

Bacterial Membrane Vesicles: The Missing Link Between Bacterial Infection and Alzheimer Disease

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Abstract

Periodontitis is a common chronic inflammatory disease, affecting approximately 19% of the global adult population. A relationship between periodontal disease and Alzheimer disease has long been recognized, and recent evidence has been uncovered to link these 2 diseases mechanistically. Periodontitis is caused by dysbiosis in the subgingival plaque microbiome, with a pronounced shift in the oral microbiota from one consisting primarily of Gram-positive aerobic bacteria to one predominated by Gram-negative anaerobes, such as *Porphyromonas gingivalis*. A common phenomenon shared by all bacteria is the release of membrane vesicles to facilitate biomolecule delivery across long distances. In particular, the vesicles released by *P gingivalis* and other oral pathogens have been found to transport bacterial components across the blood-brain barrier, initiating the physiologic changes involved in Alzheimer disease. In this review, we summarize recent data that support the relationship between vesicles secreted by periodontal pathogens to Alzheimer disease pathology.

Keywords: Alzheimer disease; bacterial vesicles; blood-brain barrier; oral microbiota; periodontitis.

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References

1. Bali J, Gheinani AH, Zurbriggen S, Rajendran L. Role of genes linked to sporadic Alzheimer's disease risk in the production of beta-amyloid peptides. *Proc Natl Acad Sci U S A* 2012; 109:15307–11. - [PMC](#) - [PubMed](#)
2. Edwards GA III, Gamez N, Escobedo G Jr, Calderon O, Moreno-Gonzalez I. Modifiable risk factors for Alzheimer's disease. *Front Aging Neurosci* 2019; 11:146. - [PMC](#) - [PubMed](#)
3. Rajan KB, Weuve J, Barnes LL, McAninch EA, Wilson RS, Evans DA. Population estimate of people with clinical Alzheimer's disease and mild cognitive impairment in the United States (2020–2060). *Alzheimers Dement* 2021; 17:1966–75. - [PMC](#) - [PubMed](#)
4. Nichols E, Steinmetz JD, Vollset SE, et al. . Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. *Lancet Public Health* 2022; 7:e105–25. - [PMC](#) - [PubMed](#)
5. Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. *Acta Neuropathologica* 1991; 82:239–59. - [PubMed](#)