IADR INTERNATIONAL ASSOCIATION FOR DENTAL, ORAL, AND CRANIOFACIAL RESEARCH

FOR IMMEDIATE RELEASE
June 29, 2025

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Brain Microvascular Cells, Oral Bacterial Dissemination to Brain in Alzheimer's

Alexandria, VA, USA – A study examining the role of periodontitis in increasing the pathology of Alzheimer's Disease was presented at the 103rd General Session of the IADR, which was held in conjunction with the IADR/Pan European Regional Congress on June 25-28, 2025 in Barcelona, Spain.

Chronic inflammation such as periodontitis (PD) elevates systemic inflammatory states, exacerbating neuroinflammation and potentially accelerating progression of Alzheimer's Disease (AD). This study tested the hypothesis that PD impairs blood-brain barrier (BBB) integrity, facilitates oral bacterial dissemination and increases AD pathology.

Human brain microvascular endothelial (HBEC-5i) cells were exposed to *Porphyromonas gingivalis* and *Fusobacterium nucleatum* at varying multiplicities of infection for 4-24 hours and were compared to human vascular endothelial cells (HUVEC). The investigators measured endothelial barrier integrity, neovascularization, tight junction protein expression, bacterial translocation in transwell coculture (HUVEC/THP-1, HBEC-5i/HMC-3) and IBA-1 expression by flow cytometry in HMC-3. In parallel, researchers used murine model of AD, induced experimental PD for 10 days, measured dissemination of *F.nucleatum* in 106 neutrophils obtained from WT donor mice using Mitotracker-labeled bacteria via intracarotid injection, and analyzed the whole brain by flow cytometry.

HBEC-5i cells were highly susceptible to transepithelial passage with a consistent increase in permeability when exposed to oral bacteria. *F.nucleatum* exhibited superior transcellular migration than P.gingivalis, compromising BBB integrity. Both pathogens significantly altered tight junctions, decreasing Occludin and Claudin-5 while increasing Tricellulin and Zonula occludens-1 as early as 4-hours, with partial reversal by 24-hours in HBEC-5i. *F.nucleatum* decreased tight junction protein expressions. There was an increase in Tricellulin/Claudin-5 ratio by 12-hours, indicating structural alterations in tight junction complexes. Neovascularization was elevated in HBEC-5i compared to HUVEC. In 5xFAD mice, there was increased translocation of neutrophils laden with *F.nucleatum* to brain compared to WT, correlated with increased IBA-1 expression in HMC-3.

These data suggested that periodontal disease compromised BBB, facilitated bacterial entry into the brain, and amplified neuroinflammation. Increased microglial activation due to increased bacterial entry into brain may exacerbate AD progression.

The abstract, “Brain Microvascular Cells, Oral Bacterial Dissemination to Brain in Alzheimer's” was presented by Zeliha Güney of the The ADA Forsyth Institute & Ankara Medipol University, Turkey during the "Systemic Consequences and Co-Morbidities Associated with Periodontitis" Poster Session that took place on June 28, 2025 at 11 a.m. CEST (UTC+2).

About IADR

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