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GRADUATION PROJECT

Degree in Dentistry

THE ROLE OF THE DENTIST IN THE EARLY DIAGNOSIS OF SYSTEMIC DISEASES WITH ORAL MANIFESTATIONS

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RESUMEN

Introducción: Las enfermedades sistémicas son cada vez más prevalentes y a menudo presentan manifestaciones orales. Investigaciones recientes destacan el papel del microbioma oral en la salud sistémica, incluyendo su posible implicación en los trastornos neuropsiquiátricos a través del eje microbiota–cerebro. Por lo tanto, los odontólogos pueden desempeñar un papel clave en la detección precoz de estas afecciones; **Objetivos:** Evaluar la asociación entre las alteraciones del microbioma oral y los trastornos neuropsiquiátricos, especialmente la depresión y la ansiedad, así como analizar el papel potencial del odontólogo en su diagnóstico precoz mediante el examen oral y el análisis salival; **Métodos:** Se realizó una revisión de la literatura utilizando bases de datos como Medline, PubMed, Access Medicine y Dentistry & Oral Science Source. Se incluyeron únicamente estudios primarios publicados en inglés durante los últimos 10 años; **Resultados:** Se incluyeron un total de 11 estudios. La mayoría mostró diferencias significativas en la composición microbiana (diversidad beta) entre individuos con trastornos neuropsiquiátricos y controles sanos. Sin embargo, los resultados sobre la diversidad alfa fueron inconsistentes. Diversos géneros bacterianos, como *Prevotella*, *Neisseria* y *Rothia*, se asociaron frecuentemente con depresión y ansiedad, aunque no se identificó un biomarcador único; **Conclusiones:** Las alteraciones del microbioma oral parecen estar asociadas con los trastornos neuropsiquiátricos, lo que respalda el concepto del eje oral–cerebro. Aunque se requieren más investigaciones, el análisis salival del microbioma podría constituir una herramienta prometedora y no invasiva para la detección precoz. Los odontólogos se encuentran en una posición estratégica para identificar signos tempranos y mejorar el manejo del paciente mediante un enfoque interdisciplinar.

PALABRAS CLAVE

Microbioma oral; Trastornos neuropsiquiátricos; Depresión; Ansiedad; Diagnóstico precoz; Análisis salival; Salud oral; Eje microbiota–cerebro

ABSTRACT

Introduction: Systemic diseases are increasingly prevalent and often present with oral manifestations. Recent research highlights the role of the oral microbiome in systemic health, including its potential involvement in neuropsychiatric disorders through the microbiota–brain axis. Dentists may therefore play a key role in the early detection of these conditions; **Objectives:** To evaluate the association between alterations in the oral microbiome and neuropsychiatric disorders, particularly depression and anxiety, and to assess the potential role of dentists in their early diagnosis through oral examination and salivary analysis; **Methods:** A literature review was conducted using databases such as Medline, PubMed, Access Medicine, and Dentistry & Oral Science Source. Only primary studies published in English within the last 10 years were included; **Results:** A total of 11 studies were included. Most studies reported significant differences in microbial composition (beta diversity) between individuals with neuropsychiatric disorders and healthy controls. However, findings regarding alpha diversity were inconsistent. Several bacterial genera, such as *Prevotella*, *Neisseria*, and *Rothia*, were frequently associated with depression and anxiety, although no single biomarker was identified; **Conclusions:** Alterations in the oral microbiome appear to be associated with neuropsychiatric disorders, supporting the concept of an oral–brain axis. Although further research is needed, salivary microbiome analysis could represent a promising, non-invasive tool for early detection. Dentists are in a strategic position to identify early signs and contribute to improved patient management through interdisciplinary collaboration.

KEYWORDS

Oral microbiome; Neuropsychiatric disorders; Depression; Anxiety; Early diagnosis; Salivary analysis; Oral health; Microbiota–brain axis

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1. INTRODUCTION

Medical advances have significantly improved patient care and decreased mortality in patients affected by systemic diseases. This explains their growing prevalence and increasingly chronic nature. This phenomenon is accompanied by a growing interest in the relationship between systemic diseases and oral pathologies, whose interactions are now recognized as an emerging field of research in both medicine and dentistry (1).

In recent years, particular attention has been given to the role of the oral microbiome in systemic health. The oral cavity hosts one of the most diverse microbial ecosystems in the human body, composed of bacteria, viruses, fungi, and protozoa. This microbial community plays a key role in maintaining oral and systemic homeostasis. However, alterations in its composition, known as dysbiosis, have been associated with numerous systemic diseases, including cardiovascular diseases, diabetes, and increasingly, neuropsychiatric disorders (2).

The concept of a microbiota–brain axis has emerged, highlighting the bidirectional exchanges between microbial communities and the central nervous system through immune, endocrine, and neural pathways. While most research has focused on the gut microbiome, recent studies suggest the concept of microbiota-brain axis and demonstrated that the oral microbiome may also influence brain function and behavior, particularly through inflammatory mediators and microbial metabolites (3).

Given that dentists routinely examine the oral cavity, they may play a crucial role in identifying early microbial and clinical alterations that could reflect systemic and neuropsychiatric conditions.

1.1. Definition and general concept

1.1.1 Generalities of systemic diseases

Beyond their diversity, systemic diseases converge around a common feature: PAIN. A real warning sign of the body, pain is usually the reason for the first consultation (4). Systemic diseases are inflammatory disorders resulting from a dysfunction in the immune system. The role of the latter is to protect us from external aggression, most often infections. When our immune system fails to work correctly, it produces hyperactivity and starts fighting against our own organs. A systemic disorder earns its name by being spread throughout the systems of the

body. Regardless of the organ they affect first, they will affect the body in its generality. Based on the site of involvement, we can classify them (5). They can be grouped by systems: cardiovascular, respiratory, endocrinology, neurology, articular, … Or also be classified into families such as autoimmune, metabolic, infectious, …(6). The cause of systemic diseases is not well known, but they may be genetic, environmental, or idiopathic (5).

In this context, the role of the microbiome has gained increasing importance. Microbial communities, particularly in the oral cavity, are involved in immune modulation. When dysbiosis occurs, it can trigger chronic inflammation, which is a key mechanism in many systemic diseases. This reinforces the idea that systemic conditions are not only organ-specific but involve complex interactions between the host and its microbiota (7).

1.1.2 Definition and classification of neuropsychiatric disorders

Among systemic diseases, special attention is given to neuropsychiatric ones. Psychological problem is a term commonly used to refer to mental disorders or neuropsychiatric disorders. Neuropsychiatric disorders are common in medical practice and may present either as a primary disorder or as a comorbid condition. The American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (APA DSM-5) defines a mental disorder as “a syndrome characterized by clinically significant disturbance in an individual’s cognition, emotion regulation, or behavior that reflects a dysfunction in the psychological, biological, or developmental processes underlying mental functioning” (8–11). Neuropsychiatric disorders are often chronic in nature (12). They are grouped into two major types: mood disorders and anxiety disorders. The major types of mood disorders are depression and bipolar disorder. Within the anxiety disorders, we can encounter panic disorders, generalized anxiety disorder, phobic disorder, stress disorders, and obsessive-compulsive disorders (9). We will focus on anxiety and depressive disorders as they are the two most prevalent ones. They often co-occur. Depression is defined by continual sadness, indifference, and loss of enjoyment; apathy or low self-esteem; disrupted sleep or appetite; feelings of fatigue, low concentration, irritability, and feelings of hopelessness; thoughts of death or dying (2,8,9,12). This depressed mood has an average duration of 2 weeks minimum (8).

Anxiety disorders are the most prevalent psychiatric condition in the general population. It is defined as a subjective sense of agitation, nervousness, unrest, apprehension, or fear. Depending on the duration, the nature of the precipitants, and the course of the illness, we may diagnose the specific type of anxiety (9).

Recent evidence suggests that neuropsychiatric disorders may not only be brain-centered conditions but also involve systemic and inflammatory components. The microbiota–brain axis plays a key role in this interaction. Alterations in microbial composition may influence neurotransmitter production (such as serotonin), immune responses, and stress regulation mechanisms (2).

1.2. Epidemiology

1.2.1 Incidence of systemic diseases with oral manifestations

About one-third of patients who attend dental clinics have systemic diseases like diabetes, hypertension,… (13). The most common systemic diseases associated with oral manifestations are hematological disorders, endocrinopathies, neurological disorders, gastrointestinal conditions, mucocutaneous disorders, rheumatic conditions, and neoplastic processes.

Among rheumatic disorders, we have Sjogren syndrome that affects 0,3-0,5 % of the population, mainly women, with a ratio of 9:1 (6,14). This syndrome is an autoimmune disorder characterized by lymphocytic infiltration of exocrine glands, mostly lacrimal and salivary (14). The main oral signs of this syndrome are hyposalivation, angular cheilitis, and ulcers. Xerostomia may be associated with fissured tongue and depapillation (15).

Concerning the mucocutaneous diseases, the main prevalent one is Lichen planus with 0,5% to 2% of prevalence. Lichen planus is a chronic inflammatory condition that affects the skin and mucous tissues. OLP concerned 4% of the population. This condition most of the time appears with oral lesions first. The tongue and buccal mucosa are affected with papules, plaque, and erosive lesions (14,16).

Amid gastrointestinal disorders, Crohn's disease is the most prevalent one in the category of inflammatory bowel disease. 1.7 million people are affected by inflammatory bowel disease, and 1 out of 60,000 presents Crohn's disease. The most common oral signs that we will see are lip swelling in minimum 50% of cases and up to 90% in some studies. Another signs that is usually present is mucosal ulcerations, angular cheilitis, and gingivitis (16).

Within hematological disorders, we have iron deficiency anemia, a condition that presents a reduction in the content of hemoglobin and oxygen. The main oral manifestations will be pale mucosa and atrophic glossitis (14).

Among endocrinopathies, we have diabetes mellitus affecting 6% of the population. Diabetes is a metabolic disorder affecting the body's metabolism, leading to structural changes in tissues (17). The oral manifestations of diabetes will appear as a form of inflammation in the gingiva

and periodontium. Around a third of patients complain of xerostomia (15). Oral signs like burning mouth syndrome, candidiasis, and ulcers are also common oral manifestations (14). Moreover, delayed healing is a common oral manifestation in those patients (15).

To continue, within neurological disorders, multiple sclerosis is one of the most prevalent ones, with more than 2.8 million people affected. It is a chronic neurodegenerative disease of the central nervous system. Concerning the oral manifestations, the main ones we will see are dry mouth, caries, TMJ disorders, and periodontal disease.

Finally, across oncological diseases, we have leukemia, which is considered one of the most life-threatening cancers. Leukemia is a malignant condition affecting the white blood cells of the bone marrow. The main oral signs include mucosa pallor, gingival bleeding and hypertrophy, opportunistic infections, petechia, and ulcers (14,16).

Many of these conditions are associated with oral manifestations, which may be linked not only to clinical symptoms but also to microbial alterations. For example, in diabetes mellitus, changes in the oral microbiome have been associated with increased inflammation, periodontal disease, and delayed healing. Similarly, autoimmune diseases such as Sjögren syndrome are associated with reduced salivary flow, which directly impacts microbial balance and promotes dysbiosis. These examples highlight that oral manifestations are not only clinical signs but may also reflect underlying microbial changes associated with systemic conditions (14,16).

1.2.2 Incidence of neuropsychiatric disorders

Neuropsychiatric disorders, also called mental disorders, are concerning more than a billion people in the world (WHO). They regroup two major types, depression and anxiety, representing the 13th and 24th leading causes of global disability (18). Depression and anxiety are often connected; they are associated with a higher risk of suicide (10). Results published by WHO estimate around 720,000 suicides in 2021 due to mental troubles. Suicide is one of the leading causes of death among young people in all countries (10,19).

Nowadays, depression concerns approximately 50% of psychiatric consultations, emphasizing the importance of mental healthcare systems. The data shows that 4 of the 10 leading causes of morbidity and the associated health care costs worldwide are psychological conditions. Anxiety is the most prevalent illness in psychiatric disorders and includes 15-20% of medical clinic patients (9). Up to 15% of the general population experiences a major depressive episode over the course of one's life (8).

Recent studies have shown that patients with neuropsychiatric disorders may present alterations in their oral microbiome. Differences in bacterial diversity and composition have been reported between individuals with depression or anxiety and healthy controls. These findings suggest that microbial biomarkers could potentially be used for early detection and monitoring of mental health conditions (20).

1.3 Clinical manifestations

Within the broad domain of human health, there is a complex and delicate interconnection between various bodily systems. Systemic and dental health are meshing in a complex interacting system. The link between systemic and dental health has a strong biological foundation, which is gaining recognition (3).

1.3.1 General clinical manifestations

Systemic diseases present a wide range of clinical manifestations depending on the affected system. Many of these manifestations are mediated by inflammatory and immune mechanisms, which are also influenced by the microbiome.

1.3.2 Oral clinical manifestations

The oral cavity is often viewed as a window into the body because many systemic diseases manifest there. In many cases, oral symptoms appear before other signs or symptoms occur elsewhere in the body. The mouth serves as a mirror of health and as an early warning method (15). The buccal cavity contains four main parts: the mucosa, tongue, dentition, and salivary glands. Inflammation of the mucosa, dental caries, reduced salivary flow, and discoloration of tissues can all be indicative signs of systemic diseases. That's why practitioners must be aware of the recognition of buccal signs (16). The mouth can be impacted by almost all of the body's system disorders (21). Soft and hard tissues of the head and neck may be involved (6). We may classify oral manifestations into mucosal alterations and salivary gland alterations. Among mucosal alterations, we encounter ulceration and patches. Ulcers are defined as a loss of substance; they may be solitary or multiple, located on keratinized mucosa or non-keratinized, and may be painful or not (22). The systemic diseases that can provoke ulcers are Herpes simplex virus infection, Behcet disease, tuberculosis, Lichen planus, Crohn's disease, Kaposi sarcoma,

varicella zoster virus, oral squamous cell carcinoma, and many others. Concerning the patches, they can be classified into adherent and non-adherent white patches, which means the patch may be wiped off or cannot be scratched. The patches can be symmetrical or not, persistent or transitory. White patches have a creamy white color. The diseases associated with patches are papillomas, mycoses, lupus disorders, and others. Other manifestations that can happen in the oral mucosa include swellings and pigmentation. The diseases associated with swelling are Sturge-Weber syndrome, Crohn's disease, tuberous sclerosis, neurofibromatosis type 1,… Concerning the pigmentation, we find Albright syndrome, metastatic malignant melanoma, hypo-adrenal cortical deficiency, Peutz-Jegher's syndrome,… (21). Within the salivary gland manifestations, we mainly see swelling or oral dryness. Diseases associated with salivary swelling and oral dryness are almost the same; we may find Sjogren disease, HIV, Sarcoidosis, HCV sialadenitis… Other signs or symptoms that are relevant in oral medicine are the loss of sensation that may be associated with diabetes mellitus. Moreover, orofacial dyskinesia associated with Parkinson's disease, rabbit syndrome, and altered tongue movement associated with bulbar palsy. Other oral manifestations we may have are halitosis, which can be caused by pulmonary tuberculosis, diabetic ketoacidosis, and end-stage hepatic and renal failure (21).

Beyond visible lesions, the oral microbiome itself can serve as an early indicator of disease. Dysbiosis may manifest through conditions such as periodontal disease, caries, mucosal inflammation, or xerostomia. Recent research suggests that specific microbial patterns may be associated with neuropsychiatric disorders. For example, increased abundance of bacteria such as *Prevotella*, *Neisseria*, and *Rothia* has been observed in patients with depression and anxiety. These microbial changes may contribute to systemic inflammation and influence brain function through the microbiota–brain axis (10). Thus, oral examination should not only focus on clinical lesions but also consider the underlying microbial environment.

1.4 Oral microbiome analysis parameters

Oral microbiome analysis was performed using salivary samples to evaluate microbial diversity and composition. Three main parameters were considered: alpha diversity, beta diversity, and taxonomic composition.

Alpha diversity refers to the diversity within a single sample, reflecting both the richness (number of species) and evenness (distribution of species). It provides information about the complexity of the microbial ecosystem.

Beta diversity measures the differences in microbial composition between groups, such as individuals with neuropsychiatric disorders and healthy controls. It allows the comparison of microbial profiles across populations.

Taxonomic analysis identifies specific bacterial groups (genera or species) present in the oral microbiome. This enables the detection of particular microorganisms associated with depression or anxiety.

1.5 Justification

WHO said that significant improvements have been made across many fields of medicine, but there are still many gaps in the global struggle against mental health (WHO). Moreover, neuropsychiatric disorders have a huge prevalence, remain poorly understood, and treatment options are still limited. It persists as a major health problem worldwide (23). This coexistence makes it even more important to recognize depression as independent but also as a common comorbidity.

It has been demonstrated that the buccal mucosa is intensely susceptible to psychological impacts like stress, anxiety, and depression. Emotions and oral pathology are directly linked. Those emotional disturbances, by affecting hormonal, vascular, and muscular functions, can cause physiological changes like pain, burning sensations, and ulcerations (24). That's why identifying the preventable risk factors by detecting the first oral signs is vital because of the harm caused by these mental illnesses (10,19). Establishing such links could enable dentists to develop a vigilance diagnostic to specifically target depression or anxiety during further questioning (25). Managing systemic diseases in those patients must be a necessity for the dentist, enabling them to provide safe dental treatment and to recognize early signs of disease (13). The identification of non-invasive biomarkers is therefore essential. In this context, the oral microbiome represents a promising diagnostic tool. Saliva-based analysis is simple, non-invasive, and easily applicable in a dental clinic. By combining clinical examination with microbiome analysis, dentists could play a key role in the early detection of neuropsychiatric disorders. This approach could improve patient management, enable earlier interventions, and contribute to better overall health outcomes.

2. OBJECTIVE

The objective is to evaluate a relationship between the oral microbiome and neuropsychiatric disorders, analyzing salivary tests, and contribute to improving patient early diagnosis.

3. MATERIAL AND METHODS

3.1 Research question

(P): Neuropsychiatric patients

(I): early diagnosis of a mental problem by saliva tests and dental examination

(C): patients without microbiome analysis

(O): early detection / improved diagnosis

To what extent can changes in the oral microbiota be an indicator of systemic diseases, particularly depression, and what role can dentists play in their early detection through oral examinations?

3.2 Eligibility criteria

The inclusion criteria are studies published within the last 10 years, studies published in English, Spanish or French; studies that are experimental (original articles), and human studies were included.

Exclusion criteria are studies on animals, articles that were not open access, and studies older than 2015. Secondary studies, like reviews, were excluded. Studies not related to mental health were excluded.

3.3 Source of information

The research was done using many databases such as Medline, PubMed, Access Medicine, Dentistry & Oral Science Source through the Learning, Research and Innovation Resource Centre Dulce Chacon Library of the European University of Madrid.

3.4 Search strategy

To conduct the research, keywords were used like depression, depressive disorders, anxiety, psychiatric disabilities, oral signs, oral symptoms, early screening, warning signs, early detection, stress, oral health, oral examination, clinical management, microbiome, and oral microbiota.

The search equation is the following one: Search: ((((mental health) OR (depression)) OR (anxiety)) AND (microbiome oral)) OR (microbiota oral)

4. RESULTS

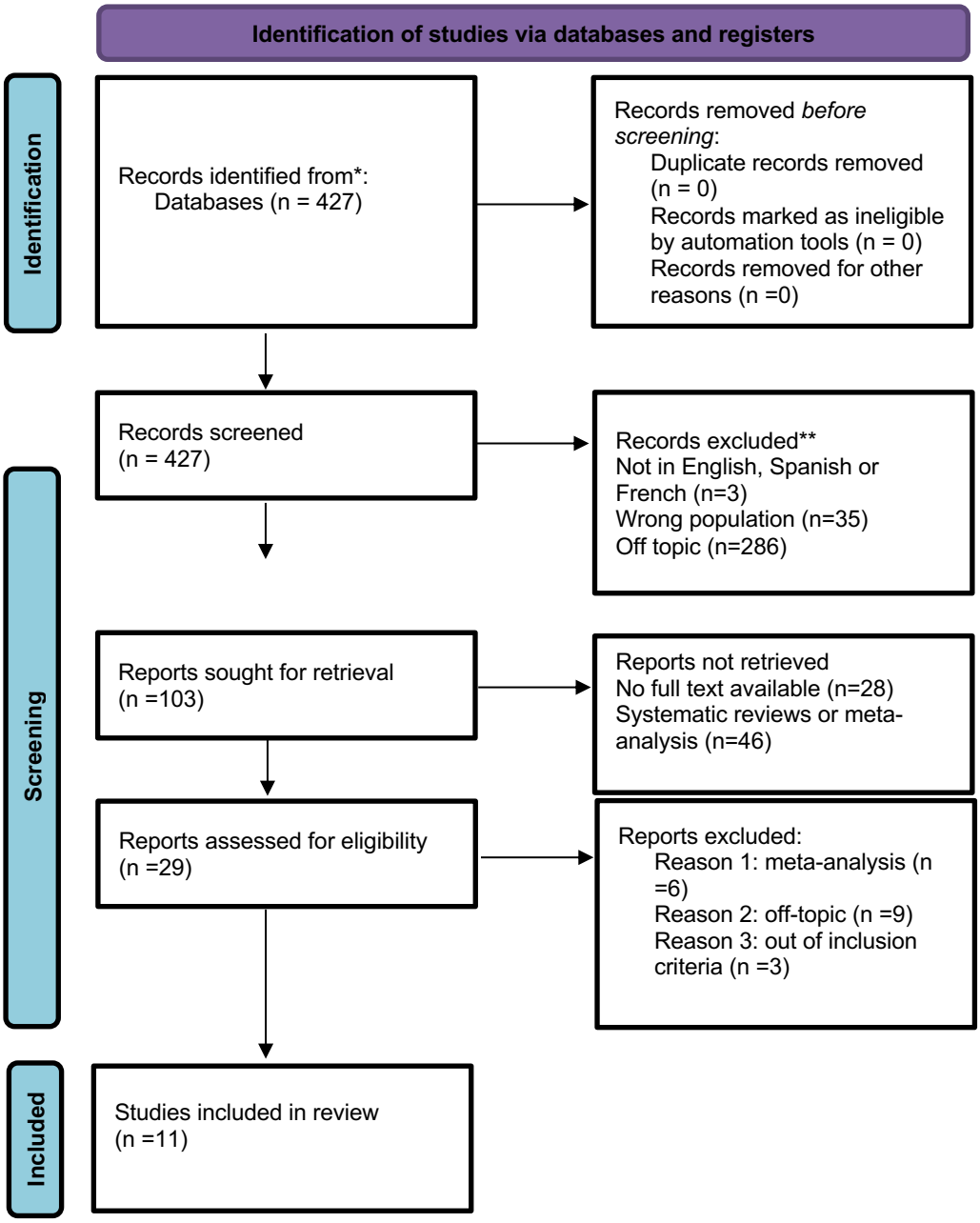


Figure 1. PRISMA flowchart diagram

TABLE 1. Summary of studies investigating the association between oral microbiome alterations and neuropsychiatric disorders

Articles	Mental health assessment tool	Population	Alpha diversity	Beta diversity	Taxa represented	Key result
2023, Richardson et al. (26)	PROMISSF-depression PROMISSF-anxiety PSQI	20 patients	Higher alpha diversity in depressive patients Lower Alpha diversity in anxiety patients No correlation in sleep disturbances	Marginal differences in depression No differences in anxiety and sleep disturbances groups	Increased abundance of *Rothia* and *scardovia* in anxiety and depression Increase abundance of *Kingella* in sleep disturbance	Suggests an association between the oral microbial diversity and anxiety and depressive symptoms
2024, Liu et al. (27)	NHANES PHQ-9 (depression)	4692 patients	Low Alpha diversity in the depression group	Distinct microbial composition in sleep deprived patient with depression	Not assessed	This study highlights the role of oral microbiome diversity in relationship between sleep duration and depression risk.
2024, Malan-Müller. Et al. (28)	CESD scale (depression) STAI (anxiety) DSM-5, PCL-5 (PTSD)	470 patients	No significant differences	Significative microbial differences between mental health group and controls	Increased abundance of *P.histicola* in depression and PTSD Increased abundance of *Oribacterium*	These results suggest a complex interplay between microbial composition, systemic neuromodulators, and health outcomes,

	CTQ-SF (trauma) WHOQOL (quality of life)				*asaccharolyticum* in anxiety	
2022, Li et al. (29)	GAD 7 (anxiety) PHQ 9 (depression)	594 patients	No differences	Significant differences microbial community between groups	Actinomyces, Neisseria, Prevotella, Porphyromonas	Changes in anxiety, depression, and oral microbiome are complex and require further research.
2023, Stoy et al. (30)	Psychological stress	37 patients	Higher richness and alpha diversity in stressed students	Distinct microbial profiles observed between groups	Higher abundance of *Corynebacterium, Eikenella, Tannerella, Rothia, Capnocytophaga, Pasteurellaceae* in stressed patients	Using the oral microbiome as an indicator of stress may provide evidence to support stress management practices
2025, Liu et al. (31)	PHQ 9 (depression)	32 patients	High alpha diversity in mild depression Low alpha diversity in high depression	Significant differences of microbial composition	Increase abundance of *Rothia, Paraclostridium, Capnocytophaga,*	This study indicates that oral microbial diversity, richness, and community structure are associated

				between the two groups	*Neisseria_elongata* in high depression Increase abundance of *Xantomonadales* in mild depression	with depression severity.
2021, Wingfield et al. (32)	DSM IV (depression)	83 patients	Marginal alpha diversity variability in the depressive group	Significant differences of microbial composition between the two. groups	Increase abundnace of *Prevotella nigrescens* *Neisseria genera* in depressive groups	It shows significant alterations in the overall bacterial composition and abundance of specific bacteria in the oral microbiome in adults with depression
2025, Kerff et al. (33)	HADS-D (depression) HADS-A (anxiety)	436 patients	No significant differences of alpha diversity in anxiety and depressive people	No significant differences of microbial composition between groups	Enriched *Prevotella nigrescens* in elevated depressive symptoms	This study shows associations between oral microbiota species and symptoms of common mental disorders, particularly for depressive symptoms.

2025, Agranyoni et al. (20)	CES-D (depression)	422 patients	No significant differences of alpha diversity between in depressive people	No significant differences of microbial composition between the two groups	*Neisseria genus* much lower in abundance in depressive symptoms	The oral microbiome may help as a potential screening tool for depression during pregnancy
2022, Aleti et al. (34)	Depression-obesity (BMI) BDI-T	60 participants	No significant differences of alpha diversity in depressive obese people	Significant differences of microbial composition between groups	*Prevotella, Aggregatibacter, Pseudomonas, Campylobacter, Clostridia* in obese depressive profile are higher in quantity	It provides evidence for a connection of the microbial oral-brain axis in the context of obesity-depression-inflammation.
2021, Xie et al. (35)	DSM-5 (depression) PHQ-9 (depression) GAD-7 (anxiety)	26 patients	Significant alpha diversity in the panic disorder group	Significant differences of microbial composition between groups	*Prevotella Veillonella* increased in PD group	It shows that oral microbes differed between patients with panic disorder and healthy subjects.

5. DISCUSSION

This study aimed to explore whether changes in the oral microbiome could be associated with neuropsychiatric disorders such as depression and anxiety, and to assess the potential role of dentists in their detection to enable early care.

5.1 Interpretation of findings

The results of the selected studies suggest that alterations in the oral microbiome may be associated with neuropsychiatric disorders such as depression and anxiety. Approximately 8 out of the 11 included studies reported significant differences in microbial composition (beta diversity) between affected individuals and healthy controls, supporting the hypothesis of a link between oral microbiota and mental health.

In contrast, findings regarding alpha diversity were more inconsistent, with only about 5 out of 11 studies reporting significant differences. This suggests that alpha diversity alone may not be a reliable biomarker for neuropsychiatric disorders.

Taxonomic analysis of the oral microbiome revealed the presence of specific bacterial patterns associated with neuropsychiatric conditions. However, no single microbial species can currently be considered a definitive biomarker. In this context, a microbial biomarker can be defined as a specific microorganism or a microbial pattern associated with a particular disease. However, no single microbial species can currently be considered a reliable biomarker for neuropsychiatric disorders. Instead, a combination of microbial alterations or a global dysbiotic profile is more likely to reflect the association between the oral microbiome and mental health conditions.

This highlights the complexity of the oral microbiome and its interaction with systemic health.

To support these conclusions, studies reported significant differences in microbial composition between affected individuals and healthy controls (beta diversity). For example, Wingfield et al. (2021) observed significant alterations in bacterial abundance and overall microbial composition in adults presenting depressive symptoms.

Similarly, Li et al. (2022) identified associations between anxiety, depression, and variations in oral bacterial taxa, including *Actinomyces*, *Neisseria*, and *Prevotella*.

Other studies also reported the presence of specific genera such as *Rothia*, *Capnocytophaga*, and *Prevotella* in individuals with depressive or anxiety symptoms (Richardson et al., 2023; Liu et al., 2025).

These findings support the idea of an oral-brain axis associating oral microbial composition to neuropsychiatric disorders. However, the results of the studies are heterogeneous. While some studies observed significant differences in alpha diversity between patients with depression and healthy controls (Wingfield et al., 2021; Liu et al., 2025), others did not find statistically significant differences (Kerff et al., 2024; Agranyoni et al., 2025).

This inconsistency suggests that alpha diversity alone may not be a reliable biomarker for neuropsychiatric disorders. Differences in sample size, study populations, diagnostic criteria for psychiatric disorders, or microbiome analysis techniques may explain these discrepancies. This shows the importance of making standardized studies in future research.

It also suggests that beta diversity, reflecting differences in microbial composition between individuals, may be more relevant than alpha diversity for identifying microbial patterns associated with neuropsychiatric disorders. Therefore, changes in microbial composition rather than overall diversity may represent a more reliable indicator in this context.

5.2 Role of oral microbiome in neuropsychiatric disorders

Several biological mechanisms may explain the relationship between the oral microbiome and neuropsychiatric disorders.

More research suggests the existence of a microbiota–brain axis, in which microorganisms can influence the central nervous system through immune, endocrine, and inflammatory pathways (2). Dysbiosis of the oral microbiome may contribute to systemic inflammation and alterations in neuromodulators, potentially influencing mood regulation and mental health. In addition, oral pathogens may induce inflammatory responses that influence cytokine production, which has been associated with depressive symptoms in several studies.

5.3 Limitations of the study

This study has several limitations. Most of the included studies were observational and therefore cannot prove a cause-and-effect link between the oral microbiome and neuropsychiatric disorders.

In addition, differences in study methods, microbiome analysis methods, and psychiatric assessment tools make comparison difficult. Further randomized clinical studies are necessary to conclude how the oral microbiota affects mental health. Nevertheless, the evidence suggests that the oral microbiome could play a role in oral health and mental health.

5.4 Clinical implications for dental practice

This reinforces the importance of an interdisciplinary approach involving dentists, doctors, and mental health professionals in the early detection and management of neuropsychiatric disorders. Because dentists routinely examine the oral cavity, they are in a privileged position to detect early oral changes that may be associated with systemic conditions. In addition to clinical examination, salivary microbiome analysis could represent a promising complementary tool in dental practice. By identifying abnormal microbial patterns or oral manifestations such as xerostomia, burning mouth syndrome, or recurrent ulcerations, dentists could help identify patients at risk of neuropsychiatric disorders and refer them to appropriate medical care (21,36). Their role is not necessarily treatment, as they are not automatically specialized in that area, but their part of the work is to take appropriate initiatives, including referring to other healthcare professionals, and to make a positive difference for the patient and their surroundings (36). Early detection can further ameliorate patient outcomes (37).

Taking psychiatry as an example, an article showed that early diagnosis is one of the most important concerns. Several studies highlighted the need to detect prodromal signs and symptoms of psychiatric diseases to establish early intervention strategies, as the lack of diagnosis and treatment during the early stages of disorders is linked to high levels of disability and a worse course of illness (38).

6. CONCLUSIONS

The findings of this study suggest that alterations in the oral microbiome are associated with neuropsychiatric disorders such as depression and anxiety. Although no single microbial biomarker has been clearly identified. Beta diversity appears to be a more relevant indicator than alpha diversity in identifying these alterations, highlighting the importance of microbial composition rather than overall diversity. However, the heterogeneity of the available studies and their predominantly observational design limit the ability to establish a causal relationship.

Furthermore, dentists play a key role in the early detection of these conditions. Through oral examination and potential salivary analysis, they are in a strategic position to identify early signs and refer patients for appropriate care.

The oral microbiome represents a promising, non-invasive tool for early screening of neuropsychiatric disorders. Salivary analysis, combined with clinical oral examination, could enhance early detection and improve patient management.

7. SUSTAINABILITY

From a social perspective, this study improves patients' quality of life by enabling early diagnosis of neuropsychiatric disorders. Non-invasive methods such as salivary analysis are more accessible, less stressful, and can reduce health inequalities by facilitating earlier and broader screening.

From an economic point of view, early detection helps reduce healthcare costs by limiting the need for complex and expensive treatments. Preventive approaches also decrease hospitalizations and long-term care expenses, contributing to a more efficient and sustainable healthcare system.

From an environmental perspective, the use of non-invasive diagnostic methods reduces the need for resource-intensive procedures. This leads to lower energy consumption, less use of medical materials, and a reduction in biomedical waste. Promoting prevention over treatment, therefore, supports more sustainable healthcare practices and reduces the environmental impact of medical care.

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