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Commentary

Ingar Olsen*

Department of Oral Biology, Faculty of Dentistry, University of Oslo, Oslo, Norway

*Correspondence to: Ingar Olsen, Department of Oral Biology, POB 1052 Blindern, 0316 Oslo, Norway, Email: ingar.olsen@odont.uio.no

DK Shoemark and SJ Alley recently launched interesting thoughts on how Alzheimer disease may relate to the oral microbiota. Their paper *The Microbiome and Disease: Reviewing the Links between the Oral Microbiome, Aging and Alzheimer Disease* was published in J Alzheimers Dis 2015; 43: 725–38. A commentary to the paper is given here:

Alzheimer disease (AD) affects old age. It represents a one in four risk in Europe for people more than 80 years old. This currently costs approximately $15 billion in the UK and $183 billion in the US respectively per year.

With increasing age our bacterial load increases and the immune defense wanes in favor of the more primitive innate immunity. Bacteria may influence how we age. Some of them can trigger damaging host responses. Important in this interplay is a possible weakening of the blood–brain barrier (BBL) by predisposing polymorphisms, e.g. in *Ephrin Type-A Receptor* (*Epha 1*). The latter is a gene associated with AD risk. Increased circulating TNFα response may also help bacteria or their lipopolysaccharide to gain access to the brain by weakening the BBL. Here they may trigger neuropathology (amyloid plaques) and change brain function. The oral epithelium releases increased TNFα and IL1β when the environmental conditions become more anaerobic. Levels of TNFα, the production ability of which is retained throughout life, increase under inflammatory conditions, e.g. in the AD brain where an inflammatory response occurs. Periodontitis, dentures and bridges tend to increase both inflammation and the oral load of anaerobes. Particularly periodontitis provides an excellent habitat for anaerobes (treponemes, *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, *Prevotella intermedia*), which are the oral bacteria so far most closely, associated with AD. An association between tooth loss in early to middle life in twins and nuns suggested that bacterial overgrowth can be involved in a sub-group of AD patients, and a clinical trial with the systemic antibiotics doxycycline and rifampicin reported beneficial effects slowing down cognitive decline.

The mouth can be a place for low-grade mucosal inflammation (mucositis) that can aggravate when saliva flow is reduced due to age, inactivity or drug side effects. Furthermore, immune-tolerant bacteria (commensals) may reach the circulation and affect host cell behavior.

Olfactory ensheathing cells (OECs) can engulf bacteria and migrate towards sites with TNFα produced by astrocytes – a sub-type of microglia. OECs help bacteria to follow nerves into the brain (Trojan horse). Infected phagocytes also help recognized CNS pathogens such as *Escherichia coli*, group B *Streptococcus* and *S. pneumoniae* to enter the brain. The original task of OECs however, is to prevent invasion of bacteria via the oronasal route. Interestingly, the odds ratio for women with anosmia was as high as 9.7 for late onset AD. Oral anaerobes tracking up the olfactory nerve may possibly destroy it. Neurodegeneration in AD11 mice (develop brain damages common with human AD) was delayed when the mice were raised under sterile conditions.

The findings listed may indicate that anaerobic oral bacteria have a role in some cases of AD. This possibility should be further elucidated. It would be important to examine if modification of the oral microbiome through improved oral hygiene habits could be effective in slowing down the disease progression of AD.

Suggested reading

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