Direct Relationship Between Periodontitis and the Progression of Alzheimer's Disease

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ABSTRACT

Alzheimer's disease is a neurodegenerative disease that contributes to about 60-70 percent of all dementia cases worldwide. Periodontitis is a peripheral chronic infection that affects the gums and can deteriorate the jawbone. Also, periodontitis causes a systemic inflammatory response and is a highly prevalent disease that can affect up to 90 percent of the population. Previous studies show that those with Alzheimer's disease have an increased likelihood of developing periodontitis. In this literature review, I sought to examine if and how periodontitis increases the progression of Alzheimer's disease. Based on this literature, This review argues that an increased risk of Alzheimer's Disease is directly related to periodontitis. From this research I found that periodontitis and Alzheimer's disease share cellular and molecular proinflammatory characteristics, such that cytokines and proinflammatory products produced from periodontitis spread from the periodontal pockets to the systemic circulation or around the trigeminal nerve terminals. Furthermore, those with periodontitis have an increased risk of cognitive decline. In addition, there are two possible pathways for periodontitis to invade the brain. Periodontitis can invade the brain through the bloodstream or through the peripheral nerves. Which allows the bacteria and proinflammatory product to have a passage to the brain. Although we know that periodontitis can invade the brain we don't know if periodontitis can trigger the neuroinflammatory response needed to cause Alzheimer's disease. Together the findings indicate that there is a relationship between periodontitis and Alzheimer's disease. This relationship shows that periodontitis is able to influence the progression of Alzheimer's disease through either the bloodstream or through the peripheral nervous system, but further research is needed to determine if periodontitis can trigger Alzheimer's disease or if it is just limited to affecting the progression of the disease.

METHODS

- For this research I completed a Literature review of 18 sources to compile data to support my thesis that periodontitis increases the risk for Alzheimer's disease

MECHANISIMS OF ALZHEIMER'S DISEASE

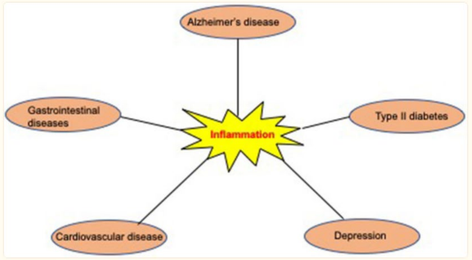

Figure 1

Most common comorbidities associated with AD. Evidence from epidemiological and molecular studies suggest that several conditions including type 2 diabetes, cardiovascular diseases, depression, and gastrointestinal diseases may be associated with an increased risk for AD. Inflammation may be a central mechanism underlying the association between AD and most of its comorbidities.

Figure 1. Comorbidities of Alzheimer's disease. This image is showing the relationship between Alzheimer's disease and other disease that are commonly associated with AD. Also, It is showing how a connection between inflammation being a mechanism that underlines the relationship between AD and its associated comorbidities.

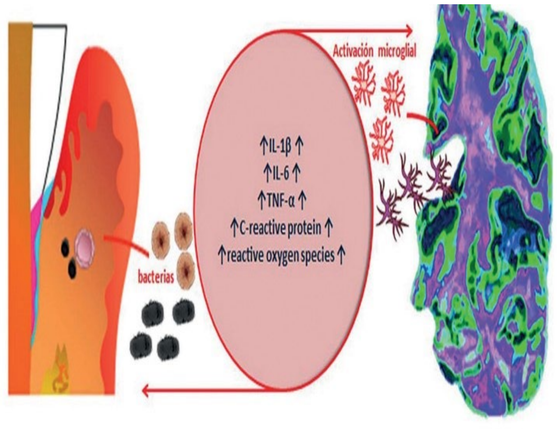

Fig. 1: Common pathophysiological pathways between AD and periodontitis. The increase in inflammatory activity is the point of confluence between AD and periodontitis. As a result of the activity of periodontopathogens on the one hand and microglial activation on the other, an increase in the levels of the main proinflammatory molecules and their metabolites is produced, when this state is maintained in the long term it generates tissue destruction.

Figure 2. Common pathways between AD and Periodontitis. An increase in proinflammatory products is the main relationship between periodontitis and Alzheimer's disease. This increase in proinflammatory products is caused by periodontal bacteria and microglia activation. Which leads to tissue destruction when these increased levels of proinflammatory products are maintained.

MECHANISIMS OF PERIODONTITIS

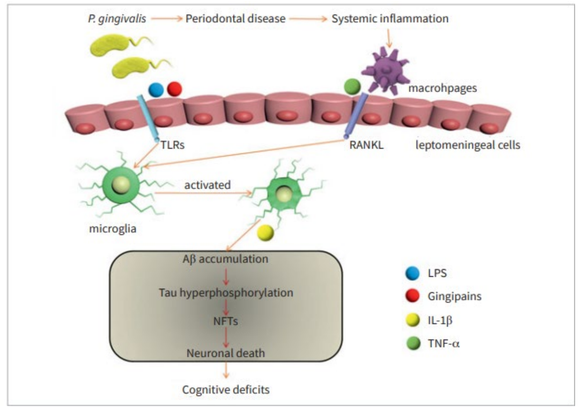

Figure 3. Periodontal bacteria inflammatory signal pathway. The bacterial signal travels through leptomeningeal cells to the microglia that are in the brain. Both the microphages and periodontal bacteria produce proinflammatory products that activate the RANKL and TLRs. This then activates the microglia and leads to an increase of proinflammatory molecules. These molecules then cause amyloid beta accumulation and tau hyperphosphorylation. The tau become hyperpolarized due to the increased amount of IL-1beta which increase tau formation. All these factors could then lead to neuronal death and cognitive deficits.

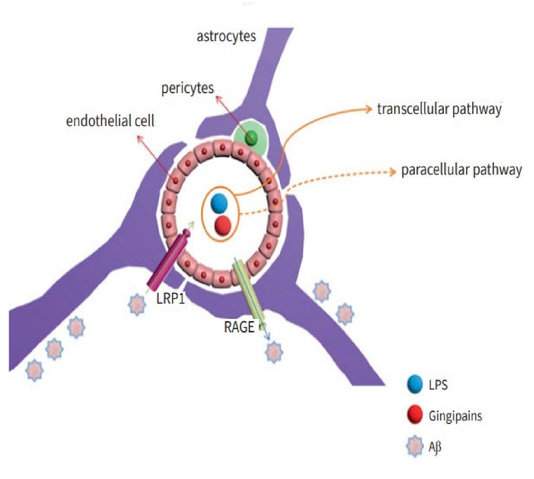

Figure 4. Structure of the blood brain barrier. The blood brain barrier consists of three parts which are the endothelial cells, pericytes, and astrocytes. Amyloid beta enters the brain tissue through the BBB with the use of LRP1 and RAGE receptors. These receptors mediate amyloid beta when entering and exiting the brain tissue to prevent the accumulation of Amyloid beta outside the neural cells. The amyloid beta would then become insoluble senile plaques.

PRELIMINARY CONCLUSIONS

- Together the findings indicate that there is a relationship between periodontitis and Alzheimer's disease.
- Further research is needed to determine if periodontitis can trigger Alzheimer's disease or if it is just limited to affecting the progression of the disease

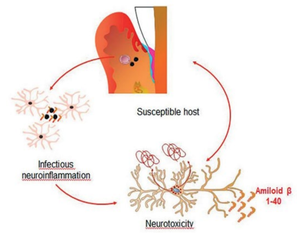

Fig. 3: Inflammatory response of brain cells to oral bacteria. Model that suggests that periodontal bacteria and their products can invade the brain via and possibly generate a local inflammatory response and neurotoxicity.

Figure 5. Brain cells response to periodontal bacterial inflammatory response. This shows how periodontitis has a possibility to invade the brain and cause a neuroinflammatory response and neurotoxicity.

SOURCES