mediterranean diet, ketogenic diet, whole-food-based nutritional models, anti-inflammatory diets, and dietary approaches rich in prebiotics and probiotics stand out as potential strategies that can positively influence OCD symptoms by reducing inflammation, improving metabolic homeostasis, regulating the gut-brain axis, and supporting neurotransmitter synthesis. However, current evidence is still limited, and well-designed prospective and randomized controlled clinical trials are needed to demonstrate the effectiveness of these nutritional models. The main dietary models, supplements, and their mechanisms of action that have a potential role in OCD management will be evaluated in light of current literature.

5.2.1. Ketogenic Diet

The ketogenic diet (KD) is a nutritional model characterized by low carbohydrate, adequate protein, and high fat content. By restricting carbohydrates, lipolysis is activated, and ketones are used as the body's primary energy source instead of glucose. Several theories have been put forward regarding the use of KD in the treatment of psychiatric disorders. It is suggested that KD may alter the ratio of GABA to glutamate in the brain, favoring GABA, and thus influence the metabolic and biochemical aspects of psychiatric illnesses (Tillery et al., 2021). However, KD has been reported to modulate mitochondrial functions, oxidative stress, and inflammatory pathways (e.g., AMPK and NLRP3 inflammasome). These multifaceted effects suggest a potential regulatory role for the underlying neurobiological processes of OCD (Lounici et al., 2024). In a case series conducted by MacDonald and Palmer (2025), a decrease in Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) scores was reported in three OCD patients after implementing a ketogenic diet; symptoms increased again when the diet was discontinued and decreased again when it was restarted (MacDonald & Palmer, 2025).

5.2.2. Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) Diet

The MIND diet is a nutritional model based on a combination of the Mediterranean and DASH diets, emphasizing plant-based foods. Rich in polyphenols, carotenoids, vitamins (E, C,

and B group), and other bioactive components, this diet is suggested to have neuroprotective effects and positively influence psychiatric symptoms (Torabynasab et al., 2023). Based on existing literature, it is thought that this nutritional model, which supports neurological health and improves mental performance, may help manage OCD symptoms by balancing anxiety levels.

5.2.3. Mediterranean Diet

The Mediterranean diet is characterized by high consumption of fruits, vegetables, unrefined grains, olive oil, nuts, and seafood; moderate consumption of chicken, dairy products, and red wine; and low consumption of red meat (Mantzorou et al., 2021). The Mediterranean diet may also play a protective role against psychological disorders thanks to its high fiber content, omega-3 fatty acids, vitamins B and E, magnesium, antioxidants, and phytoestrogens (Sadeghi et al., 2021). In a 2019 study by Briguglio et al. on nine male patients diagnosed with Obsessive-Compulsive Tic Disorder (OCTD), patients were referred to a nutritionist due to unhealthy eating behaviors and evaluated using the Mediterranean Diet Quality Index. The average Mediterranean Diet Quality Index score was found to be low. After encouraging the adoption of a Mediterranean diet and providing nutritional counseling, despite the small sample size, the Mediterranean Diet Quality Index score significantly increased, while both the Yale Global Tic Severity Scale and Y-BOCS scores significantly decreased (Briguglio et al., 2019).

5.3. Micronutrient Supplements

Pharmacotherapy and psychotherapy are prominent in psychiatric illnesses. As with other psychiatric disorders, micronutrient supplementation offers an alternative approach in OCD. Changes in vitamin levels are reported to be related to mental symptoms and therefore hold an important place in the field of nutritional psychiatry (Karcı & Celik, 2020). Vitamin D and vitamin B12 are among the most studied micronutrients in OCD.

Several mechanisms have been proposed to explain the association between vitamin D and OCD, one of which involves the relationship between $1,25(\text{OH})_2\text{D}_3$, the active form of vitamin D_3 , and the enzymes tyrosine hydroxylase and tryptophan hydroxylase, which are rate-limiting in the synthesis of dopamine, epinephrine, norepinephrine, and serotonin, and whose expression is regulated by $1,25(\text{OH})_2\text{D}_3$. Therefore, vitamin D deficiency can contribute to the etiology of OCD by affecting the serotonin and catecholamine synthesis pathways, thereby impacting neurotransmission and synaptic plasticity (Örüm, 2024). Another potential effect of vitamin D is related to its neuroprotective and antioxidant properties. Vitamin D can reduce oxidative stress by inhibiting the activity of inducible nitric oxide synthase, which plays a role in nitric oxide synthesis. Furthermore,

animal studies have shown that it strengthens brain antioxidant defenses by regulating enzymes involved in glutathione synthesis. These mechanisms suggest that vitamin D deficiency may play a role in the development of OCD by leading to weakened neuroprotection (di Michele, 2018). Studies investigating vitamin D levels in patients with OCD have found that individuals with OCD generally have low vitamin D levels (Othman et al., 2024; Soyak & Karakükcü, 2022).

Vitamin B12 and folate are micronutrients that play a critical role in homocysteine metabolism and methylation reactions. The synthesis of methionine from homocysteine depends on the provision of methyl groups via methylfolate. Folate and vitamin B12 are involved in the synthesis of S-adenosylmethionine (SAM), supporting numerous methylation reactions, including those involving proteins, phospholipids, and neurotransmitters. Deficiencies in these vitamins lead to decreased SAM synthesis, resulting in hypomethylation and negatively impacting neurotransmitter synthesis and brain structural integrity; this may contribute to the pathophysiology of OCD (Yan et al., 2022). Studies in individuals with OCD have shown elevated serum homocysteine levels and low vitamin B12 levels (Ding et al., 2025; İmre & Kocabaş, 2023; Yan et al., 2022).

6. CONCLUSION AND RECOMMENDATIONS

These findings suggest that OCD has not only a psychiatric component but also a neuroimmune and gastrointestinal component. The fact that OCD symptoms may alter the gut microbiome and these microbial imbalances (dysbiosis) may affect OCD symptoms through neuroinflammation and neurotransmitter imbalances creates a vicious cycle.

Future research should focus on a deeper understanding of these mechanisms and, in particular, evaluate the evidence-based usability of personalized microbiome modulation strategies (probiotics, prebiotics, or fecal transplants) in the treatment of OCD. Microbiota-based interventions may help achieve higher success rates in the treatment of OCD by offering a valuable complementary or alternative treatment approach to traditional pharmacological and psychotherapeutic approaches.

From a nutritional perspective, dietary fiber has been shown to exert anti-inflammatory and neuroprotective effects by increasing the production of SCFAs in the gut, which are linked to anti-inflammatory and neuroprotective effects. Therefore, increasing dietary fiber intake is considered a supportive approach for gut microbiota and mental health.

In the context of probiotic and prebiotic supplementation, it has been reported that certain probiotic strains (such as *Lactobacillus Casei* Shirota) can have positive effects on compulsive behaviors, reducing anxiety and repetitive

behaviors. These interventions need to be evaluated more comprehensively through clinical trials.

In terms of micronutrients, vitamin D, vitamin B12, and folic acid have been shown to play critical roles in neurotransmitter methylation and the reduction of oxidative stress. Therefore, monitoring these micronutrient levels and providing appropriate supplementation if deficiencies are found is recommended in individuals with OCD.

Declarations

Competing Interest

The authors declare that they have no financial or non-financial competing interests.

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Ethics Statement

Ethical approval was not required for this review because it did not involve human participants, animals, identifiable personal data, or unpublished individual-level data.

Data Availability Statement

Data sharing is not applicable to this article, as no datasets were generated or analyzed during the current study.

AI statement

Generative AI tools were used only in a limited and controlled manner for language editing. All content was reviewed and approved by the authors.

Author's Contributions

E. Kütlemmez: Visualization, Original draft writing.

M. Ünlü Söğüt: Conceptualization, Writing—review and Editing.

M. N. Çelik: Conceptualization, Visualization, Writing—review and editing.

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