

Mediating Roles Of TNF-α On Periodontitis-associated P-tau217 Elevation And Blood-brain Barrier Disruption In Alzheimer's Disease

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INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Periodontitis is as a risk factor of Alzheimer’s disease (AD). However, the interplay among inflammation, AD biomarkers and blood-brain barrier (BBB) in AD patients with periodontitis (AD-P) remains unclear.	Total 138 AD patients were classified into AD-P and AD without periodontitis (AD-nP) groups. Rating scales were used to evaluate clinical symptoms. Serum, plasma and cerebrospinal fluid (CSF) were collected to measure inflammatory factors, AD biomarkers and BBB-related indicators levels. Group differences and correlations were analyzed, and mediation analysis was performed.	(1) AD-P group showed a higher tartar index and severer probing depth, clinical attachment loss and tooth loss than AD-nP group . (2) Cognitive scores (MMSE, MoCA, AVLT and BNT) were lower and neuropsychiatric scores (NPI, HAMA, MAES) were higher in AD-P group than AD-nP group. AVLT score had significantly negative correlation with probing depth, and the scores of MMSE, MoCA, and BNT had significantly negative correlation with attachment loss. While the scores of NPI and MAES significantly positively correlated with attachment loss, and NPI scores had significantly positive correlation with tooth loss . (3) In plasma, AD-P group had higher P-tau217 than AD-nP group. In serum, H ₂ O ₂ and TNF-α were elevated in AD-P group. H ₂ O ₂ and NO correlated with probing depth, and ·OH, TNF-α and IL-1β correlated with clinical attachment loss. (4) In CSF, LRP1 and Aβ42 were decreased, while MMP-3, TNF-α and P-tau181 were elevated in AD-P group. (5) CSF NO correlated with serum TNF-α and IL-1β. CSF MMP-3 correlated with serum NO and TNF-α, whereas CSF LRP1 correlated with serum IL-1β. (6) TNF-α fully mediated (effect proportion 72.3%) periodontitis-associated plasma P-tau 217 elevation, BBB disruption and disease progression.	AD-P patients exhibit worse oral hygiene, severer cognitive and neuropsychiatric symptoms. Periodontitis-associated TNF-α elevates plasma P-tau217 and disrupts BBB, triggering a cascade of intensified inflammation, aggravated AD pathology and impaired cognition, which collectively accelerates AD progression.	1. Pruntel SM, van Munster BC, de Vries JJ, Vissink A, Visser A. Oral Health as a Risk Factor for Alzheimer Disease. J Prev Alzheimers Dis. 2024;11(1):249-258. 2. Chalmers JC, Hernandez-Kapila YL. The role of the oral microbiome, host response, and periodontal disease treatment in Alzheimer’s disease: A primer. Periodontol 2000. Published online June 11, 2025. 3. Villar A, Paladini S, Cossatis J. Periodontal Disease and Alzheimer’s: Insights from a Systematic Literature Network Analysis. J Prev Alzheimers Dis. 2024;11(4):1148-1165.
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