

## Cognitive decline and periodontitis

### Introduction

- Dementia has been defined as a clinical syndrome characterized by cognitive decline, sufficient to interfere with daily functioning
- cognitive impairment and dementia are considered as a major public health problem with large financial, human and social burdens
- Modifiable risk factors related to Alzheimer's disease are midlife obesity, midlife hypertension, diabetes, physical inactivity, smoking, low education and depression
- Patients with dementia: multiple oral health problems
  - changes in daily function affecting oral hygiene routines and thus a higher plaque index
  - influence of a peripheral inflammation
- Both clinical attachment loss (CAL) >3mm and Alzheimer's disease have reported higher brain amyloid among elderly individuals
- Higher plasma A $\beta$ <sub>1-42</sub> peptide levels were reported in individuals with severe periodontal disease
- Lipopolysaccharides from periodontal pathogens have been identified in the brain tissues of patients with AD
- Higher risk for dementia was reported among individuals with periodontitis after adjustment for socio-demographic characteristics and comorbidities
  - 3-year follow-up - a twofold higher risk for cognitive decline for individuals with severe periodontitis compared to individuals without periodontitis

### The Role of Cytokine Profile and Systemic Inflammation

(Sochocka, M. et al., 2017)

- Neuropathological features of AD
  - neuronal inflammation in the brain
  - can be enhanced by various systemic inflammatory processes
- Pro-inflammatory mediators, blood vessel damage, and oxidative stress can induce neuron degeneration

- Neuronal loss and brain injury
- Inflammation can be caused by local CNS irritants or peripheral infections
- Current theories that systemic infections in the body could aggravate inflammatory processes in the brain
- TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-8 and IL-10 are associated with the inflammatory process induced by the LPS of periodontal pathogens infiltrating into the blood
- Elevated antibodies of periodontal pathogens have been found in AD patients as well as patients with Chronic Periodontitis
- Pro-inflammatory mediators have shown to support systemic inflammation on distant organs
- Chronic exposure to these mediators can exacerbate the neurodegenerative environment by formation of amyloid- $\beta$  (A $\beta$ ) proteins
- Ultimate working hypothesis:
  - Chronic oral infection promotes inflammation, which adds to the overall inflammatory pool by contributing to pro-inflammatory mediators, and leads to confusion and dementia

## Materials and methods

- 28 participants (83 females, 45 males) aged 55-90 years
- Complete **periodontal examination**
  - Number of teeth and measures of probing depth in mm (PD), clinical attachment level in mm (CAL), and gingival inflammation measured as bleeding on probing and plaque index (API) were recorded
  - All the participants did not receive treatment for periodontal disease in the past 6 months.
- **Psychiatric Examination**
  - psychiatric and neurological examinations, as well as laboratory tests, electroencephalographic examinations (EEG) and computer tomography (CT) or MRI structural studies
  - Mini-mental State Examination (MMSE) was used for the screening of dementia
- **Isolation of Peripheral Blood Leukocytes (PBL)/Cytokine assay**
  - Freshly isolated PBL collected and stored and tested for cytokine determination.
  - Cytokine levels were determined for human IL-1 $\beta$ , IL-6, IL-10 and TNF- $\alpha$

## Discussion

- Two probable mechanisms of periodontitis leading to AD progression are proposed:
  - periodontitis preceding systemic inflammation/infection and bacterial and viral influence
  - Chronic inflammatory response that occurs in AD is a complex process that involves produced inflammatory mediators -  $\text{TNF}\alpha$ , IL-1, IL-6, IL-7, IL-10, IL-15 and IL-18 - Cytokines IL-1, IL-6, IL-10 and  $\text{TNF-}\alpha$  are involved in the pathogenesis of periodontitis
- It has been shown that the level of pro-inflammatory cytokines IL- 1, IL-6 and  $\text{TNF-}\alpha$  increases with worsened periodontal status and cognitive decline
- Studies confirmed early observations that the systemic inflammatory markers are elevated in diagnosed cognitive impairment and AD patients with periodontitis.

## Conclusion

- Periodontal health problems are a modifiable risk factor of cognitive impairment and dementia
- Early treatment of periodontitis may slow the progression of the inflammatory process on the brain

References:

1. Nilsson, H., et al. "Longitudinal evaluation of periodontitis and development of cognitive decline among older adults." *Journal of Clinical Periodontology*, vol. 45, no.10, 2018, pp/ 1142-1149-. doi:10.1111/jcpe.12992

2. Sochocka M., Sobczyński M., Sender-Janeczek A., et al. Association between periodontal health status and cognitive abilities. The role of cytokine profile and systemic inflammation. *Current Alzheimer Research*. 2017;14(9):978–990. doi: 10.2174/1567205014666170316163340.