Biology

The Link between Alzheimer's and Mouth Bacteria

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Introduction

The phrase 'A healthy mouth is a healthy body' is multifaceted, but did you know that gum disease can lead to Alzheimer's disease? The mouth can be seen as the gateway to the rest of the body, therefore poor oral hygiene can lead to a multitude of problems and perhaps chronic disease. However, recent research shows that the toxins secreted from the periodontitis - causing bacteria *Porphyromonas Gingivalis* have been found present in the brains of 96% of people with Alzheimer's - in comparison to only 39% for people without.[1] These statistics only represent a trend for the brain tissues amongst 53 Alzheimer's patients. Nonetheless, it is worth noting the possible reasons and consequences for the drastic increase in the accumulation of this bacteria and what this could mean for the future of Alzheimer's research.

Peridontitis

Firstly, the abundance of *P. Gingivalis* is the most serious cause of gum disease known as periodontitis. It is shown that 1 in 5 people under the age of 30 have low levels of this bacteria[2], however, more than half of the U.S. population aged 30 and older have some form of periodontal disease, and prevalence increases to 68 per cent for those aged 65 and older.[3]

Bacterial Translocation

Periodontitis causes the destruction of soft gum tissue and eventually reaching the pulp of the teeth, where the nerves and blood vessels are located. At this point, the bacteria can travel to the brain via a number of methods; one of which is by infecting monocytes in the blood vessels, which travel in the bloodstream to the brain, and due to the bacteria's properties, it is able to adhere to and enter other cells. Another is by damaging the endothelial cells which protect the blood-brain barrier and travelling across it via pinocytosis, gaining access to spread through cranial nerves. Therefore, those with chronic periodontitis are at a higher risk of *P. Gingivalis* reaching the brain and other parts of the body. The reticuloendothelial system is able to eliminate bacteria circulating in the bloodstream within minutes[4], however due to the fact that the mouth is closer in distance to the brain, the bacteria is less likely to be removed. Furthermore, the bacteria's ability to penetrate the cerebral barriers allows the bacteria to colonise within the brain and cause potential damage where it may not be able to do elsewhere in the body.

Despite this, the presence of *P. Gingivalis* in the blood has also been shown to affect a number of other organs such as the placenta and the liver, however it more notably contributes to cardiovascular disease, with a recent study showing that 100% of patients with cardiovascular disease had *P. Gingivalis* arterial colonisation. This is because foam cell formation is

significantly increased when this bacteria is infected into monocytes in the blood[5], leading to the accumulation of plaques in the arteries and causing strokes and heart attacks.

Formation of Alzheimer's disease

The research proposes that once the bacteria have colonised the brain, it secretes 2 proteases called gingipains which degrade the proteins in the brain. One widely accepted hypothesis suggests that Alzheimer's is caused by the accumulation of misfolded proteins in the brain. Hence,investigations have been done to investigate a chemical compound to neutralise these gingipains. A study on mice showed that when they were injected with this bacterium into their mouths, neurodegeneration in the brain occurred. However, once they were exposed to a neutralising compound, they maintained healthy brain cells. Although this has shown to be successful on mice, it has not yet proven to be safe and effective for humans.[6]

Following the damage of brain cells, a protein called amyloid beta forms a plaque over the wound as an immune response. These amyloid plaques are commonly associated with Alzheimer's as they also ultimately lead to the death of neurons. In a healthy brain, these proteins can be broken down and will not be harmful, however for someone with Alzheimer's, these plaques harden between nerve cells and become insoluble, therefore causing neurofibrillary tangles. The protein 'tau', which forms microtubules inside cells, becomes misfolded which causes twisted fibres. This prevents the transportation of important nutrients and other substances inside the cytoskeleton from one part of the cell to the other.[7] Furthermore, studies show that the presence of *P. Gingivalis* in the brain disturbs sleep patterns, which reduces the efficacy of the glymphatic system, so toxic substances, such as amyloid beta, cannot be cleared and eliminated out of the brain.[8] Evidently, the translocation of this bacteria to the brain has a domino effect which leads to the eventual damage and destruction of neurons. Despite this, research is being taken on many *P. Gingivalis* and gingipain enzyme inhibitors; for example, a study taken on mice in 2019 showed that inhibitors can be used to prevent this bacterium from reaching the brain. The inhibitor, TLR-4, prevented the bacteria's ability to respire and gain energy, therefore they could not continue the pathway to the brain, resulting in a significant decrease in amyloid beta plaques and cognitive defects in the mice's brains.[9]

Discussion

It is difficult to distinguish whether the accumulation of bacteria in the brain is a cause or a consequence of Alzheimer's disease. The symptoms of Alzheimer's usually appear many years after the damage to the brain has already started, therefore if *P. Gingivalis* was the cause of Alzheimer's, the build-up of this bacteria must begin from a younger age than the diagnosis. The rate of periodontitis increases with age, and the presence of bacteria in the brain is a consequence of poor oral health, but this can easily be avoided by regular brushing and flossing. For someone with Alzheimer's, they are more likely to forget to maintain this routine due to memory loss. Nevertheless, keeping the rate of this bacterium under control can delay the symptoms and the presence of this bacterium in the brain could even be used as a biomarker to assess the chances of someone developing Alzheimer's in the future.

For references, footnotes and endnotes, click here.