www.sada.co.za / SADJ Vol. 80 No.10
https://doi.org/10.17159/sadj.v80i10.22087

The Oral Microbiome and Mental Health: An Emerging Paradigm

SADJ NOVEMBER 2025, Vol. 80 No.10 P550-P554
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ABSTRACT

Recent research highlights the human microbiome as a significant determinant of systemic health. While the gut microbiome has been extensively studied, growing evidence suggests that the oral microbiome is implicated in a range of systemic and neurological disorders. This review examines the emerging relationship between the oral microbiome and mental health, with a focus on mechanisms including inflammation, neurotransmitter modulation and microbial translocation. Dysbiosis within the oral cavity may contribute to neuroinflammatory and neurodegenerative conditions. Understanding these associations provides a foundation for novel therapeutic and preventive strategies that integrate oral health into broader neuropsychiatric care.

INTRODUCTION

The human oral cavity is home to a diverse microbial community, collectively known as the oral microbiome, which is the second largest set of bacteria in the human body and plays a vital role in maintaining oral and systemic health.[1] Over 600 bacterial species, along with fungi, viruses and archaea colonise the oral environment, forming a complex ecosystem.[2] These microorganisms form biofilms on various oral surfaces, contributing to a balanced oral environment that prevents pathogenic invasion.[3] The oral microbiome plays a crucial role in metabolic homeostasis and immune regulation. Commensal bacteria aid in the digestion of dietary carbohydrates, producing short chain fatty acids (SCFAs) that support oral and gut health.[4] Additionally, the microbiome modulates immune responses, preventing excessive inflammation and maintaining mucosal integrity.[5] The balance of this microbiome is crucial, as disruptions can contribute to both local and systemic diseases. Disruptions in this balance, termed dysbiosis can contribute to chronic inflammation and systemic conditions including cardiovascular disease, diabetes and neuropsychiatric disorders.[6]

Bacteria are the most extensively studied components of the oral microbiome. The predominant phyla include Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria and Spirochaetes.[2] Within these phyla, species such as *Streptococcus*, *Veillonella*, *Fusobacterium*, *Porphyromonas* and *Prevotella* are common inhabitants of the oral cavity, each contributing to ecological balance and immune regulation.[7] While many of these bacteria are commensals, certain pathogenic strains such as *Porphyromonas gingivalis* and *Treponema denticola* are associated with periodontal disease and systemic inflammation.[8] Fungi, particularly *Candida* species are also present in the oral microbiome typically existing in low numbers in healthy individuals. However, in cases of dysbiosis or immunosuppression, *Candida albicans* can overgrow leading to opportunistic infections such as oral thrush.[9] Viruses, including bacteriophages and human viruses like herpes simplex virus (HSV) and Epstein Barr virus (EBV) interact with bacterial populations and contribute to microbial balance or disease progression.[10]

In recent years, research has increasingly highlighted the link between oral microbiome dysbiosis and various mental health disorders, suggesting that microbial imbalances in the oral cavity may influence brain function and behaviour. [11]

Mechanisms Linking Oral Dysbiosis to Mental Health

Neuroinflammation and Cytokine Transport:

Neuroinflammation and cytokine transport is one of the primary mechanisms connecting the oral microbiome to mental health.[12] Periodontal disease, characterised by chronic inflammation due to microbial overgrowth has been associated with increased levels of proinflammatory cytokines such as interleukin 6 (IL-6) and tumor necrosis factor-alpha (TNF-α) which can cross the blood-brain barrier and contribute to neuroinflammatory processes linked to depression and anxiety.[12,13] Furutama (2020) demonstrated that periodontal inflammation increases systemic IL-6 which induces neuroinflammation in the hippocampus.[13] Oral bacteria such as *Porphyromonas gingivalis* and *Fusobacterium nucleatum* have been found in the bloodstream of individuals with systemic inflammatory conditions further supporting the role of oral microbes in influencing overall health including neurological function.[14]

Neurotransmitter modulation:

Neurotransmitter modulation is another critical link between the oral microbiome and mental health. Some bacteria within the oral microbiota are known to influence the production of neurotransmitters including serotonin, dopamine and gamma-aminobutyric acid (GABA) all of which play essential roles in mood regulation and cognitive function.[15] Bacteria from the *Lactobacillus and Bifidobacterium* genera have been shown to enhance GABA production which has calming effects on the nervous system.[15] Conversely, the presence of pathogenic bacteria and the resultant dysbiosis may lead to imbalances in these neurotransmitters, potentially contributing to mood disorders and neuropsychiatric conditions.[16]

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Declaration:
- Both authors contributed equally to the article and approved the submitted version.
- The authors declare there is no conflict of interest

https://doi.org/10.17159/sadj.v80i10.22087

Microbial Translocation:
Pathogens like *Fusobacterium nucleatum* and *P. gingivalis* can breach mucosal barriers, enter the systemic circulation and potentially access the brain, triggering neurodegenerative processes.[17,18]

Hypothalamic Pituitary Adrenal (HPA) Axis Dysregulation:
Chronic oral infections activate the HPA axis, elevating cortisol and disrupting stress regulation pathways implicated in anxiety and depression.[19] This study found that individuals with periodontitis exhibited significantly higher salivary cortisol levels and these levels correlated with measures of stress and depression.[19] The findings suggest that chronic oral infections may activate the HPA axis leading to elevated cortisol and contributing to the pathophysiology of anxiety and depression.[19]

Epidemiological evidence

Epidemiological evidence also supports the connection between oral health and mental well-being.[20,21] Individuals with poor oral hygiene and periodontal disease are at an increased risk of developing depression and cognitive impairment.[22] Additionally, a bidirectional relationship exists between oral health and mental illness; psychiatric disorders often lead to neglect of oral hygiene which exacerbates dysbiosis and inflammation creating a vicious cycle that worsens both oral and mental health outcomes.[23] Thus, understanding the composition and function of the oral microbiome is fundamental to recognising its role in health and disease. As research continues to uncover these interactions between oral microbes and systemic health new therapeutic strategies targeting microbial balance are emerging, highlighting the importance of maintaining oral microbiome stability through proper oral hygiene, dietary interventions and probiotic use.[24]

Oral Dysbiosis in Specific Mental Health Conditions

Oral dysbiosis, an imbalance in the microbial community of the oral cavity has been increasingly linked to various mental health disorders. The disruption of a healthy oral microbiome leads to systemic inflammation, microbial translocation and neurotransmitter imbalances all of which play a role in the pathophysiology of psychiatric conditions. Below, we explore how oral dysbiosis is associated with specific mental health disorders including depression, anxiety, schizophrenia, bipolar disorder and neurodegenerative diseases.

Depression and Oral Dysbiosis

Major depressive disorder (MDD) is a prevalent and debilitating condition marked by persistent low mood, anhedonia and cognitive dysfunction. The pathophysiology of depression includes dysregulated hypothalamic-pituitary-adrenal (HPA) axis activity, proinflammatory cytokine elevation and serotonin (5-HT) imbalance.[25] Increasing evidence suggests that oral dysbiosis may act as both a contributor to and consequence of depression.[26] Disruption of the oral microbial ecosystem particularly an overgrowth of periodontal pathogenic species such as *Porphyromonas gingivalis, Fusobacterium nucleatum* and *Treponema denticola* is associated with elevated levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) and C-reactive protein (CRP) markers consistently elevated in depressive states.[27] These inflammatory mediators cross the blood-brain barrier and alter neurotransmitter metabolism, including the depletion of tryptophan, a serotonin precursor.[28] Pathogens such as *Porphyromonas gingivalis* and *Fusobacterium nucleatum* can enter systemic circulation triggering systemic inflammation and increasing the risk of depression.[29,30]

Shared biomarkers, IL-6 and TNF-α, may suggest a common inflammatory pathway in periodontitis and depression.[31] The oral microbiome plays a role in modulating neurotransmitters like serotonin, dopamine and GABA levels.[32] Dysbiosis can reduce the production of these neurotransmitters leading to symptoms of depression.[32] Moreover, poor oral health behaviour is common in depressed individuals, including reduced tooth brushing frequency, increased smoking and high carbohydrate intake which promotes microbial dysbiosis and further propagates systemic inflammation.[32] This bi-directional relationship underscores the role of oral health in both the onset and maintenance of depressive disorders.

Anxiety Disorders and the Oral Microbiome

Anxiety disorders including generalised anxiety disorder, panic disorder and social anxiety share features such as heightened stress responsiveness and autonomic nervous system dysregulation. Emerging evidence indicates a crucial role for the microbiota-gut-brain axis in anxiety with oral microbiota increasingly recognised as a contributor to this axis. Gamma aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the brain is produced by certain commensal oral bacteria such as *Streptococcus salivarius* and *Lactobacillus rhamnosus*.[33,34] Dysbiosis characterised by a reduction in GABA producing species may lead to central disinhibition, manifesting as increased anxiety.[35] Additionally, dysbiosis promotes reactive oxygen species (ROS) formation and oxidative stress, which damage neuronal tissues and exacerbate anxiety like behaviors.[35] Chronic oral pain syndromes including burning mouth syndrome and temporomandibular disorders (TMD) are frequently comorbid with anxiety and may be associated with altered oral microbial profiles suggesting a shared pathophysiological substrate involving neuroimmune dysregulation with microbial imbalance.[36]

Schizophrenia is a complex neurodevelopmental disorder characterised by delusions, hallucinations, disorganised thought and cognitive impairment. Individuals with schizophrenia are at increased risk for periodontal disease, dental caries and poor oral hygiene often due to neglect, medication side effects and cognitive impairment. Studies have demonstrated increased *Porphyromonas and Treponema* species among others in patients with schizophrenia contributing to oral and systemic inflammation.[36] These bacteria release endotoxins such as lipopolysaccharides (LPS) which activate toll like receptors (TLRs) on immune cells triggering neuroinflammatory cascades implicated in dopaminergic dysregulation, a central mechanism in schizophrenia.[37] Furthermore, emerging data suggest that oral microbial metabolites including short chain fatty acids (SCFAs) can influence brain function by modulating dopamine synthesis and receptor activity.[37] Antipsychotic medications particularly first generation agents may further alter oral microbial communities via anticholinergic-induced xerostomia and immunomodulatory effects.[38]

Bipolar disorder (BD) is a mood disorder characterised by alternating episodes of mania and depression with a psychosocial impact. The role of systemic inflammation in BD has gained attention with elevated levels of proinflammatory cytokines such as IL-1β and TNF-α

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https://doi.org/10.17159/sadj.v80i10.22087

reported during both manic and depressive phases.[39] Oral dysbiosis may influence circadian rhythm regulation which play a role in mood regulation in bipolar disorder. It has been shown to alter melatonin production and clock gene expression possibly contributing to circadian misalignment in BD.[40] Pharmacologic treatments for BD, including lithium and valproate frequently induce salivary gland hypofunction and xerostomia, reducing the mechanical clearance of pathogens and fostering anaerobic bacterial overgrowth.[41] These medication induced oral changes may potentiate microbial translocation and neuroinflammation, potentially impacting mood regulation. Whether immune dysfunction is a direct cause or a consequence is still an object of intense debate in what concerns the pathophysiology of psychiatric disorders. Nevertheless, interventions that modulate the immune system may be helpful.[39] It has been shown that mild anti-inflammatory effects were described in studies for antidepressants, mood stabilizers and antipsychotics, proposing that by contolling inflammation may relieve psychiatric symptoms. [42]

Neurodegenerative disorders, such as Alzheimer's disease and Parkinson's disease have been linked to microbial imbalances including those in the oral cavity. Alzheimer's disease, the most common cause of dementia is histopathologically defined by amyloid beta plaques and neurofibrillary tangles. A growing body of evidence implicates the oral pathogen *Porphyromonas gingivalis* in AD pathogenesis. Gingipains, cysteine proteases secreted by *P. gingivalis,* have been detected in post mortem brain samples of AD patients suggesting microbial infiltration across a compromised blood-brain barrier[43] These virulence factors promote amyloidogenesis, exacerbate tau hyperphosphorylation and activate microglia thereby perpetuating neuroinflammation.[43] Longitudinal studies have shown that individuals with chronic periodontitis are at significantly increased risk of cognitive decline.[44] In this six month observational cohort study, 60 community-dwelling participants with mild to moderate Alzheimer's disease were assessed for periodontal health and cognitive function. The study found that the presence of periodontitis at baseline was associated with a sixfold increase in the rate of cognitive decline over the follow up period.[44] The presence of bacterial DNA from oral pathogens in the cerebrospinal fluid of Alzheimer's patients suggests direct microbial translocation to the brain.[45] The systemic dissemination of oral pathogens and their endotoxins may serve as persistent neuroinflammatory stimuli hastening the progression of neurodegeneration.

Parkinson's disease is a progressive neurodegenerative disorder marked by bradykinesia, rigidity and tremor associated with loss of dopaminergic neurons in the substantia nigra. Gastrointestinal dysfunction is a prominent non-motor symptom of PD often preceding motor manifestations by years.[46] Although the gut microbiome has received significant attention in PD research, the role of the oral microbiome remains underexplored. Oral dysbiosis, particularly elevated levels of *Aggregatibacter actinomycetemcomitans*, *Prevotella intermedia* and *Campylobacter rectus* may contribute to systemic inflammation and gut barrier dysfunction.[47] These bacteria have been implicated in promoting the misfolding of alpha synuclein, a key protein in PD pathophysiology.[48]Additionally, oral inflammation can influence vagus nerve signaling and modulate enteric nervous system integrity mechanisms believed to be central to PD pathogenesis. Patients with PD frequently exhibit sialorrhea or xerostomia, both of which alter salivary flow and microbial composition. This dysregulation may foster a pro-inflammatory oral environment that facilitates peripheral to central immune activation further accelerating neuronal loss.[49]

The oral brain axis as a potential therapeutic target

Improving oral hygiene may reduce anxiety or depressive symptoms by restoring microbial balance, lowering systemic inflammation and potentially normalising neurotransmitter associated pathways. While direct interventional studies remain limited, observational evidence supports the idea that poor periodontal health correlates with worse mental health outcomes.[21] Regular oral care can reduce the abundance of pathogenic bacteria that promote inflammatory and neurotoxic metabolites, thereby diminishing prodepressive physiological signals. Reduction in pathogenic taxa like *Shuttleworthia* and increases in beneficial microbes such as *Fusobacterium* (associated with healthier mental states) have been observed in individuals without anxiety or depressive symptoms.[20] These findings collectively support the hypothesis that oral hygiene may play a preventive or adjunctive therapeutic role in managing mental health.

While the associations between oral health and mental illness are compelling, current evidence is largely correlative and preclinical. Many studies rely on animal models or cross sectional human data. Longitudinal and interventional studies are needed to establish causality, especially concerning oral probiotics' direct effects on neuropsychiatric outcomes. Additionally, confounding variables such as socioeconomic status, diet and medication use complicate interpretation. However, given the mounting evidence linking oral microbiome health to mental well being, it is important to explore interventions aimed at maintaining microbial balance.

Role of probiotics in the oral microbiome

Although much of the evidence regarding probiotics and mental health focuses on the gut microbiome, early findings suggest that oral probiotics may indirectly influence brain health by reducing peripheral inflammation and supporting mucosal integrity.[50] Strategies such as maintaining good oral hygiene, using probiotics and adopting a diet rich in prebiotic fibers may help modulate the oral microbiome and mitigate risks associated with mental health disorders.[50] The effect of *Lactobacillus reuteri* against one of the major cariogenic organism, *Streptococcus mutans* was studied.[51] Yogurt products containing *L. reuteri* showed a significant growth inhibitory effect against *S. mutans*. *L. reuteri* and *L. kefiranofaciens* inhibit cariogenic bacteria like *S.mutans* promote mucosal health and support anti-inflammatory cytokine profiles.[51,52] *L. kefiranofaciens* DD2 from kefir was shown to effectively inhibit *S. mutans* and *S. sobrinus i*n an in-vitro oral environment.[53] The precise mechanisms underlying these interactions needs further research which may pave the way for new and innovative therapeutic approaches that can integrate oral health into a more holistic mental health care regime.

Role of Dentists in maintaining healthy oral microbiome

As frontline healthcare providers, dentists play a crucial role in maintaining not only oral health but also overall systemic

https://doi.org/10.17159/sadj.v80i10.22087

well-being including mental health. The emerging research on the oral microbiome's impact on neurological and psychiatric disorders suggests that dental professionals should adopt a more holistic approach to patient care. Understanding the connections between oral health, inflammation and mental well-being allows dentists to contribute to both preventive and therapeutic strategies that extend beyond the oral cavity.

Recommendations for Practitioners

Dentists should educate patients on the importance of the oral microbiome, emphasising that the oral cavity hosts a complex microbial ecosystem essential for both oral and systemic health. Patients should understand that maintaining a balanced microbiome not only prevents cavities and gum disease but also helps reduce systemic inflammation linked to mental health outcomes. While good oral hygiene is crucial, excessive use of antimicrobial mouthwashes can disrupt beneficial bacterial communities. Practitioners should therefore encourage effective hygiene practices without over-sterilization and recommend alcohol-free, mild antiseptic rinses that preserve microbial balance rather than eradicating all bacteria.

Promoting the use of probiotics and prebiotics can further support oral and systemic well-being. Products such as probiotic lozenges or mouthwashes containing *Lactobacillus* and *Bifidobacterium* strains may help stabilize the microbiome while a diet rich in prebiotic foods such as fibre rich vegetables, fermented foods and dairy products with active cultures provides a nutritional foundation for beneficial bacteria. Addressing periodontal disease should also be considered a systemic concern given its contribution to systemic inflammation and potential links to neuroinflammation. Personalized management plans for periodontitis should combine mechanical debridement with microbiome supportive therapies.

Clinicians should also remain vigilant in screening for oral systemic health links particularly in patients with mental health disorders such as depression, anxiety or neurodegenerative diseases. These individuals may experience poor oral health due to neglect or medication induced xerostomia and would benefit from tailored oral care strategies including fluoride applications, saliva substitutes and more frequent hygiene visits. Dietary advice should emphasize reducing sugar intake which fuels pathogenic bacteria while encouraging the consumption of anti-inflammatory foods rich in omega 3 fatty acids, polyphenols (such as those found in green tea, berries and dark chocolate) and fibre rich vegetables. Stress management is another important consideration as stress contributes to both periodontal disease and microbiome imbalance; dentists can collaborate with other healthcare professionals to encourage mindfulness practices, exercise and adequate sleep as part of comprehensive care.

As technology advances, personalized oral microbiome testing may allow dentists to integrate microbial profiling into routine care enabling more targeted prevention and treatment strategies.

CONCLUSION

Emerging evidence supports the view that oral health extends beyond the mouth with implications for neurological and psychiatric well-being. Oral dysbiosis may contribute to the pathophysiology of depression, anxiety, schizophrenia, bipolar disorder and neurodegenerative diseases through inflammation, microbial translocation and neurotransmitter modulation. By integrating oral microbiome management into preventive care and interdisciplinary collaboration, dental professionals can contribute meaningfully to public mental health.

By adopting a proactive approach to microbiome health, dental practitioners can move beyond the traditional management of caries and periodontal disease to play a pivotal role in promoting overall systemic health and supporting their patients' mental well-being.

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