Cognitive dysfunction and salivary metabolome in young subjects with periodontal disease

Simona I Hategan D.M.D., Ph.D,[1] Angela R. Kamer D.M.D., Ph.D,[2] Sabrina Kamer, D.M.D[2], Catalin Jianu D.M.D. Ph.D.[1], Catalin Marian D.M.D. Ph.D[1], Bianca Bora[1], Diana Nitusca,[1] Sinescu Cosmin D.M.D., Ph.D[1], Meda Lavinia Negrutiu D.M.D., Ph.D[1]

1. University of Medicine and Pharmacy ''Victor Babes'', Faculty of Dential Medicine, Timisoara, Romania
2. NYU College of Dentistry, New York, USA

INTRODUCTION

Latest epidemiological data that links periodontal disease (PD) and Alzheimer's disease (AD) reported that measures of PD were associated with cognitive dysfunction, Cognitive decline, dementia and AD, with odds and hazard risk ratios in the mild to moderate range. Most studies, investigated these relationships in elderly and only a few studies included young populations.[1,2] Therefore it is unclear whether these relationships are also found in youth.

Studying younger populations is significant for several reasons: AD pathology starts early in life with a long preclinical phase and longer periodontal exposure increases the AD risk.

In addition, the young population are most likely to lack other comorbidities that would affect AD and preventive measures could be implemented early. [3]

We hypothesized that young subjects with periodontal disease would have impaired episodic memory compared to controls. We also hypothesized that salivary proinflammatory molecules (IL-1β ,TNF-α) would inversely correlate with delayed memory and to verify the hypothesis of certain metabolites having increased levels in aggressive periodontitis (AgP) stage relative to other stages, in order to expand existent data literature regarding the metabolomic signature of PD.

METHODS & MATERIAL

This was a cross-sectional comparative study of 3 clinical groups of young medically healthy subjects from the western region of Romania.[4] Forty subjects were recruited: 10 with AgP, 20 with chronic mild-moderate periodontitis CrP and 10 with no signs of periodontitis (NL_P). General and neurological health status was determined by three neurological specialists and the neuropsychological assessments was performed by a clinical psychologist.[5]

Interleukin-1 (IL-1 β) and tumor necrosis factor- α as well as the targeted metabolomics were measured using saliva samples from 40 participants (Figure 1).

Figure 1. – Processing of saliva samples

Proinflammatory cytokines were measured using commercially available ELISA kits and targeted metabolomics was performed using "CHIP BASED NANOESI QTOF MS" analysis.

RESULTS

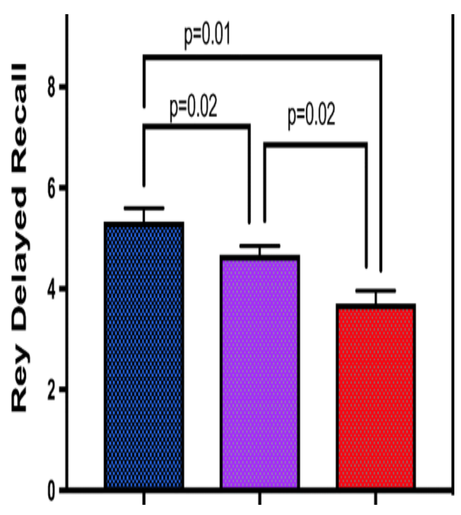

Figure 2. RAVLT among groups

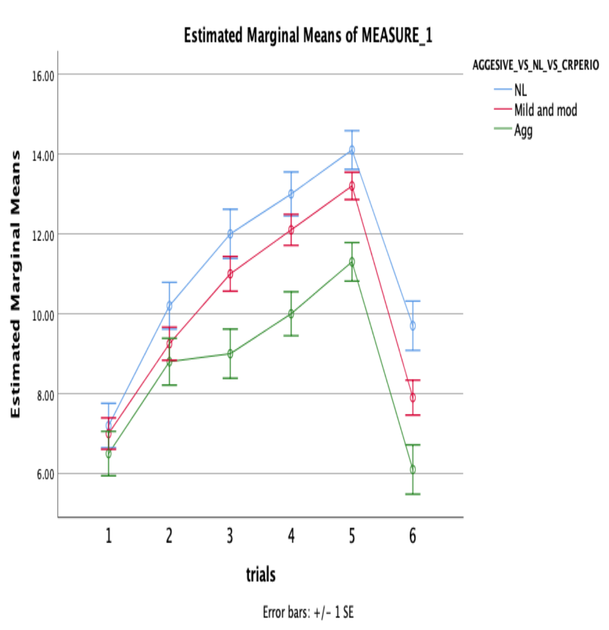

Figure 3 Learning performance among groups

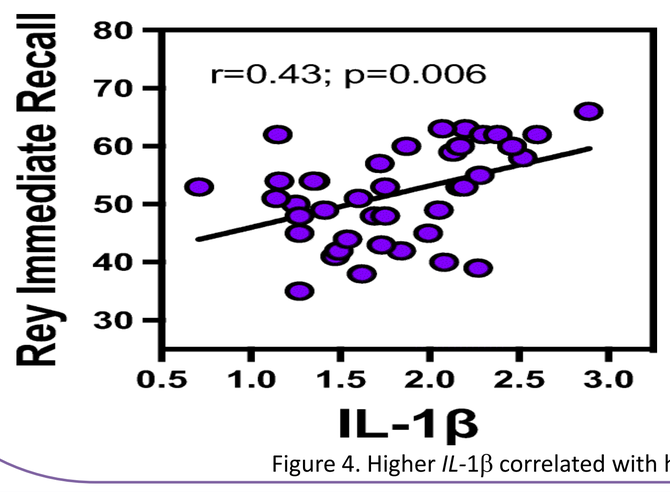

Figure 4. Higher *IL*-1β correlated with higher immediate memory

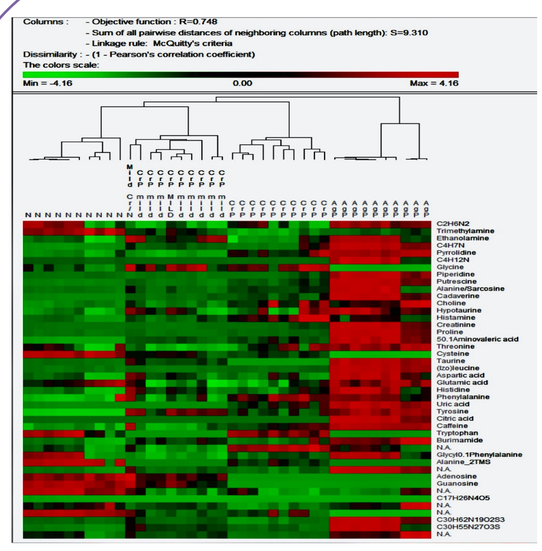

Figure 5. – Metabolites heat map

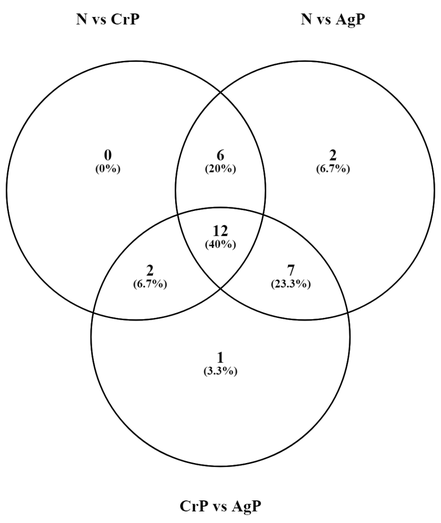

Figure 6.- Venn diagram

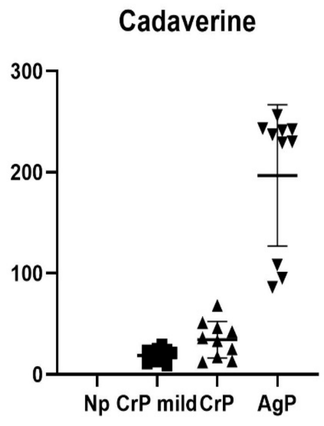

Figure 7. - Cadaverine gradual increase

CONCLUSIONS

- We showed that young subjects with periodontal disease had lower cognition. There is a need for more observational studies on this topic with control of modifiable variables (diagnostic criteria, time of diagnosis and follow-up between periodontitis and cognitive decline, level of education, etc.) to investigate the cause-effect relationship between the pathologies.
- **Our findings from the third study suggest that salivary metabolites levels, taken from subjects with various stages of periodontitis compared to healthy controls, exist.**

REFERENCES

1.Kamer A, Malvin N. Janal, Mony J. de Leon. Letter to the editor regarding: Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective. Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring. 2015

2. Kamer AR, Pirraglia E, Tsui W, Rusinek H, Vallabhajosula S, Mosconi L, et al. Periodontal disease associates with higher brain amyloid load in normal elderly. Neurobiol Aging. 2015 Feb;36(2):627-33. PubMed PMID: 25491073. PMCID: PMC4399973. Epub 2014/12/11. eng.

3. Kamer AR, Ronald G. Craig, Richard Niederman, Juan Fortea, Mony J. de Leon. Periodontal Disease as a Possible Cause for Alzheimer's Disease. Periodontology 2000. 2020;83(1):242-71.

4. Hategan SI, Kamer AR, Sinescu C, Craig RG, Jivanescu A, Gavrilovici AM, et al. Periodontal disease in a young Romanian convenience sample: radiographic assessment. Bmc Oral Health. 2019 May;19. PubMed PMID: WOS:000469470400004.

5. Hategan SI, Kamer SA, Craig RG, Sinescu C, de Leon MJ, Jianu DC, et al. Cognitive dysfunction in young subjects with periodontal disease. Neurol Sci. 2021 Feb 19. PubMed PMID: 33606127. Epub 2021/02/20. eng.

Presented at the 97th Annual Session of the Greater New York Dental Meeting in 2021