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STUDENT PAPER

MOUTH-BRAIN CONNECTION: EXPLORING HOW ORAL BACTERIA AFFECT BRAIN HEALTH

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Oral health is connected to brain health. Recent studies suggest that infectious bacteria found in the mouth and oral tract may have a direct relation to the health of our brains. These microorganisms have been connected to the occurrence and progression of cognitive dysfunction and disease. Microorganisms in the oral cavity are linked to neuro degenerative disease, such as Alzheimer's because they can migrate to the central nervous system, cause inflammation, and alter the formation of Proteins.

According to the Canadian Dental Association (2017), 7 out of 10 Canadians will, at some point, develop gum disease. Additionally, the Alzheimer's Society of Canada (2024) estimates that around 771,939 people in Canada are living with dementia, Alzheimer's disease being its leading cause. Now the real question is, how do these relate? Or do they even relate at all?

Gum disease is subtle yet destructive. According to the Centers for Disease Control and Prevention (2024), the most common gum diseases are gingivitis and chronic periodontitis (CP). Both issues occur when an over accumulation of bacterial biofilms (dental plaque) sit where the teeth meet the gingiva (Gums). Gingivitis is a mild case of gum disease caused by the accumulation of oral bacteria on the tooth. At this stage of gum disease, the bacteria adhering to the tooth's surface has formed plaque. Neglecting plaque can result in the formation of calculus, a mineralized form of plaque that can only be removed by professionals. The presence of calculus near the gum line will result in swollen gums and irritation or bleeding while brushing and flossing. In the progression and later stages of gingivitis, swelling and infection prompt the reproduction of a more pathogenic bacteria known as *Porphyromonas gingivalis* (*P. gingivalis*). CP is often the result of untreated gingivitis and the reproduction of *P. gingivalis* beneath

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the gum line along with the presence of calculus. CP occurs when the infection moves below the gum line and begins to attack vital tooth structures such as the periodontal ligament and bone, both of which are responsible for tooth stability. This can cause gum recession, pocket formation, (which encourages further infection) and eventually the loss of teeth (Wilson and Wilson 2021).

Alzheimer's disease (AD) remains an active area of research for scientists in an attempt to understand its main cause and how to prevent its progression. Generally speaking, AD can be characterized by the buildup of plaques and tangles within the brain, leading to disturbance between neuron communication, and thus causing nerve damage. This results in a gradual decline of brain tissue known as atrophy, which is directly related to memory loss, alteration in personality and the hindrance in one's ability to perform physical activities (Braak, Griffing, Arai and Braak 1999). Thousands of Canadians suffer from the symptoms and consequences that come with this neurodegenerative disease (Alzheimer Society of Canada 2024) and their families are forced to watch their loved ones slowly lose what makes them who they are. The need to understand this disease and discover ways to prevent it is self-evident.

Recent studies have proven that oral bacteria can migrate from the mouth to the central nervous system. Though many bacteria fail to reach the brain due to its highly specialized defence wall known as the blood brain barrier (BBB), some microorganisms have developed mechanisms to cross this barrier (Coureuil *et al*. 2017). Kerstens *et al*. (2024) explains that bacteria which originated in the oral cavity have been detected in the bloodstream after gum manipulation. Stimulation such as flossing, tooth brushing, or dental procedures in which the gums or oral surfaces experience minor abrasions, allow bacteria to enter the bloodstream. In fact, microbes such as *P. gingivalis* and its outer membrane known as Lipopolysaccharide (LPS) have been found in the brains of AD patients (Narengaowa *et al*. 2021). This does not suggest the abandonment of procedures which may disrupt the gums as even the consumption of hard foods or unrelated injury provide a similar window for bacteria to enter the blood stream, rather, this suggests the importance of maintaining a healthy oral microbiome to avoid complications. Lipid A in LPS acts as the bacterium's main source of pathology, often triggering immune responses like pro-inflammatory

cytokines from the host, resulting in damage to surrounding tissues (Alexander and Rietschel 2001).

A study by Wu *et al*. (2017) performed on mice found that the LPS from *P. gingivalis* can induce biochemical reactions within the brain, causing numerous malfunctions for neuronal health and longevity. Neurons are responsible for sending signals, while glial cells act as protection and support. When foreign microorganisms like *P. gingivalis* enter the brain, the glial cells react to the bacteria as a threat. They signal pro-inflammatory molecules known as cytokines to the location in order to prevent the spread of bacteria and recruit other immune cells. Neuroinflammation plays a huge role in neurodegeneration, cognitive dysfunction and even nerve cell death (necrosis) (Narengaowa *et al*. 2021). Interestingly, research suggests that although dementia and its mechanisms are not fully understood, inflammation plays a major role in its development and progression (Guo *et al*. 2021).

Chronic inflammation in the brain can promote the over production of naturally occurring proteins such as Amyloid-beta (Aβ) and tau, resulting in the formation of neurodegenerative substances. Researchers hypothesise that the presence of bacteria such as *P. gingivalis* in the brain can stimulate the overproduction of Aβ (Zhao *et al*. 2023). *P. gingivalis* has been found to induce excess production of Aβ which forms a sticky plaque-like residue between the neurons. Ironically, much like the plaque on our teeth, Aβ must be regularly maintained in order to avoid damage to the brain and neuronal health. Glial cells are responsible for the management of this, and so, when bacteria signal the overproduction of plaque, glial cells respond and it can lead to severe inflammation.

Similar to the Aβ's response to oral bacteria in the brain, tau proteins may be influenced by the presence of oral bacteria. Tau is a protein that stabilises microtubules, which act as intracellular transport structures within neurons. Zhao *et al*. (2023) suggest that the translocation of oral microorganisms from the mouth into the brain can be linked to tau hyperphosphorylation, a process in which tau proteins form abnormally, detaching themselves from the microtubules and instead, stick together, forming tau tangles. Wozniak *et al*. (2009) states that "neurofibrillary (tau) tangles are one of the main neuro pathological features of Alzheimer's disease". These tangles are associated with disrupted intracellular transport and neuronal dysfunction, which contributes to neurodegenerative processes. Ultimately, the hindrance

of the tau proteins in the brain by oral bacteria may play a role in mechanisms involved in Alzheimer's disease progression.

In conclusion, it is clear that oral bacteria do indeed play a role in the health of our brains. The effects of these microorganisms match with the characteristics of cognitive dysfunctional diseases such as Alzheimer's. The migration of microorganisms through the bloodstream and into the brain is the beginning of brain altering reactions like the immune response of inflammation, the overproduction of Aβ causing plaque build up, and tau tangles. This field has room for exploration, as there are still many questions to answer regarding the relationship between the mouth and brain. How early do these bacteria affect our brains before symptoms appear? Can the damage be reversed? Understanding how the microorganisms in the mouth affect the brain is important because it may introduce new ways to slow down or prevent the onset of neurodegenerative disease. Understanding the oral cavity, the second most diverse microbiome in the body, continues to prove significant beyond its role in digestion, respiration, and speaking. Brushing twice daily and flossing every 24 hours seems to offer more than a healthy smile, rather, keeping up with oral hygiene is an easy way to foster a healthy brain. The efficiency and health of our brain is affected by the management of oral bacteria through good hygiene, so make sure to keep brushing!

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