



# Periodontitis and Increased Cognitive Decline in Alzheimer's Disease

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## Introduction

Periodontitis and its relation to Alzheimer's Disease can be described partly by the role systemic pro-inflammatory mediators such as Tumor Necrosis Factor alpha, (TNF- $\alpha$ ), Interleukin 1 Beta and 6 (IL1- $\beta$ , IL-6) play in both pathologies. The purpose of this investigation is to make a case for the possible feedback loop involving the secretion of similar pro-inflammatory cytokines in both pathoses.

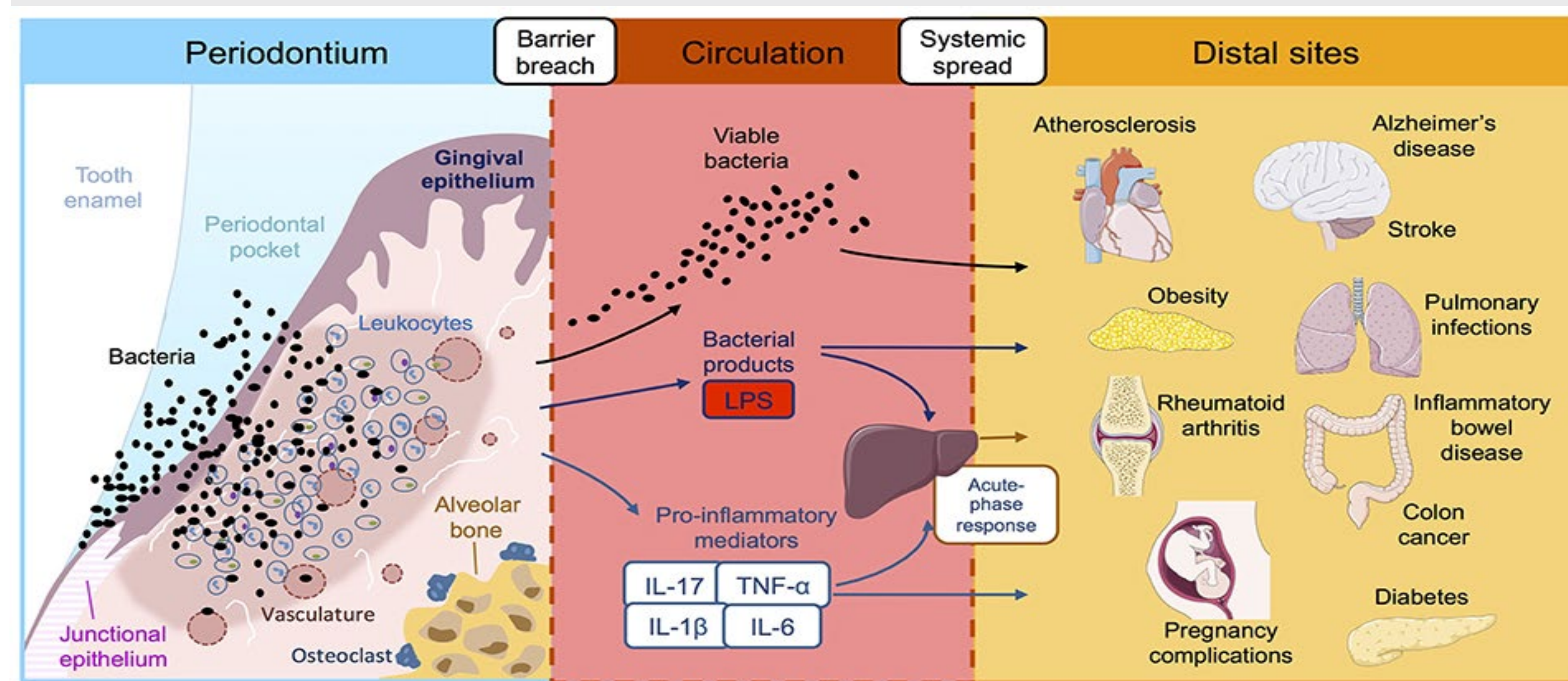


Figure 1. Diagram of the connections observed between Periodontitis & Alzheimer's Disease

## Methods

A broad search was conducted mainly on PubMed and Google Scholar for articles listed in the inclusion criteria. Keywords like Periodontitis, Alzheimer's Disease, IL-6, Pro-Inflammatory Mediators, Amyloid Beta (A $\beta$ ), Tau, Brain-Derived Neurotrophic Factor and the Blood-Brain Barrier were used to collect articles. A total of 50 articles were collected and used.

	Inclusion	Exclusion
<b>Time Period</b>	Literature published anytime up to the current date	Literature published before 2015
<b>Language</b>	English	Non-English
<b>Proteins/Cell Types &amp; Structures</b>	A $\beta$ -Peptide, Tau, Brain-Derived Neurotrophic Factor, Lipopolysaccharides, Amyloid-Precursor Protein, IL-6, IL-1, IL-1 $\beta$ , TNF- $\alpha$ , Blood-Brain Barrier, T-cells, Microglia, Astrocytes	All other proteins and cell types.
<b>Article Type</b>	Journal Articles, Systematic Reviews, Peer-Reviewed Articles	All other Articles
<b>Article Criteria</b>	Periodontitis and Alzheimer's Disease	Periodontitis and other chronic disease.

Table 1. Inclusion/Exclusion Criteria For Periodontitis & Increased Cognitive Decline In Alzheimer's Disease

## References

Miralda, I., & Uriarte, S. M. (2021). Periodontal Pathogens' strategies disarm neutrophils to promote dysregulated inflammation. *Molecular Oral Microbiology*, 36(2), 103-120. doi:<https://doi.org/10.1111/omi.12321>

Naseri, N. N., Wang, H., Guo, J., Sharma, M., & Luo, W. (2019). The complexity of tau in Alzheimer's disease. *Neuroscience letters*, 705, 183-194. doi:10.1016/j.neulet.2019.04.022

Zenaro, E., Piacentino, G., & Constantin, G. (2017). The blood-brain barrier in Alzheimer's disease. *Neurobiology of disease*, 107, 41-56. doi:10.1016/j.nbd.2016.07.007

Miranda, M., Morici, J. F., Zanon, M. B., & Bekinschtein, P. (2019). Brain-Derived Neurotrophic Factor: A Key Molecule for Memory in the Healthy and the Pathological Brain. *Frontiers in Cellular Neuroscience*, 13(363). doi:10.3389/fncel.2019.00363

Lee, D. C., Rizer, J., Selenica, M.-L. B., Reid, P., Kraft, C., Johnson, A., . . . Morgan, D. (2010). LPS- induced inflammation exacerbates phospho-tau pathology in rTg4510 mice. *Journal of neuroinflammation*, 7, 56-56. doi:10.1186/1742-2094-7-56

## Established Periodontal Pathogens Affect Neutrophil Functions to Sustain Dysregulated Inflammation

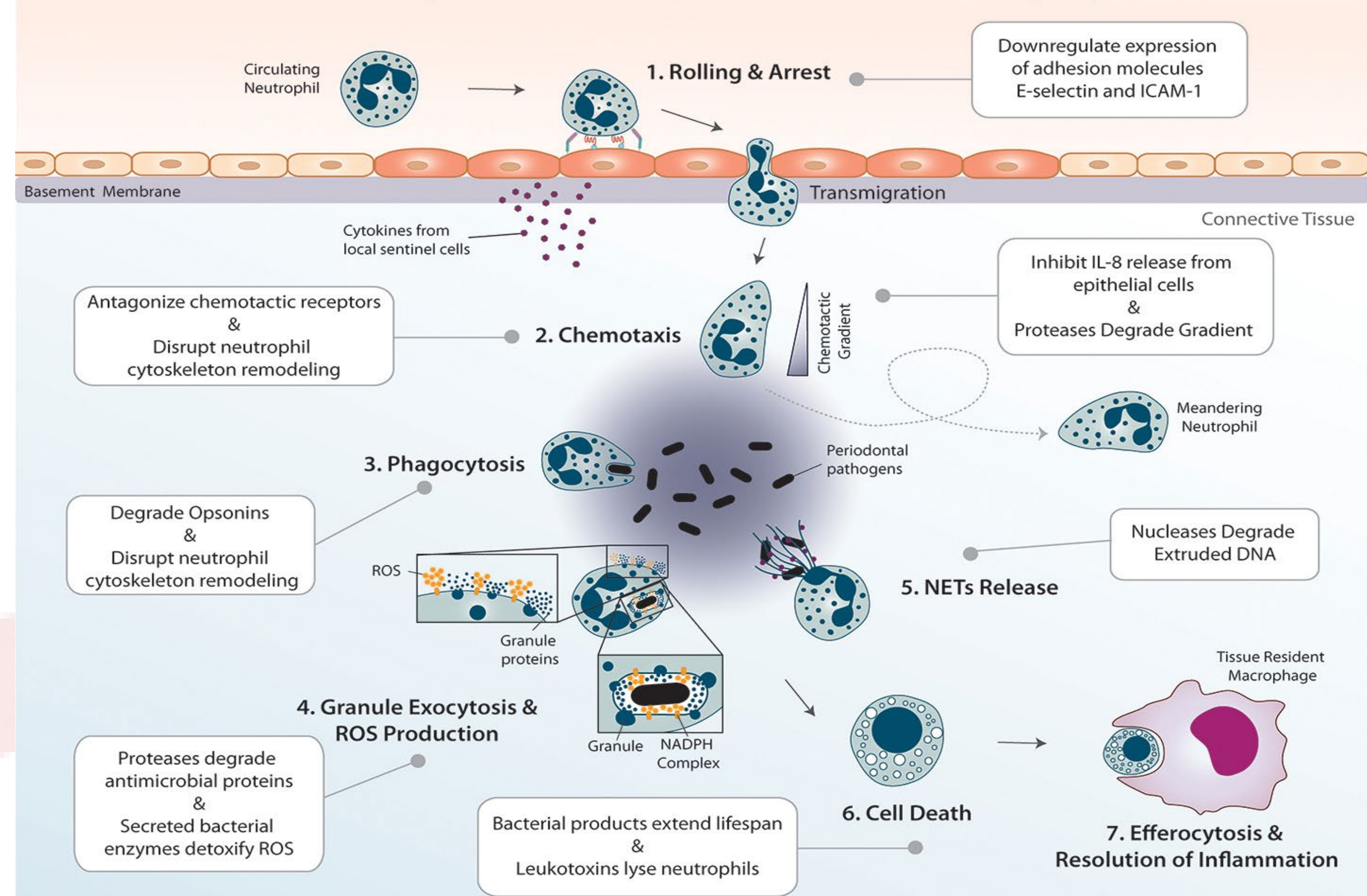


Figure 2. Diagram showing how periodontal pathogens can sustain a dysregulated immune response

## Results

Five areas of interest were isolated to describe the possible feedback loop between Periodontitis and Alzheimer's Disease in relation to pro-inflammatory mediators. The A $\beta$  peptide and the Amyloid Precursor Protein, Tau, Brain-Derived Neurotrophic Factor, Lipopolysaccharides, and the Blood-Brain Barrier.

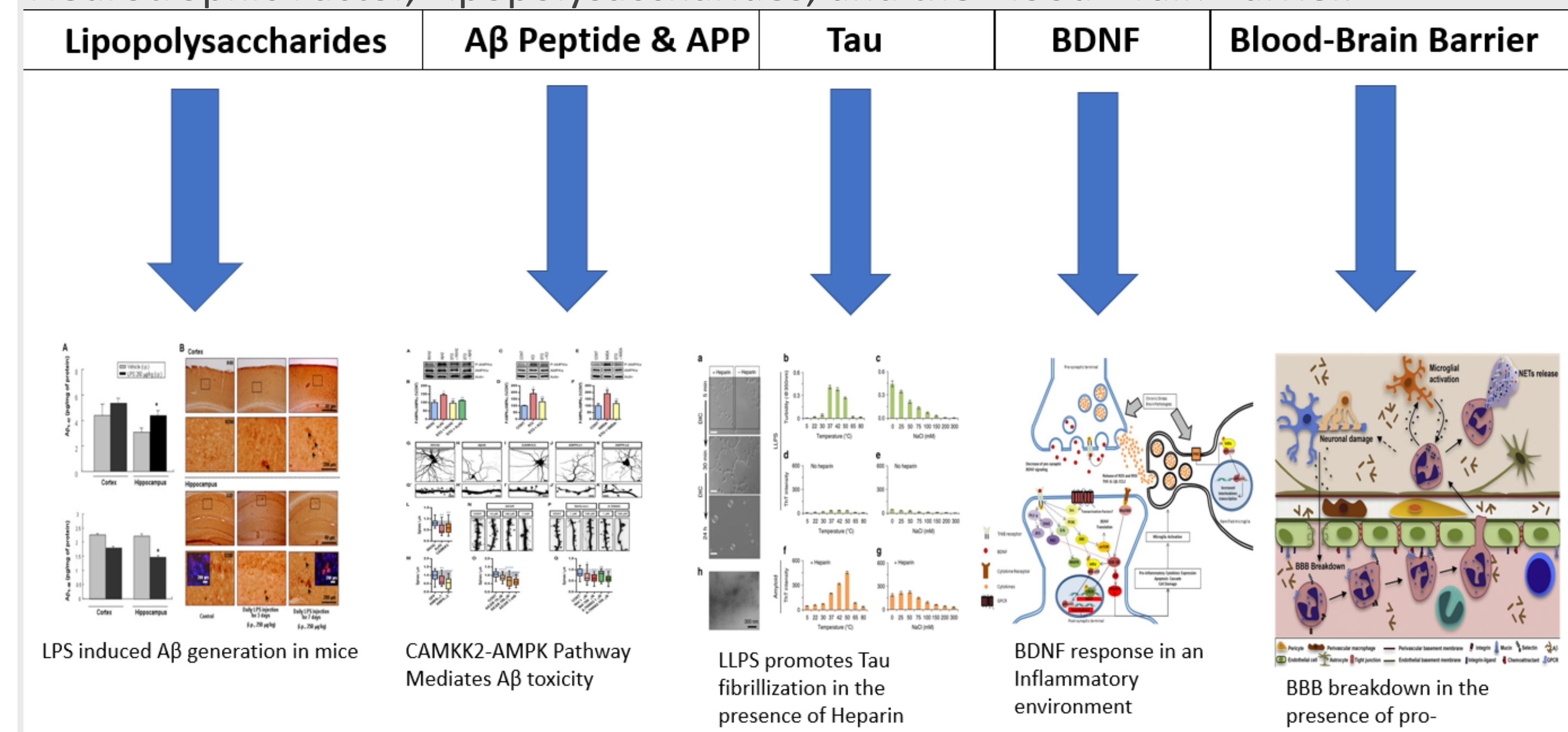


Figure 3. Diagram of the five areas of interest

## Conclusions and Future Directions

At the root, a dysregulated immune response resulting in a negative feedback loop seems to be the most likely explanation for the increased cognitive decline. Based on the current literature, there is sufficient evidence that periodontitis and Alzheimer's disease onset work under similar proinflammatory cytokine secretion pathways. See Figure 4. Future Directions should include *in vivo* studies in rat and human models that provide more real time evidence for how Periodontitis and Alzheimer's Disease evolve together and how Periodontitis may lead to and worsen symptoms of Alzheimer's Disease.

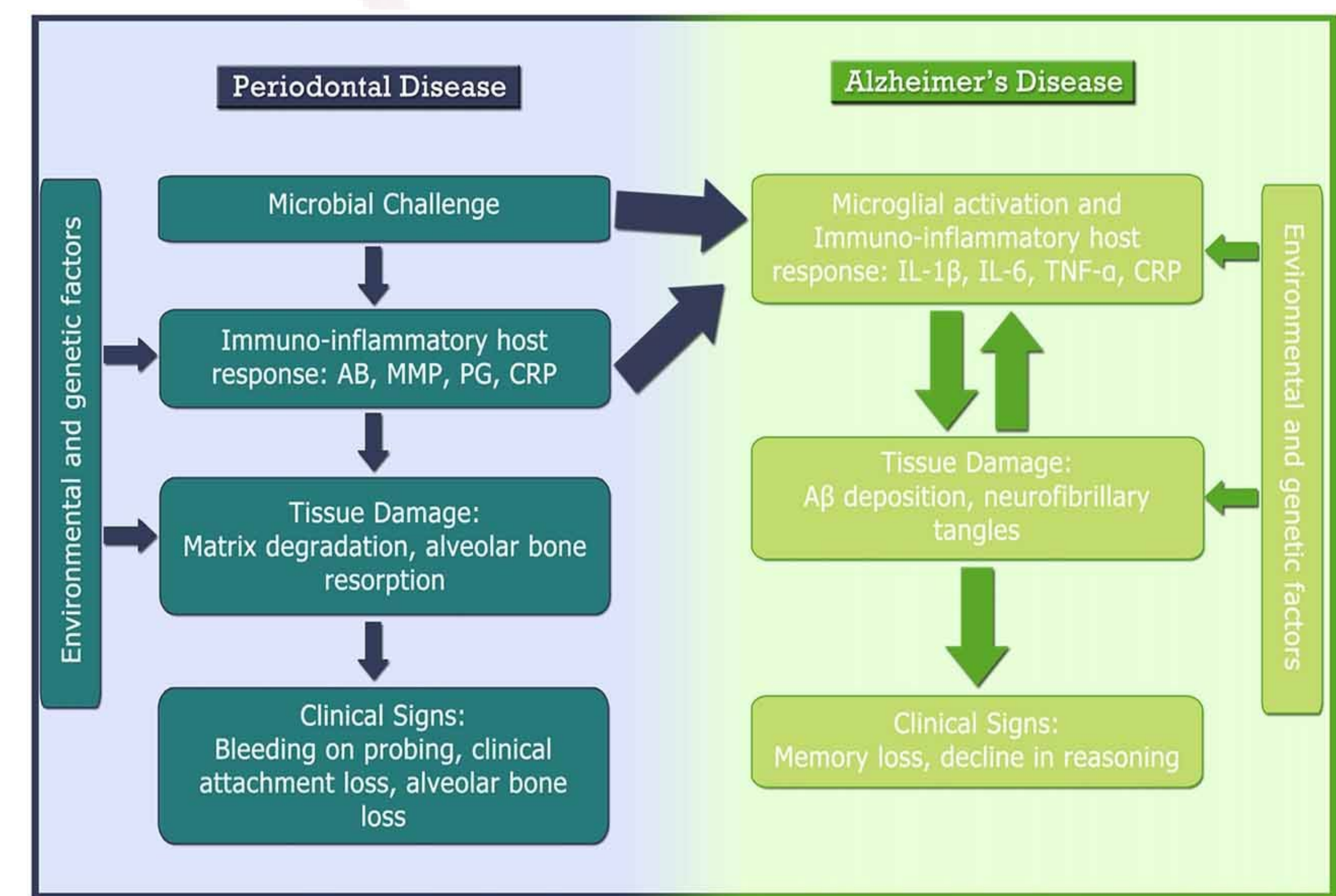


Figure 4. In-Depth Diagram explaining the correlation between Periodontitis and Alzheimer's Disease