The Role of *Porphyromonas gingivalis* in Endothelial Dysfunction and Vascular Cognitive Impairment

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Introduction

- **Vascular cognitive impairment (VCI) is strongly linked to damage of small blood vessels in the brain, leading to reduced blood flow, inflammation, and cognitive decline.**
- ***Porphyromonas gingivalis (P. gingivalis)* is a major periodontal pathogen that produces virulence factors (gingipains, LPS) and can promote chronic inflammation and endothelial dysfunction.**
- ***P. gingivalis* DNA, LPS, and gingipain proteases have been detected in the brain of Alzheimer's disease patients, suggesting a possible link between periodontal infection and neurodegeneration.**
- **This review examines how *P. gingivalis* contributes to endothelial dysfunction, blood-brain barrier (BBB) disruption, inflammation, and vascular cognitive impairment.**

https://www.denteric.com/patients-periodontal-disease/

Objective

- **Examine the effects of *P. gingivalis* on endothelial cells and vascular function.**
- **Explore how *P. gingivalis*-induced inflammation and BBB dysfunction contribute to vascular cognitive impairment.**
- **Evaluate clinical and experimental evidence linking periodontal disease with cognitive decline.**

KEY TAKEAWAY

***P. gingivalis*-associated endothelial dysfunction and chronic inflammation may promote vascular injury, BBB dysfunction, and neuroinflammation, providing a potential pathway to vascular cognitive impairment**

Methods

A literature review was conducted through primary sources, including cellular studies, animal models, and human clinical studies. Key topics include *P. gingivalis* virulence factors, endothelial cell responses, inflammation, BBB integrity, and cognitive outcomes.

Results

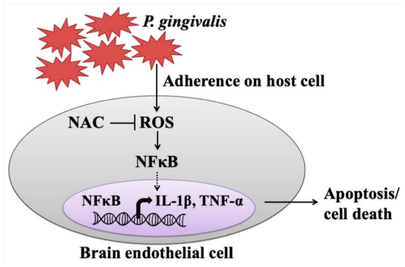

Figure 1. Proposed mechanism of P. gingivalis-induced brain endothelial cell injury through ROS production, NF-κB activation, and inflammatory cytokine release. Reproduced from Charoensaensuk et al. (2021).

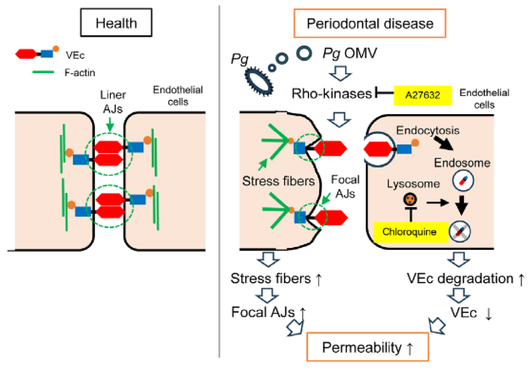

Figure 2. *P. gingivalis* outer membrane vesicles disrupt endothelial junctions and promote VE-cadherin degradation, increasing vascular permeability. Reproduced from Mekata et al. (2025).

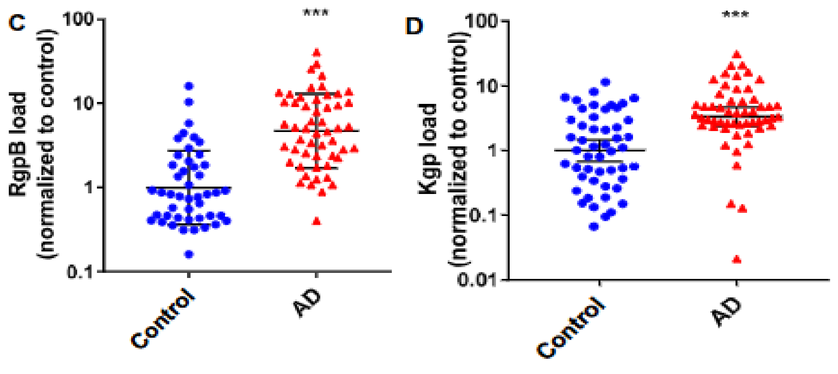

Figure 3. RgpB and Kgp gingipain loads were significantly higher in Alzheimer's disease (AD) brain tissue compared with nondemented controls (***P < 0.0001). Adapted from Dominy et al. (2019).

Conclusion

- ***P. gingivalis* virulence factors induce endothelial dysfunction, oxidative stress, and inflammatory cytokines.**
- **These effects may weaken BBB integrity, potentially facilitating neuroinflammation and exposure of brain tissue to circulating bacterial products and inflammatory mediators.**
- **Clinical and experimental studies connect periodontal disease with vascular dysfunction and cognitive decline.**
- **Current evidence supports a contributory role of *P. gingivalis* in vascular cognitive impairment through vascular injury, BBB dysfunction, and neuroinflammation.**

Future Directions

- **Conduct longitudinal clinical studies to establish causality.**
- **Investigate the therapeutic potential of gingipain inhibitors and anti-inflammatory strategies.**
- **Use geriatric animal models to mimic human aging and disease progression better.**
- **Explore diagnostic biomarkers of *P. gingivalis* infection in CSF and blood.**

References