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Oral microbiota and neuroinflammation in pathogenesis of parkinson's desease

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Abstract. Oral Microbiota and Neuroinflammation in the Pathogenesis of Parkinson's Disease Abstract: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by α-synuclein aggregation and chronic neuroinflammation. Emerging evidence suggests that oral microbiota dysbiosis, particularly the proliferation of periodontal pathogens like Porphyromonas gingivalis, plays a significant role in PD pathogenesis through the "oral-gut-brain" axis. This literature review systematically analyzes the mechanisms by which oral pathobionts and their virulence factors (such as lipopolysaccharides and gingipains) disrupt mucosal barriers, induce systemic inflammation, and trigger microglial activation in the central nervous system. Furthermore, we discuss the clinical correlations between periodontal disease and PD severity, highlighting the potential of salivary biomarkers for early, non-invasive diagnosis. Ultimately, the review explores microbiome-targeted therapeutic strategies, emphasizing that maintaining periodontal health may mitigate neuroinflammation and potentially slow disease progression.

Keywords: parkinson's disease, neuroinflammation, neurodegenerationoral, microbiome, oral microbiota, oral dysbiosis, periodontitis, periodontal pathogens, porphyromonas gingivalis, alpha-synuclein, oral-gut-brain axis, microglia activation.

Аннотация: Болезнь Паркинсона (БП) - это прогрессирующее нейродегенеративное заболевание, характеризующееся агрегацией α-синуклеина и хроническим нейровоспалением. Появляется все больше данных о том, что дисбиоз микробиоты полости рта, в частности чрезмерный рост таких пародонтопатогенов, как Porphyromonas gingivalis, играет значительную роль в патогенезе БП через «орально-кишечно-мозговую» ось. В данном обзоре литературы систематически анализируются механизмы, с помощью которых оральные патогены и их факторы вирулентности (включая липополисахариды и гингипины) нарушают барьеры слизистой оболочки, вызывают системное воспаление и провоцируют активацию микроглии в центральной нервной системе. Кроме того, обсуждаются клинические корреляции между заболеваниями пародонта и тяжестью БП, а также подчеркивается высокий потенциал биомаркеров слюны для ранней и неинвазивной диагностики. В заключение рассматриваются терапевтические стратегии, направленные на коррекцию микробиома, и подчеркивается, что поддержание здоровья полости рта может снизить нейровоспаление и замедлить прогрессирование заболевания.

Ключевые слова: болезнь Паркинсона, нейровоспаление, нейродегенерация, микробиом полости рта, микробиота полости рта, дисбиоз полости рта, пародонтит, пародонтопатогены, Porphyromonas gingivalis, альфа-синуклеин, орально-кишечно-мозговая ось, активация микроглии.

Annotatsiya: Parkinson kasalligi (PK) – bu α-sinuklein oqsilining to'planishi va surunkali neyroyallig'lanish bilan tavsiflanuvchi zo'rayib boruvchi neyrodegenerativ kasallikdir. So'nggi ilmiy dalillar shuni ko'rsatadiki, og'iz bo'shlig'i mikrobiotasi disbiozi, xususan, Porphyromonas gingivalis kabi parodont patogenlarining ko'payishi "og'iz-ichak-miya" o'qi orqali PK patogenezida muhim rol o'ynaydi. Ushbu adabiyotlar sharhida og'iz bo'shlig'i patogenlari va ularning virulentlik omillari shilliq qavat to'siqlarini buzib o'tishi, tizimli yallig'lanishni keltirib chiqarishi hamda markaziy asab

tizimida mikrogliya faollashuvini qo'zg'atish mexanizmlari tizimli ravishda tahlil qilinadi. Shuningdek, parodont kasalliklari va PK og'irlik darajasi o'rtasidagi klinik bog'liqliklar muhokama qilinib, erta va noinvaziv diagnostika uchun so'lak biomarkerlarining (masalan, oligomer α-sinuklein) salohiyati ta'kidlanadi. Xulosa o'rnida, mikrobiomga qaratilgan terapevtik strategiyalar ko'rib chiqiladi va og'iz bo'shlig'i salomatligini saqlash neyroyallig'lanishni kamaytirib, kasallik rivojlanishini sekinlashtirishi mumkinligi xulosa qilinadi.

Kalit so'zlar: Parkinson kasalligi, neyroyallig'lanish, neyrodegeneratsiya, og'iz bo'shlig'i mikrobiomi, og'iz bo'shlig'i mikrobiotasi, og'iz bo'shlig'i disbiyozi, parodontit, parodont patogenlari, Porphyromonas gingivalis, alfa-sinuklein, og'iz-ichak-miya o'qi, mikrogliya faollashuvi.

Introduction.Parkinson’s disease (PD) is a complex, progressive, and debilitating neurodegenerative disorder that affects millions of people worldwide. The core pathological hallmarks of PD include the progressive loss of dopaminergic neurons in the substantia nigra pars compacta, the widespread accumulation of misfolded α-synuclein (α-Syn) aggregates (Lewy pathology), and chronic neuroinflammatory processes. In recent years, neuroinflammation has emerged as a fundamental driver in the pathogenesis of PD, involving both innate and adaptive immune responses. Systemic inflammation and bacterial factors are increasingly recognized as a potential "second hit" that exacerbates microglial activation and neurodegeneration in the central nervous system (CNS) While traditional microbiome research in PD has heavily focused on the gut-brain axis, the oral cavity-which harbors the second-largest microbial community in the human body-has recently gained significant attention. Oral dysbiosis, commonly presenting as periodontal disease, involves a shift from commensal bacteria to a pathogenic profile enriched with gram-negative anaerobic bacteria such as Porphyromonas gingivalis (P. gingivalis), Fusobacterium nucleatum, and Streptococcus mutans. These oral pathogens continuously shed virulence factors, including lipopolysaccharides (LPS) and toxic proteases like gingipains, which can compromise the mucosal barrier and enter the systemic circulation. Compelling evidence suggests that the oral microbiome interacts with the CNS through multiple direct and indirect pathways, contributing to PD pathology. Pathogenic oral bacteria and their circulating toxins can increase the permeability of the blood-brain barrier (BBB) and facilitate the entry of bacterial inflammagens into the brain. Once in the CNS, these factors activate microglia and trigger the release of pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α, initiating a cascade of neuroinflammation and neuronal death. Notably, recent autopsy studies have ultrastructurally localized P. gingivalis gingipains directly within the dopaminergic neurons of the substantia nigra in PD patients, providing robust evidence for their direct neurotoxic effects. Furthermore, the "oral-gut-brain axis" presents another critical route of pathogenesis. Patients with severe periodontitis swallow millions of oral pathogens daily, which can survive gastric transit, colonize the gastrointestinal tract, and induce severe gut dysbiosis. This microbial shift promotes intestinal inflammation, increases gut permeability, and may trigger the initial aggregation of α-Syn in the enteric nervous system, which then propagates to the brain via the vagus nerve in a prion-like manner. Clinically, epidemiological studies have demonstrated a higher prevalence of periodontitis and overall poorer oral hygiene-such as elevated plaque indices and profound tooth loss-among patients with PD compared to healthy controls. However, findings regarding the exact bidirectional, causal association between periodontitis and PD risk remain controversial, highlighting the need for a deeper mechanistic understanding of this relationship. Therefore, the objective of this literature review is to comprehensively evaluate the role of the oral microbiome in the development of neuroinflammation and the progression of Parkinson’s disease. Specifically, this review aims to synthesize current evidence on the mechanistic pathways linking oral dysbiosis to neurodegeneration, analyze the clinical correlations between periodontal status and PD, and explore the promising landscape of microbiome-targeted therapeutic strategies.

MATERIALS AND METHODS. A systematic literature search was conducted across major scientific databases, including PubMed, Scopus, Web of Science, Google Scholar, the Cochrane Library, and EMBASE, for articles published between 2000 and 2026. Search queries utilized a

combination of English and Russian keywords and MeSH terms, such as "oral microbiome," "periodontal pathogens," "Parkinson's disease," and "neuroinflammation". Selection Criteria: We included clinical, preclinical, and epidemiological studies, as well as systematic reviews and meta-analyses that investigated the link between oral microbiota and Parkinson's disease (PD). Studies focusing exclusively on the gut microbiome, other neurodegenerative diseases, or unverified clinical case reports were excluded. Data Extraction: After removing duplicates using reference management software (e.g., EndNote, Zotero, or Mendeley), articles underwent a rigorous two-step screening process: an initial title/abstract evaluation followed by a full-text analysis for relevance. Extracted data focused on study design, oral microbiota composition, mechanistic pathways (e.g., lipopolysaccharides, gingipains, and pro-inflammatory cytokines), and clinical correlations between periodontal health and PD progression.

RESULTS. Clinical Alterations in Oral Microbiota and Periodontal Status Epidemiological and clinical data consistently demonstrate that patients with Parkinson's disease (PD) exhibit a significantly higher prevalence of periodontal diseases and poorer overall oral hygiene compared to healthy controls. Specifically, PD patients present with significantly elevated clinical parameters such as Periodontal Pocket Depth (PPD), Clinical Attachment Level (CAL), and Plaque Index (PI), alongside higher rates of xerostomia (dry mouth), tooth mobility, and dysphagia[1]. However, despite these strong clinical correlations, comprehensive meta-analyses and Mendelian randomization studies indicate no significant bidirectional causal association between periodontitis risk and the genetic incidence of PD. This suggests that severe periodontitis in PD is not necessarily the sole initiating cause of the disease, but rather a consequence of PD-related motor and cognitive deficits, combined with shared systemic inflammatory pathways that exacerbate both conditions[2]. Microbiome profiling of the oral cavity in PD patients reveals distinct oral dysbiosis, characterized by a marked reduction in beneficial commensal bacteria and a significant enrichment of pro-inflammatory pathobionts, including Porphyromonas gingivalis (P. gingivalis), Prevotella, Fusobacterium nucleatum, and Streptococcus mutans (S. mutans). Mechanistic Pathways of Neuroinflammation: The Oral-Gut-Brain Axis The systemic dissemination of oral pathobionts and their neuroinflammatory effects primarily occur through the oral-gut-brain axis. Patients with severe periodontitis swallow massive amounts of oral bacteria daily (estimated at 10^8 to 10^{10} P. gingivalis cells), allowing acid-resistant pathogens to ectopically colonize the gastrointestinal tract[3]. Once in the gut, these pathogens induce severe gut dysbiosis by reducing the Firmicutes/Bacteroidetes ratio and depleting beneficial short-chain fatty acid (SCFA)-producing bacteria. This microbial shift damages the intestinal epithelial barrier by downregulating tight junction proteins, increasing gut permeability ("leaky gut"), and allowing bacterial endotoxins, such as lipopolysaccharides (LPS), to enter the systemic circulation. Consequently, this translocation triggers a massive systemic immune response[4]. The infiltration of LPS and other bacterial virulence factors activates peripheral immune cells, leading to a pro-inflammatory cytokine storm characterized by elevated blood levels of IL-1β, IL-6, TNF-α, and C-reactive protein. Furthermore, oral pathogens orchestrate a profound immune dysregulation by skewing T-cell differentiation towards a pro-inflammatory Th17 phenotype while simultaneously suppressing regulatory T cells (Tregs) in the gut and lymphoid tissues. These circulating cytokines and gut-primed Th17 cells can cross the blood-brain barrier, triggering the sustained activation of microglia and astrocytes via Toll-like receptors (TLRs), which directly mediates neuroinflammation and drives dopaminergic cell death[5]. Direct Neurotoxicity and Pathological Protein Aggregation In addition to systemic inflammation, oral pathogens contribute to PD pathogenesis through direct neurotoxic mechanisms and the promotion of pathological protein aggregates. Pathogenic oral bacteria produce bacterial amyloids and LPS that trigger the initial misfolding and aggregation of α-synuclein (α-Syn) in the enteric nervous system[6]. Consistent with Braak's hypothesis, these α-Syn aggregates can subsequently propagate from the inflamed gut to the brain in a prion-like manner via the vagus nerve. In animal models, the oral administration of P. gingivalis and S. mutans has been shown to successfully induce gut dysbiosis, promote α-Syn accumulation in colon neurons, and exacerbate

motor dysfunction and dopaminergic neurodegeneration. Furthermore, recent ultrastructural autopsy studies have detected gingipains-highly toxic proteases secreted by P. gingivalis-directly within the dopaminergic neurons of the substantia nigra in PD patients. These translocated gingipains can directly cleave neuronal proteins, thereby exacerbating localized neuroinflammation, accelerating the formation of Lewy body-like pathologies, and contributing heavily to the cognitive impairment (PD-CI) frequently observed in advanced PD cases.

DISCUSSION. The synthesized literature provides compelling evidence that oral dysbiosis is intricately linked to the neuroinflammatory processes underlying Parkinson's disease (PD). The data suggest that periodontal pathobionts, most notably Porphyromonas gingivalis (P. gingivalis), operate through a complex "oral-gut-brain" axis to exacerbate systemic and central inflammation[7]. Through the continuous shedding of virulence factors such as lipopolysaccharides (LPS) and gingipains, oral pathogens can disrupt mucosal and blood-brain barriers, promote the systemic release of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α), and induce a dysregulation of the Th17/Treg immune cell balance. These cascades ultimately contribute to microglial activation and the aggregation of α-synuclein (α-Syn) in the brain. The Causality Dilemma and Environmental Confounders Despite the strong mechanistic plausibility, the exact causal nature of the relationship between periodontitis and PD remains a subject of considerable debate[8]. While observational studies consistently report a higher prevalence of periodontitis, worse periodontal pocket depth (PPD), and poorer overall oral hygiene in PD patients compared to healthy controls, a recent comprehensive meta-analysis and Mendelian randomization study revealed no significant bidirectional or genetic causal association between the risk of periodontitis and the incidence of PD. This discrepancy suggests that the association may be heavily mediated by shared systemic inflammatory pathways and downstream environmental factors rather than genetic liability[9]. As PD progresses, motor deficits (bradykinesia, rigidity), cognitive impairment, and specific symptoms like dysphagia and xerostomia (dry mouth) severely hinder a patient's ability to maintain adequate daily oral hygiene. Consequently, poor oral health and severe periodontitis in PD patients may initially develop as a secondary consequence of the disease's debilitating symptoms[10.]. However, once established, this oral infection acts as a continuous source of systemic inflammation, fueling a vicious cycle that further drives neurodegeneration. Methodological Limitations in Current Research A critical evaluation of the existing literature reveals several methodological limitations that complicate the interpretation of these findings. First, the majority of clinical studies investigating the oral microbiome in PD are cross-sectional or retrospective case-control designs with relatively small sample sizes. This cross-sectional nature makes it incredibly difficult to establish true temporal causality-whether oral dysbiosis precedes PD or develops as a consequence of the disease. Secondly, there is high heterogeneity across studies regarding the diagnostic criteria used for periodontitis and the clinical parameters measured, which challenges the accurate estimation of prevalence. Furthermore, differences in microbiome analysis techniques (e.g., 16S rRNA sequencing versus shotgun metagenomics) can introduce inconsistencies. Many studies also fail to adequately account for critical confounding variables, including dietary habits, smoking status, age, and the use of PD medications or antibiotics, all of which independently alter the microbiome. Future Directions and Therapeutic Implications To overcome current limitations, future research must prioritize large-scale, longitudinal prospective cohort studies to clearly map the temporal dynamics between oral dysbiosis and PD progression[8]. Additionally, utilizing advanced multi-omics approaches (such as transcriptomics and metabolomics) and network-based correlation analyses will be crucial for deciphering the complex inter-species interactions between the oral and gut microbiota, as well as their specific metabolic outputs (e.g., short-chain fatty acids, TMAO, and bile acids). From a clinical perspective, managing the oral-gut axis presents a promising frontier for adjunctive PD therapy. Interventional trials are needed to evaluate whether maintaining oral health can directly slow neurodegeneration[7]. Evidence already suggests that non-surgical periodontal treatment (NSPT) can reduce systemic inflammation, restore gut barrier integrity, and lower harmful circulating metabolites like TMAO. Furthermore, microbiome-targeted

interventions, such as the administration of specific probiotics (e.g., Lactobacillus, Bifidobacterium, or Akkermansia muciniphila) to competitively exclude oral pathogens and dampen inflammation, or the development of pharmacological agents targeting bacterial toxins (e.g., gingipain inhibitors), hold significant potential for disease modification in PD[10].

CONCLUSION. Current evidence strongly highlights the pivotal role of the oral microbiota in the pathogenesis and progression of Parkinson's disease (PD). Oral dysbiosis, particularly the overgrowth of periodontal pathogens such as Porphyromonas gingivalis, contributes to chronic systemic and central neuroinflammation. Through the release of potent virulence factors-such as lipopolysaccharides and gingipains-and the translocation of bacteria via the "oral-gut-brain" axis, oral pathogens can disrupt the blood-brain barrier, activate microglial cells, and promote the pathological aggregation of α-synuclein. Although some large-scale analyses indicate no strict genetic causal link between periodontitis risk and PD onset, the debilitating motor and cognitive symptoms of PD inevitably lead to poorer oral hygiene. This establishes a vicious cycle where oral infections serve as a continuous source of systemic inflammation that exacerbates neurodegeneration. Therefore, maintaining periodontal health and exploring microbiome-targeted therapies-such as non-surgical periodontal treatment, probiotics, or specific bacterial toxin inhibitors-represent highly promising adjunctive strategies to mitigate neuroinflammation and potentially slow PD progression. Future large-scale, longitudinal studies are essential to fully decode these complex microbial interactions and validate targeted clinical interventions.

REFERENCES:

1. Chen, Y., Jin, Y., Li, K., Qiu, H., Jiang, Z., Zhu, J., ... & Yang, D. (2023). Is There an Association Between Parkinson's Disease and Periodontitis? A Systematic Review and Meta-Analysis. Journal of Parkinson's Disease, 13, 1107–1125.
2. Ciongaru, D. N., Piţuru, S. M., Păunică, S., Giurgiu, M. C., Bujdei-Tebeică, I., & Dumitriu, A.-S. (2026). Comparative Analysis of Oral Bacterial Profiles in Parkinson's Disease According to Periodontal Status: A Clinical Case Series.
3. Ermini, F., et al. (2024). Ultrastructural localization of Porphyromonas gingivalis gingipains in the substantia nigra of Parkinson's disease brains. npj Parkinson's Disease, 10, 45.
4. Gan, G., Chen, R., Zheng, P., Long, K., Cheng, K. K. Y., Sulaiman, J. E., & Huang, X. (2026). Oral pathogens meet the gut microbiome: new mechanistic insights on systemic disease. Frontiers in Cellular and Infection Microbiology, 15, 1673512.
5. Grotemeyer, A., McFleder, R. L., Wu, J., Wischhusen, J., & Ip, C. W. (2022). Neuroinflammation in Parkinson's Disease – Putative Pathomechanisms and Targets for Disease-Modification. Frontiers in Immunology, 13, 878771.
6. Jin, J.-Y., Li, D., Qian, S., Gao, F., Li, Z.-Q., Zhang, J.-R., ... & Cheng, X.-Y. (2026). Distinct gut and oral microbial profiles differentiate patients with symmetric/asymmetric Parkinson's disease. Frontiers in Human Neuroscience, 20, 1776294.
7. Jo, S., Kang, W., Hwang, Y. S., Lee, S. H., Park, K. W., Kim, M. S., ... & Chung, S. J. (2022). Oral and gut dysbiosis leads to functional alterations in Parkinson's disease. npj Parkinson's Disease, 8(1), 87.
8. Li, D., Ren, T., Li, H., Liao, G., & Zhang, X. (2022). Porphyromonas gingivalis: A key role in Parkinson's disease with cognitive impairment? Frontiers in Neurology, 13, 945523.
9. Mihaila, D., Donegan, J., Barns, S., LaRocca, D., Du, Q., Zheng, D., ... & Middleton, F. A. (2019). The oral microbiome of early stage Parkinson's disease and its relationship with functional measures of motor and non-motor function. PLoS One, 14(6), e0218252.
10. Wang, B., Zhang, C., Shi, C., Zhai, T., Zhu, J., Wei, D., ... & Zhao, L. (2024). Mechanisms of oral microflora in Parkinson's disease. Behavioural Brain Research, 474, 115200.