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# Active invasion of Porphyromonas gingivalis and infection-induced complement activation in ApoE-/- mice brains

Sophie Poole [1], Sim K Singhrao [1], Sasanka Chukkapalli [2], Mercedes Rivera [2], Irina Velsko [2], Lakshmyya Kesavalu [3], StJohn Crean [1]

Affiliations
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## Abstract

Periodontal disease is a polymicrobial inflammatory disease that leads to chronic systemic inflammation and direct infiltration of bacteria/bacterial components, which may contribute to the development of Alzheimer's disease. ApoE-/- mice were orally infected (n = 12) with Porphyromonas gingivalis, Treponema denticola, Tannerella forsythia, and Fusobacterium nucleatum as mono- and polymicrobial infections. ApoE-/- mice were sacrificed following 12 and 24 weeks of chronic infection. Bacterial genomic DNA was isolated from all brain tissues except for the F. nucleatum mono-infected group. Polymerase chain reaction was performed using universal 16 s rDNA primers and species-specific primer sets for each organism to determine whether the infecting pathogens accessed the brain. Sequencing amplification products confirmed the invasion of bacteria into the brain during infection. The innate immune responses were detected using antibodies against complement activation products of C3 convertase stage and the membrane attack complex. Molecular methods demonstrated that 6 out of 12 ApoE-/- mice brains contained P. gingivalis genomic DNA at 12 weeks (p = 0.006), and 9 out of 12 at 24 weeks of infection (p = 0.0001). Microglia in both infected and control groups demonstrated strong intracellular labeling with C3 and C9, due to on-going biosynthesis. The pyramidal neurons of the hippocampus in 4 out of 12 infected mice brains demonstrated characteristic opsonization with C3 activation fragments (p = 0.032). These results show that the oral pathogen P. gingivalis was able to access the ApoE-/- mice brain and thereby contributed to complement activation with bystander neuronal injury.

**Keywords:** Alzheimer's disease; chronic periodontitis; inflammation; periodontal bacteria.

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