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# The Relationship Between Neuropsychiatric Disorders and the Oral Microbiome

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## Abstract

The oral microbiome, a highly diverse and intricate ecosystem of microorganisms, plays a pivotal role in the maintenance of systemic health. With the oral cavity housing over 700 different bacterial species, the body's second most diverse microbial community, periodontal pathogens often lead to the dysregulation of immune responses and consequently, neuropsychiatric disorders. Emerging evidence suggests a significant link between the dysbiosis of oral taxa and the progression of neurogenic disorders such as depression, schizophrenia, bipolar disorders, and more. In this paper, we show the relationship between mental health conditions and shifts in the oral microbiome by highlighting inflammatory responses and neuroactive pathways. The connection between the central nervous system and the oral cavity highlights its role as a modulator of mental health. Clinically, these findings have significant importance as dysbiosis could compromise quality of life. The weight of mental health is often compounded with treatment resistance, non-adherence, and relapse, causing a further need for treatment development. This review seeks to underscore the crucial role of the proposed oral–brain axis in hopes of increasing its presence in future intervention strategies and mental health therapies.

**Keywords:** microbiome; oral dysbiosis; schizophrenia; anxiety; depression; Alzheimer's; Parkinson's; autism

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## 1. Introduction

The relationship between mental health and the oral microbiome is an intricate and increasingly recognized area of concern. The oral cavity, which hosts the second-largest microbiome after the gut, harbors over 700 microorganisms, including bacteria, fungi, viruses, and protozoa, that are crucial in maintaining oral and systemic health [1]. Groups of bacteria that are heavily associated with oral disease, particularly within periodontitis, are categorized by color into bacterial complexes, such as red, orange, yellow, green, and purple [2,3]. The red complex, which includes *Porphyromonas gingivalis*, is the most strongly associated with severe periodontal disease, including the characteristics of bleeding upon probing and high inflammation [3].

Increases or decreases in particular microorganisms or changes in the overall diversity in the oral microbiome, known as dysbiosis, can be traced to conditions such as caries and periodontal disease, which affected approximately 32.26% and 42.44% of the population, respectively, in 2020 and these numbers are expected to rise [4,5]. Various factors include

poor oral hygiene, diet, smoking, stress, and more, which can disrupt the microbial equilibrium [6]. Since the mouth serves as an entry point to the gastrointestinal and respiratory tracts, disruptions in its composition can have widespread effects and can cause several systemic diseases.

Research has drawn significant attention to the link between mental health conditions and microbial dysbiosis [7]. The recent rise of such conditions is particularly concerning. Depression, for instance, accounts for approximately 50% of psychiatric consultations, highlighting its burden on mental healthcare systems [8]. The mechanisms through which mental health disorders can emerge from dysbiosis include translocated bacteria, detrimental microbial byproducts, and systemic inflammation [9]. The nature of this relationship also suggests that mental health conditions themselves exacerbate changes in the oral microbiome. Alterations in immune function and stress-related physiological responses associated with these disorders influence the activity of the oral microbiota [10]. Often, patients are prescribed medications to manage their conditions, yet pharmacological treatments can impact the balance of microbes. A common side effect of medication includes dry mouth, leaving the oral mucosa more vulnerable to pathogen colonization as salivary flow is important in the maintenance of homeostasis [11,12]. Beyond medication effects, individuals with neurodegenerative disorders contribute to shifts in oral microbiota due to a lack of motivation or motor dysfunction, increasing susceptibility to infections, and further worsening cognitive decline.

This review explores the role of microbial dysbiosis in the development and progression of neuropsychiatric disorders, including depression, anxiety, schizophrenia, bipolar disorder, Alzheimer's disease, Parkinson's disease, and autism. By examining the underlying mechanisms associated with oral dysbiosis, we highlight the importance of oral health on overall well-being and aim to explore potential interventions to reduce the incidence of neurological conditions, which have become an increasing problem worldwide.

## 2. Methods

To create this descriptive literature review, Google Scholar was used to identify pertinent peer-reviewed journal articles, and results were screened by date, with preference given to those within the past 10 years. Keywords including microbiome, oral dysbiosis, and mental health were utilized to refine the scope of the search. Canva was used to design visual figures that effectively summarize the key concepts of our findings.

## 3. Depression and Stress-Related Disorders

Depression has been highlighted as the leading cause of disability worldwide, characterized by loss of interest, persistent sadness, and feelings of hopelessness [13]. Beyond its psychological framework, depression also has physiological dimensions that require exploration, especially its connection to the oral microbiome. Shifts in taxa in the microbiome are mediated by immune responses and metabolites that have an impact on well-being through neural pathways [14]. Depression is associated with the release of stress hormones, including elevated levels of salivary cortisol, which has been linked to higher amounts of plaque, inflammation, and periodontitis symptoms. While a significant stress biomarker, cortisol may also act locally by modulating microbial gene transcription, which may contribute to periodontal dysbiosis alongside immune and inflammatory responses [15]. Specifically, an increase in transcriptional expression is seen in *Fusobacterium nucleatum* [16]. With its activity elevated, *F. nucleatum* is often involved in the pathogenesis of periodontitis as it upregulates pro-inflammatory cytokines and metalloproteases, such as collagenase 3, which promote cell migration [17]. Additionally, *F. nucleatum*'s ability to secrete serine proteases often leads to the damage of periodontal tissue through the degradation of extracellular

matrix proteins. Chronic stress-induced cortisol release in the oral cavity also further amplifies depression as it impairs the function of the hypothalamic–pituitary–adrenal (HPA) axis, reducing neurogenesis and impairing neuron signaling [18]. Ultimately, the interaction between depression, cortisol, and the oral microbiome creates a vicious cycle (Figure 1).

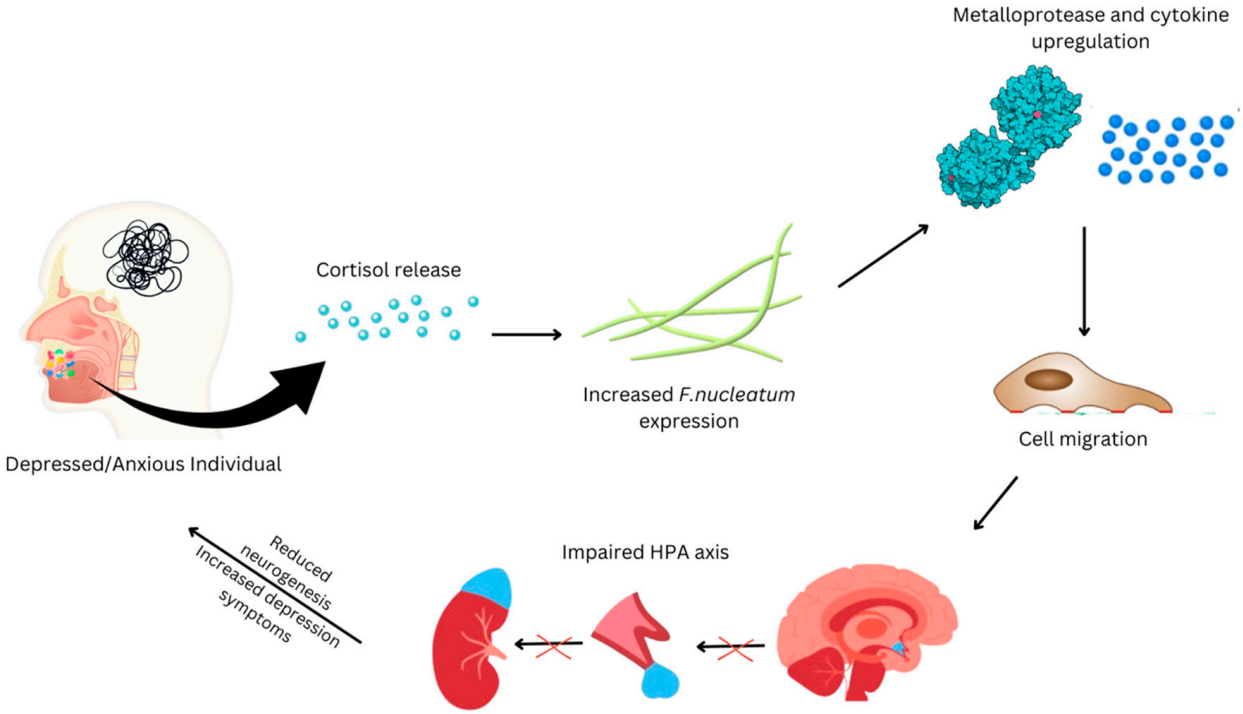



**Figure 1.** The mechanistic pathway illustrating the cycle of psychological stress and microbial dysbiosis through cortisol release.

An increased amount of anxiety and depression is seen to correlate with a decreased amount of tooth brushing and oral hygiene maintenance, indicating the emergence of harmful bacteria [19]. Poor hygiene habits are seen as individuals struggling with mental health challenges may have reduced motivation for self-care routines. This is often associated with the prevalence of caries and periodontal disease because of the disruption of salivary components. In patients with depression and anxiety, there is a notable abundance of *Spirochaetes*, which are equipped with a wide range of virulence factors that allow them to continually induce tissue damage within the gingival pocket [20,21]. Their ability to undermine critical immune defenses, such as neutrophil activity, ensures a long-term presence of chronic inflammation. The disruption of immune responses is highly prevalent during chronic stress, leading to susceptibility to infection and diminished wound-healing abilities [22]. In addition, patients with panic disorder, another form of anxiety that is characterized by sudden and intense episodes of fear along with several physical symptoms, have shown an increase in *Prevotella* and *Veillonella*, which are bacterial genera that contribute to periodontal disease through inflammatory responses [23]. Individuals with suicidal ideation, strongly linked to major depressive disorders and anxiety, also present with elevated levels of *Megasphaera micronuciformis* [24]. *M. miconuciformis*, frequently detected on tongue coatings in gastric cancer patients, has been linked to several diseases, as it is seen to promote cell death and inflammation [24]. Additionally, a study conducted on students at the University of Florida found that those without suicidal thoughts showed a significantly higher abundance of *Alloprevotella rava*, a Gram-negative bacterium responsible for the fermentation of glucose to succinate, which enhances glucose oxidation and supports overall brain function [25].

Simultaneously, there is a decreased prevalence of *Lactobacillus* bacteria, which is a Gram-positive microbe that has been seen to have potential benefits to health [26,27]. The species has been identified as a probiotic bacterium that can be used mostly against gut disorders but has been proven to fight against oral diseases as well [27]. Specifically, *Lactobacillus plantarum* exhibits properties that help prevent dental caries, including modulation of *Streptococcus mutans* and *Candida albicans* virulence [28]. Additionally, treatment using such bacteria regulates the immune system by inhibiting IL-8 expression by TNF-α and the production of regulatory T cells in rats, managing mood and anxiety [29]. Colonizing mucosal surfaces, *Lactococcus* bacteria are often introduced through the mouth and can travel through the digestive tract into the gut [30]. Two strains, *L. lactis* WHH2078 and *L.cremoris* WHH2080, have been shown to enhance the secretion of 5-hydroxytryptophan (5-HTP), a precursor to serotonin (5-hydroxytrptamine), which can cross the blood–brain barrier, and be converted within the central nervous system, thus playing a key role in regulating emotional well-being [30].

In individuals with depression, the disruption of the blood–brain barrier, an important regulator in central nervous system homeostasis, is a prominent characteristic [31]. Primarily driven by tight junction breakdown, the progression of depression is associated with increased blood–brain barrier permeability [32]. Therefore, there is a greater risk of pathogenic bacteria entering and altering the central nervous system (CNS). These pathogens also implicitly promote pro-inflammatory cytokine production that triggers cells expressing tumor necrosis factor (TNF)-α and interleukin-1 (IL-1) β receptors, contributing to neuroinflammation [33]. The activation of (TNF)-α has been seen to interfere with serotonin balance in the brain by increasing its reuptake through serotonin transporters, contributing to depressive symptoms [34].

Although herpes is not a native component of the oral microbiome, it becomes highly relevant when considering the impact of depression and stress on health. Oral herpes, or herpes simplex (HSV) type I, often remains dormant but can be reactivated by chronic stress [35]. Increased cortisol interacts with glucocorticoid receptors (GR) and enters the nucleus, where the complex reacts with GR response elements, leading to the upregulation of target genes [36]. This affects pathways such as the suppression of immune processes and elevated pro-inflammatory markers such as interleukin-6 and C-reactive protein [37]. Additionally, CD8+ T cells play a crucial role in controlling HSV-1 latency within the trigeminal ganglion as the immune cells remain active to continuously monitor the infected neurons [38]. By weakening the body's defense mechanism, stress can compromise the integrity of the CD8+ T cells, leading to an increased likelihood of symptomatic outbreaks [38].

In terms of depression, it is also important to note that perinatal and postnatal depression among expecting mothers remains prevalent, with rates as high as 27.6% according to a review written in 2023 [39]. With this, the susceptibility of caries in children is elevated through the disruption of the gestational formation of primary teeth enamel [40]. Any stressor, including maternal depression, can interfere with the critical window of enamel mineralization, impairing ameloblast function and causing hypoplasia or the discoloring of teeth and softening of enamel. Furthermore, vertical transmission of cariogenic bacteria such as *Streptococcus mutans* increases the risk of caries within children through sharing of genotypic strains [41]. Beyond oral health, prenatal stress can reprogram the child's HPA axis, contributing to cognitive impairments later in life [42].

## 4. Schizophrenia

Schizophrenia is a condition characterized by hallucinations, delusions, and disorganized thoughts. If left untreated, it may lead to thoughts of suicide, anxiety disorders, social isolation, substance abuse, etc. [43]. The causes of schizophrenia cannot be traced back to a concrete cause, but research suggests that a mix of brain chemistry, genetics, and external environment play roles [44]. To truly understand the bidirectional link between the oral microbiome and the brain, it is important to examine oral health as a factor for schizophrenia risk. Periodontal disease has been shown to promote neuroinflammation, causing the release of inflammatory cytokines in the central nervous system, which can be tied back to the mechanism by which inflammation affects schizophrenia. Along with this, dysbiosis of the saliva's microbiome can also be traced back to schizophrenia through causing oxidative stress, permeability of the blood–brain barrier, and disordered tyrosine metabolism [45]. When compared to control patients, those with schizophrenia were seen to have higher levels of several hydrogen sulfide ($H_2S$)-producing bacteria, including *Veillonella, Actinomyces, Leptotrichia, Atopobium, Prevotella, and Porhromonas* [46]. Hydrogen sulfide acts as an important neuroprotector, antioxidant, vasodilator, and immune regulator. Despite exhibiting such properties, excess $H_2S$ has been tied to schizophrenia pathology as heightening of its antioxidative role can cause bioenergetic deficits [47].

When analyzing the different taxonomic levels in the tongue coating microbiota, it was found that schizophrenic patients exhibited higher levels of *Proteobacteria*, *Fusobacteria*, *Spirochaetes*, *Acidobacteria*, and *Synergistetes* [48]. Overall, indicated imbalance can lead to systemic inflammation. For example, *Fusobacterium nucleatum* is one of the species known to trigger systemic inflammation, resulting in endotoxin production like lipopolysaccharides (LPS) [49,50]. LPS is known to infiltrate the bloodstream, causing the release of inflammatory cytokines such as IL-6, (TNF)-α, and (IL-1) β, all of which have been implicated in schizophrenia pathogenesis [51,52].

This bidirectional relationship is further amplified as schizophrenia often hinders oral hygiene maintenance. It has been found that toothbrushing habits were often reduced in 50–78% of patients diagnosed with schizophrenia [53]. Along with this correlation, there is also a significant positive association between the amount of periodontitis symptoms, such as gingival inflammation and plaque, and the patients' duration of schizophrenia [54]. Along with inflammatory defects, there has also been a correlation between patients and periodontal pockets, as well as loss of connective tissue attachment [55]. With this increase in dental disease among schizophrenia patients, there is also a decrease in seeking care for these ailments. Compared to healthy control patients, schizophrenia patients had higher scores of caries and decayed teeth and lower scores of filled teeth [56]. Possible oral neglect caused by schizophrenia can also be compounded with antipsychotic drug use, which has been seen to induce xerostomia. Hyposalivation during xerostomia results in the worsening of periodontal disease and rapid development of oral caries [57]. Specifically, the *Candida* species has been strongly correlated with antipsychotic drugs and salivary flow. Patients who were currently on antipsychotic medications such as fluphenazine—a schizophrenia medication—were highly colonised with *Candida* compared to a group of age-matched, healthy individuals [58]. Specifically, proliferation of Candida albicans is strongly correlated with xerostomia as well as root caries and difficulties in speech [59]. Another mechanism for antipsychotics to worsen dental conditions is through Parkinsonian symptoms, a common side effect of schizophrenia medications. These symptoms include tremors, which make it difficult to hold toothbrushes and other oral care products. Without the proper motor skills to carry out these functions, the oral cavity is left to house detrimental microbiomes [60].

Treatment for this bidirectional disease pathway typically involves a combination of good oral hygiene, decreased substance use, and evaluation of different psychotropic

medications. Along with changes in the patient's practices, it is encouraged that dentists receive additional training in the care of vulnerable groups, helping them be more adherent in treatment [61]. Another proposed route of treatment is reducing the dose of antipsychotic medications, though it should be conducted with extreme caution to prevent worsening of chronic mental effects [62].

Schizophrenia is often categorized with bipolar disorder, as recent genetic results have pointed to possible common causative factors between the two [63]. Bipolar disorders are categorized as bipolar I and bipolar II, the two differing primarily in the severity and nature of mood episodes experienced [64]. Considering this, it is also important to dive into the relationship between the oral microbiome and bipolar disorder. Along with an increased frequency of periodontopathogens, bipolar disorder has also been associated with higher bacterial load, such as *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*. These increased bacterial loads were especially correlated with depressive aspects of the disorder compared to the manic or euthymic phases [65]. *A.actinomycetemcomitans* is a facultative anaerobic bacillus that can cause diseases such as localized aggressive periodontitis and, as a result, bone reabsorption. This is performed through the production of pro-inflammatory cytokines such as IL-1 [66]. *P. gingivalis* uses several virulence factors, such as lipopolysaccharides, proteases, and fimbriae, to increase its bacterial load. After increased colonization, it can also reduce T cell response during periodontitis. This is using gingipain Rpgs, which downregulate IL-2 production and T-cell proliferation. Gingipains also aid in the invasion of the host immune system by degrading T Cell receptors such as CD4 and CD8 [67]. This bacterial buildup can be traced back to patterns of poor oral hygiene among patients, leading to accumulations of calculus, increased dental caries, and missing teeth [68].

## 5. Alzheimer's and Parkinson's Disease

Alzheimer's Disease (AD) refers to the most common form of dementia, a progressive neurodegenerative disorder that is characterized by declining cognitive function with age [69]. As of 2018, about 44 million people were estimated to have dementia, with rates projected to triple by 2050 [70]. Recent research suggests a mutual relationship between the progression of AD and the dysbiosis of the oral microbiome. Specifically, a lower diversity of microorganisms was present in patients with Alzheimer's, with a higher prevalence of periodontal bacteria, *Porphyromonas gingivalis*. The presence of *P. gingivalis* seen in the hippocampus of mice indicates its potential ability to cross the blood–brain barrier [71]. Periodontitis caused by *P. gingivalis* correlates with the increase in beta-amyloid (Aβ), a protein whose buildup is characteristic in AD, that causes neurodegeneration through excessive release of pro-inflammatory cytokines [72]. Additionally, *P. gingivalis* releases cysteine proteases, Arg-gingipain (Rgp) and Lys-gingipain (Kgp), that are able to degrade basal membrane proteins, leading to vascular porosity and subsequent infiltration of *P. gingivalis* into the brain [73]. These gingipains are often secreted in outer membrane vesicles (OMVs), quickly absorbed by mammalian cells, and trigger NLRP3 inflammasome, leading to ASC speck and Aβ plaque formation [74].

*Treponema* is a pathogenic genus known to cause damage to periodontal tissue and is seen in cases of peri-implantitis, a condition that affects the tissues around a dental implant [75,76]. These spirochetes are neutropenic and have the ability to spread through lymphatic vessels and nerve fibers, which explains their high prevalence in the trigeminal ganglia of Alzheimer's patients [77,78]. Its frequency induces the deposition of amyloid and disturbance in norepinephrine, leading to early signs of AD and cognitive decline [79]. *Treponema denticola* particularly produces a feature of Alzheimer's disease, the accumulation of tau protein forming neurofibrillary tangles, by activating GSK3β [80]. GSK3β

is a phosphokinase whose activity is responsible for the hyperphosphorylation of tau protein. Additionally, *T. denticola* produces lipopolysaccharides that stimulate neuroinflammation, increasing the expression of GSK3β and ultimately promoting the development of tau tangles.

Considering the connection between changes in the oral microbiome and Alzheimer's Disease, recent advancements in treatment planning have begun to explore how targeting oral bacteria can lead to potential management of neurodegenerative conditions. The use of tetracycline antibiotics such as doxycycline and minocycline has recently sparked interest due to their effectiveness against Gram-positive and Gram-negative bacteria, but also for their ability to cross the blood–brain barrier and neuroprotective benefits [81,82]. These antibiotics have shown promise in reducing oxidative stress and inhibiting matrix metalloproteases, which are mechanisms valuable in addressing neuroinflammation in AD [81]. However, the dosages required to achieve such effects are higher than typically prescribed for standard anti-inflammatory purposes [81]. This raises concerns regarding long-term safety, particularly due to the possible disruption of gut microbiota, highlighting the need to discover more alternative treatment strategies.

As the second most common neurodegenerative disease, Parkinson's Disease (PD) is a multi-system disorder that primarily affects movement and impairs various neurological functions [83]. It is characterized by damage to dopaminergic neurons in the substantia nigra and the emergence of Lewy bodies, which are abnormal protein deposits [83,84]. Parkinson's link to oral dysbiosis manifests in significant alterations to the microbiome, including an increase in pro-inflammatory cytokines in the gingival crevicular fluid [85]. With localized inflammation, the emergence of *Streptococcus mutans* is highly notable, especially in its ability to form amyloid [85]. *S. mutans'* ability to adhere to surfaces is facilitated by the surface protein P1 that plays a crucial role in the formation of dental caries and plaque [86]. The presence of β-sheet structures in the V- and C-terminal domains suggests a potential role in the aggregation of amyloid-like proteins [86]. The most amyloidogenic proteins, alpha-synuclein, and their clustering in the central nervous system, are key markers of PD pathology [85,87]. Being a major component of Lewy bodies, alpha-synuclein aggregates contribute to neuroinflammation by activating microglia [88,89]. As a result of the over-stimulation, activated microglia can produce pro-inflammatory cytokines that could convert astrocytes from a neuroprotective to a neurotoxic state, making the brain more susceptible to neurodegeneration [89].

Gram-negative bacteria represent a prominent component of the oral microbiome. Their outer membrane contains lipopolysaccharides (LPS) that act as toxins with the ability to destroy the blood–brain barrier and promote PD progression through attachment to LPS-binding proteins [84]. The complex binds to Toll-like receptors (TLR), and this interaction involves two pathways that can cause degeneration of neurons (Figure 2). One pathway includes the binding of LPS to TLR2 that can activate T cells, which in turn differentiate into different subsets such as Th1, Th2, or Th17 cells that release cytokines, leading to inflammation through recruitment of several immune cells [84]. The second pathway involves LPS being presented to TLR4 and activating microglia [89]. This can lead to the upregulation of nitric oxide synthase, a process that has been linked to DNA damage and cytotoxicity, causing increased apoptosis sensitivity [90].

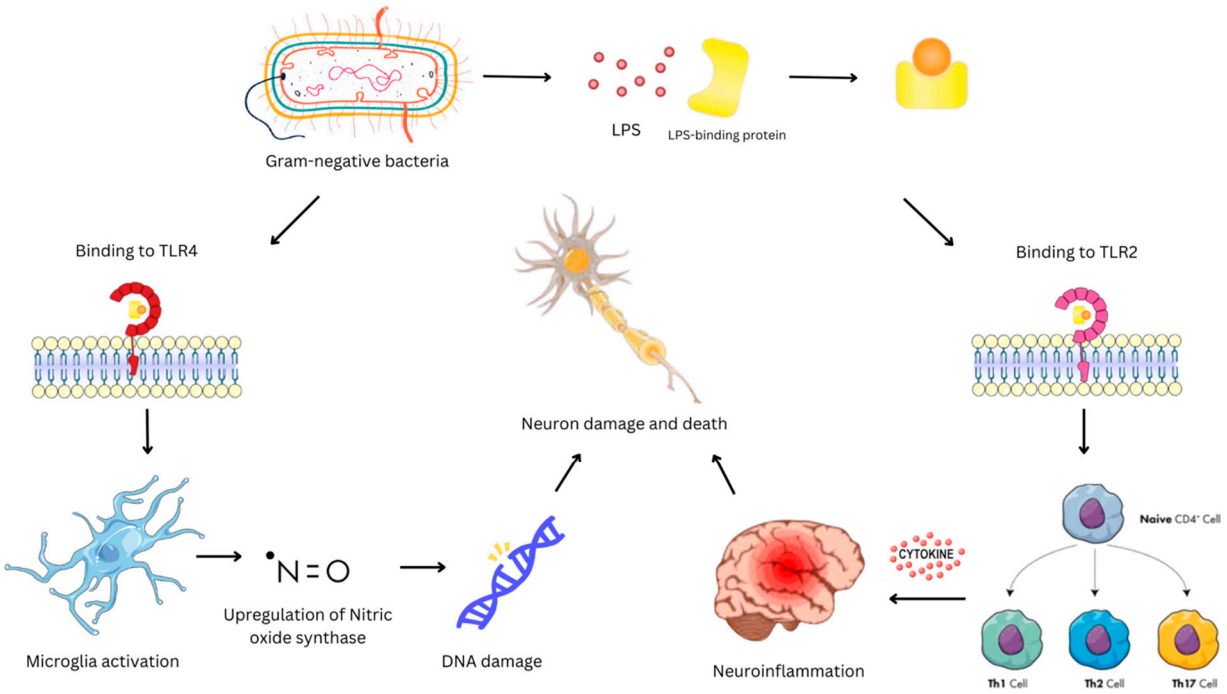



**Figure 2.** The pathway by which Gram-negative bacteria contribute to neuronal damage and neuroinflammation.

## 6. Autism

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition that entails atypical social communication and difficulties in everyday interaction [91]. With the prevalence of ASD increasing over the past decades, there has been growing interest in understanding its underlying etiology, which is believed to involve a complex interplay of genetic, environmental, and neurobiological factors [91]. Emerging evidence suggests that the oral microbiome might play a substantial role in influencing the process of neurodevelopment. Specifically, the *Prevotella* genus is the most significantly altered genus within autistic patients [92]. *Prevotella* are core anaerobic commensals that are frequently found in the oral cavity of healthy individuals [92,93]. They can be found in the digestive system and lower respiratory tract because of the swallowing of saliva, where they break down a variety of saccharides [92]. However, ASD subjects present with a decreased abundance within their feces, suggesting dysfunctional carbohydrate digestion that such patients often struggle with [92,94]. Additionally, gastrointestinal issues common in ASD, like acid reflux or constipation, may also affect oral health by causing oral discomfort or changes in microbiota composition [95].

One potential mechanism through which the microbiome may influence ASD is the production of neuroactive metabolites, such as short-chain fatty acids (SCFAs) [96]. After swallowing, these metabolites can enter systemic circulation through the oral mucosa or GI tract and can either cross the BBB directly or trigger immune responses that influence brain function [97]. Increased levels of some SCFAs, such as acetate and propionate, cause the cessation of pyruvate dehydrogenase, depleting energy levels in cells [96]. However, not all SCFAs have detrimental effects, but butyrate has been shown to enhance CNS function by inhibiting histone deacetylases (HDACs) and modulating gene expression [96]. Sodium butyrate, an HDAC inhibitor, can contribute to the potential therapeutic effect in ASD by supporting neuronal energy metabolism [96].

Enzymes involved in the degradation of neurotransmitters like serotonin, GABA, and dopamine are associated with distinct microbial communities in ASD [98]. These

findings constitute potential directions for investigating the ASD oral microbiome at the enzymatic level, indicating a possible connection to cognitive and behavioral functions [98]. Researchers reported that in previous studies, cytokines and chemokines were found to be elevated in the cerebrospinal fluid in ASD patients. From this evidence, authors argue that the chronic inflammatory state generated by bacterial pathogenicity factors (especially LPS) can alter the functioning of the synapses and the activity of the microglia, which are critical elements for the generation and progression of ASD [99]. ASD-specific changes also include reduced plasma amino acids and over-stimulation of glutamate [100]. Glutamate in excess, as an excitatory neurotransmitter, can induce excitotoxicity, leading to neuronal damage through mitochondrial dysfunction and atypical cerebral development from altered glutamate metabolism [100]. It should be noted that the glutamatergic–kyrurenine pathway's mediation of excitotoxicity and neuroprotective tryptophan metabolites is not limited to just autism, and is also observed in schizophrenia, substance use disorders, major depressive disorder, and post-traumatic stress disorder [101].

A significant increase in the abundance of *Streptococcus* and *Haemophilus*, and a decrease in *Selenomonas*, *Actinomyces*, *Porphyromonas*, and *Fusobacterium* in their saliva suggests a complex relationship with ASD, with specific bacteria potentially influencing the disorder through various biological pathways [102,103]. Most notably, the prevalence of *Tannerella,* which was recovered from 86.7% of ASD patients in one study, has been heavily associated with greater challenges in social interactions and repetitive behaviors [104,105]. The species is a major periodontal pathogen that has been identified as a microbial marker for autism through immune dysregulation [106].

## 7. Conclusions

The rise in neuropsychiatric disorders has prompted a deeper exploration into potential contributing factors beyond genetic and traditional neurological explanations. Emerging research suggests that the oral microbiome plays a significant role in influencing systemic inflammation, immune responses, and even neurological pathways through mechanisms such as the hypothalamic–pituitary–adrenal axis or the blood–brain barrier [18,32,45]. Specific bacteria, such as *P. gingivalis*, release pro-cytokines that can ultimately influence neuroinflammation and contribute to the progression of Alzheimer's disease, schizophrenia, and depression [107]. Additionally, *F. nucleatum* and other periodontal pathogens can activate signaling pathways that disrupt neurovascular integrity, further intensifying cognitive decline [108]. The infiltration of pathogens in the central nervous system depends heavily upon the integrity of the blood–brain barrier, as its disruption is a key factor in many of the diseases discussed.

These findings emphasize the need for further research into preventative strategies and therapeutic interventions targeting the oral microbiome, as individuals tend to neglect oral health without being aware of the dire consequences on mental health. The research on gut microbiome therapy has demonstrated significant potential, as microbiota transfer therapy (MTT) has been shown to reduce behavioral symptoms in children with autism by 45%, with long-lasting effects [102]. This emphasizes the need to extend similar strategies to the oral microbiome, as it can offer ways to mitigate mental health issues. Some potential approaches include the use of probiotics to balance microbial environments, which have had promising effects for individuals with depression [11]. In addition, strategies such as oral microbial transplants (OMTs) are being explored [108]. These transplants consist of introducing beneficial microorganisms from a healthy donor into a recipient, which has been successful in fecal transplants. Although in its early stages, OMTs may provide a novel method for combating oral dysbiosis by controlling caries production and periodontitis, thereby potentially alleviating systemic inflammation linked to mental health

conditions [108]. Other factors, such as environmental influences and diet considerations, impact the composition and stability of the oral microbiome, affecting overall health outcomes. Integrating dental care into broader practices may offer a promising avenue for reducing the burden of neuropsychiatric disorders.

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