Researchers Link Herpes To Alzheimer's Disease; "Cold Sores" Connected To Cognitive Decline

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Laboratories at the University of New Mexico (UNM), Brown University, and House Ear Institute (HEI) have developed a new technique to observe herpes simplex virus type 1 (HSV1) infections growing inside cells. HSV1, the cause of the common cold sore, persists in a latent form inside nerve cells. Re-activation and growth of HSV1 infections contribute to cognitive decline associated with Alzheimer's disease. Details are published in the March 31 issue of PLoS ONE magazine from the Public Library of Science.

"Herpes infects mucous membranes, such as the lip or eye, and generates viral particles," submits study Principal Investigator Elaine Bearer, M.D., Ph.D., Harvey Family Professor and Vice Chair for Research, Department of Pathology, UNM School of Medicine. "These viral particles burst out of the cells of the mucous membrane and enter sensory nerve cells where they travel inside the nerve toward the brain. We now can see this cellular transportation system and watch how the newly formed virus engages cellular APP on its journey out of the cell."

Tagging herpes virus inside cells with green fluorescent protein, scientists used live confocal imaging to watch HSV1 particles emerge from infected cells. Newly produced viral particles exit the cell nucleus and then bud into cellular membranes containing amyloid precursor protein (APP). Electron microscopy at HEI detailed the ultrastructural relationship between HSV1 particles and APP.

This dance between viral particles and cellular APP results in changes in cellular architecture and the distribution of APP, the major component of senile plaques found in the brains of Alzheimer's disease patients. Results from this study indicate that most intracellular HSV1 particles undergo frequent, dynamic interplay with APP, which facilitates viral transport while interfering with normal APP transport and distribution. This dynamic interaction reveals a mechanism by which HSV1 infection leads to Alzheimer's disease.

In developed countries such as the U.S., approximately 20 percent of children are infected with HSV1 prior to the age of five. By the second and third decades of life, as much as 60 percent of the population is infected, and late-in-life infection rate reaches 85 percent.

Symptoms of primary HSV1 infection include painful blisters of the mouth, lips or eyes. After infection, HSV1 persists in nerve cells by becoming latent. Upon re-awakening, new viral particles are made in the neuron and then travel back out its pathways to re-infect the mucous membrane. Many infected people experience sporadic episodes of viral outbreaks as the well-known recurrent cold sore.

"Clinicians have seen a link between HSV1 infection and Alzheimer's disease in patients, so we wanted to investigate what might be going on in the body that would account for this," adds Dr. Shi-Bin Cheng, post-doctoral associate, Department of Pathology and Laboratory Medicine, Alpert Medical School, Brown University. "What we were able to see in the lab strongly suggests a causal link between HSV1 and Alzheimer's Disease."

"It's no longer a matter of determining whether HSV1 is involved in cognitive decline, but rather how significant this involvement is," Bearer asserts. "We'll need to investigate anti-viral drugs used for acute herpes treatment to determine their ability to slow or prevent cognitive decline."
Researchers recommend people treat a cold sore as quickly as possible to minimize the amount of time the virus is actively traveling through a person's nervous system. The faster a cold sore is treated, the faster the HSV1 returns to a dormant stage.

Source: House Ear Institute

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NYU dental researchers have found the first long-term evidence that periodontal (gum) disease may increase the risk of cognitive dysfunction associated with Alzheimer's disease in healthy individuals as well as in those who already are cognitively impaired.

The NYU study offers fresh evidence that gum inflammation may contribute to brain inflammation, neurodegeneration, and Alzheimer's disease.

The research team, led by Dr. Angela Kamer, Assistant Professor of Periodontology & Implant Dentistry, examined 20 years of data that support the hypothesis of a possible causal link between periodontal disease and Alzheimer's disease.

"The research suggests that cognitively normal subjects with periodontal inflammation are at an increased risk of lower cognitive function compared to cognitively normal subjects with little or no periodontal inflammation," Dr. Kamer said.

Dr. Kamer's study, conducted in collaboration with Dr. Douglas E. Morse, Associate Professor of Epidemiology & Health Promotion at NYU College of Dentistry, and a team of researchers in Denmark, builds upon a 2008 study by Dr. Kamer which found that subjects with Alzheimer's disease had a significantly higher level of antibodies and inflammatory molecules associated with periodontal disease in their plasma compared to healthy people.

Dr. Kamer's latest findings are based on an analysis of data on periodontal inflammation and cognitive function in 152 subjects in the Glostrop Aging Study, which has been gathering medical, psychological, oral health, and social data on Danish men and women. Dr. Kamer examined data spanning a 20-year period ending in 1984, when the subjects were all 70 years of age. The findings were presented by Dr. Kamer at the 2010 annual meeting of the International Association for Dental Research July 16, in Barcelona, Spain.

Dr. Kamer's team compared cognitive function at ages 50 and 70, using the Digit Symbol Test, or DST, a part of the standard measurement of adult IQ. The DST assesses how quickly subjects can link a series of digits, such as 2, 3, 4, to a corresponding list of digit-symbol pairs, such as 1/-,2/- ... 7/Λ,8/X,9=-.

Dr. Kamer found that periodontal inflammation at age 70 was strongly associated with lower DST scores at age 70. Subjects with periodontal inflammation were nine times more likely to test in the lower range of the DST compared to subjects with little or no periodontal inflammation.

This strong association held true even in those subjects who had other risk factors linked to lower DST scores, including obesity, cigarette smoking, and tooth loss unrelated to gum inflammation. The strong association also held true in those subjects who already had a low DST score at age 50.

Dr. Kamer plans to conduct a follow-up study involving a larger, more ethnically diverse group of subjects, to further examine the connection between periodontal disease and low cognition.

In addition to Dr. Morse, Dr. Kamer's coinvestigators included Dr. Poul Holm-Pedersen, Professor and Director of the Gerontology & Oral Health Research Center; Dr. Erik Lykke Mortensen, Professor of Psychology; and Dr. Birita Ellefsen, Assistant Professor of Gerontology & Oral Health,
all at Copenhagen University in Denmark; and Dr. Kirsten Avlund, Professor of Social Medicine at the Institute of Public Health in Copenhagen.

Source: New York University

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Alzheimer Disease and Oral Health
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Oct 04, 2012

Oral Health of the Elderly With Alzheimer's Disease
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Alzheimer Disease

Alzheimer disease is the most common form of dementia, a process characterized by development of neuritic plaques and neurofibrillary tangles, ultimately leading to cortical dysfunction and progressive neurologic damage.[1] The prevalence of Alzheimer disease increases with age, and it is estimated that more than 13 million people in the United States may be diagnosed with Alzheimer disease by 2050.[1] Patients with dementia experience higher rates of oral diseases than healthy persons, and they may present with a higher burden of periodontal disease markers, such as gingival bleeding.

Study Summary

This study by Ribeiro and colleagues provides data on the subjective and objective oral health findings of elderly patients diagnosed with Alzheimer disease. This cross-sectional study included 60 volunteer participants: 30 with various stages of Alzheimer disease (mild, moderate, and severe) and 30 without Alzheimer disease or other forms of dementia who served as the control group. Data obtained from the participants included dental and medical histories and sociodemographic characteristics, including age, educational level, and monthly income.

Subjective assessment of oral health problems was evaluated using the validated General Oral Health Assessment Index (GOHAI). The participants with Alzheimer disease completed the GOHAI in the presence of their caregivers, whereas the control participants completed their assessments independently. The GOHAI score could range from 12 to 36; scores of 34-36 are classified as high, scores of 31-33 moderate, and scores less than 30 low. Lower GOHAI scores indicated more self-reported oral health problems, and these participants were expected to have poorer oral health conditions.

Objective clinical examination used the decayed, missing, and filled teeth (DMFT) index, evaluation of biofilm and calculus on exposed teeth surfaces reflected by the Oral Hygiene Index (OHI), general evaluation, and stability of removable prostheses and presence of biofilm on these prostheses.

The major findings of this study were:

- The Alzheimer disease group presented at a more advanced age and had a lower education level than the control group;
- The GOHAI scores were similar between the Alzheimer disease group and the control group and were considered moderate, indicating a positive self-perception of oral health;
- The group with Alzheimer disease presented with a fewer number of natural teeth and higher DMFT and OHI scores, especially with advancing severity of Alzheimer disease, indicating worsening oral health compared with healthy control participants; and
Upon analyzing removable prosthetic conditions, there was a significant association between the presence of oral pathology and Alzheimer disease.

Viewpoint

It is important to appreciate the differences in subjective and objective perceptions of health status, especially in individuals with conditions associated with cognitive impairment, such as Alzheimer disease. This study demonstrates the necessity of professional oral health evaluations at regular intervals in this population, because self-perception of oral health may differ significantly from clinically observed oral health.

Preventive oral health measures should be reinforced to patients with Alzheimer disease and their caregivers, because it may become more challenging to maintain and deliver oral healthcare in the context of advanced Alzheimer disease. As the US population continues to age, the prevalence of Alzheimer disease is expected to increase, and oral healthcare providers will play a critical role in the overall care of these patients.

Abstract

References


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Alzheimer's disease linked to poor dental health

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A study has found that people with poor oral hygiene or gum disease could be at higher risk of developing Alzheimer's compared with those who have healthy teeth.

Researchers from the University of Central Lancashire (UCLan) in the UK, discovered the presence of a bacterium called *Porphyromonas gingivalis* in the brains of patients who had dementia when they were alive. The bug is usually associated with chronic periodontal (gum) disease.

For the study, published in the *Journal of Alzheimer's Disease*, 10 brain samples from patients with dementia were donated for analysis by a scheme called Brains for Dementia Research, alongside 10 brain samples from people who had not had the disease.

Examination of the samples revealed the presence of the *Porphyromonas gingivalis* in the samples of the brains affected by Alzheimer's.

**Need for invasive dental treatment 'increases the bacterial risk'**

This bacteria is usually found in oral cavities, and enters the blood stream through a variety of daily activities, such as chewing, eating and brushing teeth. However, it is more likely to enter the blood stream after invasive dental treatment, where it is possible that the bacteria can enter the brain regularly, the researchers say.

Each time the bacteria enter the brain, the researchers note, this could potentially trigger immune system responses, causing the release of excess chemicals that can kill neurons.

The researchers say that this activity could lead to symptoms such as confusion and deteriorating memory - typical symptoms of Alzheimer's disease.

**Study adds to previous findings**

The study adds to previous findings that Alzheimer's is linked to poor oral health. Research from New York University in 2010 revealed long-term evidence that linked gum inflammation and Alzheimer's disease, finding that gum disease could increase the risk of cognitive dysfunction.

Another study has suggested that other bacteria and viruses are linked to the disease. Research from the University of New Mexico suggested that Herpes simplex virus type 1 (HSV-1) was linked to Alzheimer's. See "Cold sores" connected to cognitive decline.
Professor St John Crean, from the School of Medical Dentistry at UCLAN, says of this most recent research:

"Whereas previous studies have indicated a link between dementia and other bacteria and viruses such as the Herpes simplex virus type 1, this new research indicates a possible association between gum disease and individuals who may be susceptible to developing Alzheimer's disease, if exposed to the appropriate trigger."

"Research currently under way at UCLan is playing an active role in exploring this link," Prof. St John Crean continues, "but it remains to be proven whether poor dental hygiene can lead to dementia in healthy people, which obviously could have significant implications for the population as a whole. It is also likely that these bacteria could make the existing disease condition worse."

The researchers hope that continued donation of brain tissue will enable examination of more samples from people with and without Alzheimer's disease who have relevant dental records.

They add that future research will involve determining whether the Porphyromonas gingivalis could be used as a marker for a blood test that predicts the development of Alzheimer's disease in patients who are at higher risk.

Written by Honor Whiteman

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