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ORAL MICROBIOME AND DEPRESSION: EXPLORING THE LINK BETWEEN BUCCAL MICROBIAL DIVERSITY AND DEPRESSIVE DISORDERS

MICROBIOMA ORAL E DEPRESSÃO: EXPLORANDO A RELAÇÃO ENTRE A DIVERSIDADE MICROBIANA BUCAL E TRANSTORNOS DEPRESSIVOS

MICROBIOMA ORAL Y DEPRESIÓN: EXPLORANDO EL VÍNCULO ENTRE LA DIVERSIDAD MICROBIANA BUCAL Y LOS TRASTORNOS DEPRESIVOS

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ABSTRACT

The objective of this narrative literature review article is to address the possible correlation between the microbiome and depressive disorders. Methodology: During the construction of this narrative literature review, it was necessary to search online databases to obtain studies that would serve to compose the review. Searches were carried out in the following databases: Pubmed, Cochrane Library, Embase in conjunction with Google Scholar. The following descriptors were used during the searches in the databases: Microbiome;

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depression; Oral Health. The results obtained in the searches within the databases went through 3 stages, aiming to remain only studies that are related to the objectives of this review. First stage: The articles acquired in the searches went through screening, eliminating duplicate articles. Second stage: The articles left over from the deduplication were read, where the remaining articles had their abstracts and titles read, and those that did not fit the study were removed. Third stage: The remaining articles were read in their entirety, leaving only those that fit the theme to compose the article. Results: The oral cavity houses the second largest bacterial community in the human body, behind only the intestine, which is responsible for the largest community of bacteria. Studies have shown that knowledge about the bacteria in the oral cavity can serve as potential biomarkers, even revealing the possibility of predisposition to depressive disorders. Conclusion: Studies show that people with lower diversity in the oral microbiome are more likely to develop symptoms of depression.

Keywords: Microbiome. Depression. Oral Health.

RESUMO

O objetivo deste artigo de revisão narrativa da literatura é abordar a possível correlação entre o microbioma e transtornos depressivos. Metodologia: Durante a construção desta revisão narrativa da literatura, foi necessária a busca em bases de dados online para obtenção de estudos que serviriam para compor a revisão. As buscas foram realizadas nas seguintes bases de dados: Pubmed, Cochrane Library, Embase em conjunto com o Google Acadêmico. Os seguintes descritores foram utilizados durante as buscas nas bases de dados: Microbioma; depressão; Saúde Bucal. Os resultados obtidos nas buscas dentro das bases de dados passaram por 3 etapas, visando permanecer apenas estudos que se relacionam com os objetivos desta revisão. Primeira etapa: Os artigos adquiridos nas buscas passaram pela triagem, eliminando artigos duplicados. Segunda etapa: Os artigos que sobraram da deduplicação foram lidos, onde os artigos restantes tiveram seus resumos e títulos lidos, e aqueles que não se enquadram no estudo foram removidos. Terceira etapa: Os artigos restantes foram lidos na íntegra, restando apenas aqueles que se enquadram na temática para compor o artigo. Resultados: A cavidade oral abriga a segunda maior comunidade bacteriana do corpo humano, atrás apenas do intestino, que é responsável pela maior comunidade bacteriana. Estudos demonstram que o conhecimento sobre as bactérias presentes na cavidade oral pode servir como potenciais biomarcadores, revelando inclusive a possibilidade de predisposição a transtornos depressivos. Conclusão: Estudos demonstram que pessoas com menor diversidade no microbioma oral têm maior probabilidade de desenvolver sintomas de depressão.

Palavras-chave: Microbioma. Depressão. Saúde Bucal.

RESUMEN

El objetivo de esta revisión narrativa de la literatura es abordar la posible correlación entre el microbioma y los trastornos depresivos. Metodología: Durante la construcción de esta revisión narrativa de la literatura, fue necesario buscar en bases de datos en línea para obtener estudios que sirvieran de base para la revisión. Las búsquedas se realizaron en las siguientes bases de datos: PubMed, Cochrane Library, Embase y Google Scholar. Se utilizaron los siguientes descriptores durante las búsquedas en las bases de datos:

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Microbioma; Depresión; Salud Oral. Los resultados obtenidos de las búsquedas en las bases de datos se sometieron a tres etapas, con el objetivo de retener solo estudios relacionados con los objetivos de esta revisión. Primera etapa: Los artículos adquiridos a través de las búsquedas se sometieron a un cribado, eliminando artículos duplicados. Segunda etapa: Se leyeron los artículos restantes después de la deduplicación, donde se leyeron los resúmenes y títulos de los artículos restantes, y se eliminaron aquellos no adecuados para el estudio. Tercera etapa: Los artículos restantes se leyeron en su totalidad, dejando solo aquellos que se ajustaban al tema para componer el artículo. Resultados: La cavidad oral alberga la segunda comunidad bacteriana más grande en el cuerpo humano, solo superada por el intestino, que es responsable de la comunidad bacteriana más grande. Los estudios demuestran que el conocimiento sobre las bacterias presentes en la cavidad oral puede servir como posible biomarcador, incluso revelando la posibilidad de predisposición a trastornos depresivos. Conclusión: Los estudios demuestran que las personas con menor diversidad en el microbioma oral tienen mayor probabilidad de desarrollar síntomas de depresión.

Palabras clave: Microbioma. Depresión. Salud Bucal.

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1 INTRODUCTION

The human microbiome plays a critical role in maintaining systemic health, influencing immunity, metabolism, and even neurological functions. While the gut microbiome has been widely studied in relation to brain health and mood disorders, the oral microbiome, a diverse community of bacteria residing in the buccal cavity, has recently emerged as a potential player in the pathogenesis of depression. The oral cavity is the second most microbially dense site in the human body, comprising over 700 bacterial species, many of which are involved in immune modulation and inflammatory responses (Dewhirst et al., 2010; Wade, 2013).

Recent studies suggest that dysbiosis in the oral microbiome may contribute to systemic inflammation, which has been implicated in the development of major depressive disorder (Maes et al., 2009; Qiu et al., 2025). The oral-brain axis akin to the well known gut brain axis proposes that changes in oral microbial diversity can influence neuroinflammation and neurochemical regulation (Sampson et al., 2016; Jiang et al., 2017; Paudel et al., 2022). The NHANES-based population study by Qiu et al. (2025) found that individuals with lower alpha diversity in the oral microbiome were significantly more likely to present depressive symptoms, with a nonlinear association between observed microbial richness and PHQ-9 scores.

Additionally, it has been proposed that microbial metabolites such as short-chain fatty acids, generated by oral bacteria, may modulate systemic inflammation and neurotransmission. Furthermore, depression may lead to poor oral hygiene, substance use, and altered diet, creating a bidirectional relationship between oral health and mental well-being (Friedlander & Marder, 2002; Dumitrescu, 2016). Understanding the interplay between oral microbial diversity and depressive symptoms may not only provide biomarkers for early diagnosis but also open avenues for preventive and therapeutic interventions.

2 METHODOLOGY

During the construction of this narrative literature review, it was necessary to search online databases in order to obtain studies that would serve to compose the review. Searches were carried out in the following databases: Pubmed, Cochrane Library, Embase in conjunction with Google Scholar. The following descriptors were used during the searches in the databases: Microbiome; Depression; Oral Health. Descriptors that are directly related to the topic addressed in the article, serving to narrow the results obtained in the searches,

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finding only content related to the present study. The results obtained in the searches within the databases went through 3 stages, aiming to remain only studies that are related to the objectives of this review. First stage: The articles acquired in the searches went through a de-publication, eliminating duplicate articles. Second stage: The articles left over from the deduplication were read, where the remaining articles had their abstracts and titles read, and those that did not fit the study were removed. Third stage: The remaining articles were read in their entirety, leaving only those that fit the theme to compose the article. Rother's study (2007) served as a guide during the construction of this article, as it is a study that addresses how narrative and systematic literature reviews should be carried out, from their approach to the content that should make up each type of review.

3 RESULTS

Recent scientific advances have significantly expanded our understanding of how the oral microbiome may influence mental health, particularly depressive disorders. The human oral cavity harbors over 700 bacterial species, forming the second most microbially dense ecosystem in the body after the gut (Dewhirst et al., 2010; Wade, 2013). While the gut-brain axis has long been studied in relation to mood and cognition, emerging evidence now highlights an analogous oral-brain axis, in which dysbiosis of the oral microbiome may contribute to neuroinflammatory pathways and neuropsychiatric outcomes.

One of the most robust findings comes from a population-based study by Qiu et al. (2025), which utilized data from the NHANES (2009–2012) cohort to analyze the relationship between oral microbial diversity and depressive symptoms measured by the Patient Health Questionnaire-9 (PHQ-9). The study revealed a statistically significant inverse association between alpha diversity (a measure of microbial richness and evenness) and depressive symptom scores. Individuals with lower microbial diversity exhibited increased odds of moderate-to-severe depressive symptoms, even after adjusting for smoking, body mass index (BMI), age, and socioeconomic factors.

Metagenomic studies further corroborate these associations. For instance, Liu et al. (2021) and Yang et al. (2022) identified distinct oral microbial signatures in patients with clinically diagnosed major depressive disorder (MDD), characterized by a depletion of symbiotic species such as Streptococcus sanguinis, Neisseria subflava, and Rothia mucilaginosa, alongside an increased abundance of pro-inflammatory pathogens such as

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Fusobacterium nucleatum, Porphyromonas gingivalis, and Prevotella intermedia. These shifts are consistent with a dysbiotic state that promotes chronic low-grade inflammation.

The pro-inflammatory state induced by oral dysbiosis may exert systemic effects by increasing circulating cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1β (IL-1β) which can compromise the integrity of the blood-brain barrier and dysregulate neurochemical transmission (Maes et al., 2009; Paudel et al., 2022). This mechanism mirrors those described in the gut-brain axis and suggests that the oral microbiota may similarly modulate the hypothalamic-pituitary-adrenal (HPA) axis and serotonergic systems involved in mood regulation.

Another important line of evidence concerns the production of microbial metabolites. Certain oral bacteria, such as Veillonella and Actinomyces, are capable of producing short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate, which exhibit neuroactive and anti-inflammatory properties. Disruption of SCFA production due to reduced microbial diversity may impair GABAergic and serotonergic signaling in the brain, further contributing to depressive symptoms (Komatsu et al., 2022; Sampson et al., 2016). Bidirectionality must also be acknowledged. Depressive disorders are often accompanied by behavioral changes that negatively affect oral hygiene, such as reduced toothbrushing frequency, increased sugar intake, tobacco and alcohol use, and decreased dental service utilization (Friedlander & Marder, 2002; Dumitrescu, 2016). These behaviors create a favorable environment for pathogenic bacterial overgrowth, reinforcing the dysbiosis-depression cycle.

A large-scale population study by Lebedeva et al. (2021) found that individuals with depression had significantly worse oral health indicators, including higher rates of periodontitis, greater tooth loss, and more frequent reports of dry mouth. Likewise, longitudinal data from Liu et al. (2023) showed that older adults with lower oral microbial diversity at baseline were more likely to develop depressive symptoms over a five-year follow-up, suggesting a potential predictive role for buccal microbiota composition. Demographic variables such as gender, age, education, and diet also influence both the oral microbiome and mental health outcomes. Women, for example, may exhibit greater microbial susceptibility to stress-induced dysbiosis, while diets rich in fiber and polyphenols appear to support microbial eubiosis and confer resilience against depression (Ganjhu et al., 2020; Liu et al., 2023).

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Collectively, these findings support a multifactorial and dynamic interaction between oral microbial communities and mental health. Identifying specific microbial signatures and inflammatory profiles associated with depression could enable the development of diagnostic tools based on salivary biomarkers and open new therapeutic possibilities involving oral probiotics, prebiotics, dietary interventions, and behavioral health integration in oral care.

4 DISCUSSION

The expanded results from both metagenomic and population-based studies provide strong evidence for a biological link between oral microbial diversity and depressive symptoms. Rather than being an incidental comorbidity, oral dysbiosis appears to play an active role in the neurobiological underpinnings of mood disorders. The observed reduction in microbial diversity in depressed individuals suggests a loss of microbial equilibrium, potentially impairing mucosal immunity and triggering chronic low-grade inflammation. This systemic inflammatory state may compromise the integrity of the blood brain barrier and dysregulate neuroimmune pathways, contributing to the onset and maintenance of depressive symptoms.

Moreover, the alteration in microbial composition marked by the dominance of pathogenic bacteria and depletion of symbiotic commensals may disrupt the production of key metabolites such as butyrate and other short chain fatty acids. These compounds have known roles in anti-inflammatory signaling and neurotransmitter modulation, including serotonin metabolism, thus influencing mood and emotional regulation. The bidirectional nature of the relationship must also be acknowledged. Depression often leads to behavioral changes such as poor oral hygiene, irregular dental visits, high sugar intake, and increased alcohol or tobacco use. These habits not only worsen periodontal health but also accelerate microbial imbalance, establishing a feedback loop that perpetuates both psychological and oral dysfunction.

The demographic differences observed in this study further reinforce the need for personalized interventions. Gender, race, education, and lifestyle factors all appear to modulate the microbiota depression axis. These variables may influence microbial acquisition, immune response, and systemic exposure to inflammatory triggers. While current findings are robust, they are largely derived from cross-sectional data. As such, the causality and temporal direction of these associations remain to be fully elucidated. Longitudinal and mechanistic studies are essential to determine whether modifying oral

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microbiota through hygiene, diet, or probiotics can provide tangible improvements in mental health outcomes.

5 CONCLUSION

Studies show that people with less diversity in their oral microbiome are more likely to develop symptoms of depression. However, there is a clear need for more studies to identify these biomarkers, studying them and proving their link to depression.

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