**Familial Alzheimer’s Disease Linked to Aluminum Levels in Brain Tissue**

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**Familial Alzheimer’s Disease is one form of Alzheimer’s disease (AD) that is characterized as a genetic mutation that allows the production of clumping Beta-Amyloid proteins in the brain. This causes the early onset of the disease. In the case of fAD, this mutation is being passed genetically from a parent to offspring. There is an increasing pressure in the research field to know more about familial AD as more people are diagnosed through the years. It is estimate that approximately 44 million people are diagnosed with AD worldwide. As our population pyramid is slowly flipping to be top heavy, there is an expected increase in the diagnoses as the flip cycles. Researchers have long hypothesized that a link exists between aluminum exposure and AD but there has been controversy over the topic for the last 40 years. Newly published research supports this hypothesis but goes on to show that there is a direct, yet complex, relationship between the clusters of the Amyloid-β proteins and deposits of aluminum in the brain tissue. With the new research comes loose ends and connections yet to be found relating to our genes and their influence on toxin retention, ultimately leading to diseases ranging from Autism to Alzheimer’s Disease.**

**Introduction**

Familial Alzheimer’s Disease (fAD) is passed down genetically and accounts for roughly 1 in 20 of every cases of Alzheimer’s Disease (AD) diagnoses worldwide. There are rare cases of fAD where the parent was not diagnosed (or a carrier who did not live long enough to be diagnosed) and there is a new genetic mutation at creates a carrier (Strobel). Neurologists agree that fAD and AD are essentially the same disease, but very in the genetic cause and age of onset. Like AD, fAD has no cure, and is aggressively researched to hopefully reach a day that fAD is treatable. There are three genetic mutations identified that are responsible for causing fAD: amyloid precursor protein (APP), presenilin-1 (PS1), and presenilin 2 (PS2). Those who are diagnosed with fAD have a mutation in at least one of these three genes, which are known to affect the expression of the toxic Amyloid-β protein. This protein is responsible for the plaque buildup in brain tissue that is a hallmark of Alzheimer’s Disease (Mould et al., 2020). Those diagnosed with both AD and fAD display a distinct set of symptoms, but the degree of severity and display other symptoms vary on a case by case basis. Both fAD and AD have stages that increase as symptoms worsen and the level of dependence increases in the patient. In the early stages, a person with AD or fAD will suffer from memory loss and mild cognitive impairment. As the disease progresses, symptoms can include repetitive behavior, weight loss, an increase in sleep, incontinence, using nonverbal communication, hallucinations, depression, anxiety, and the list goes on. The final stage of AD leaves one completely dependent on others for care, and most often, nonverbal. Unlike Alzheimer’s Disease, those diagnosed with fAD typically display early stage symptoms by their 40s to 50s and the full onset happens earlier than those with AD.

Human exposure to aluminum has increased over the years with the access to things such as advanced farming technology, food processing, pharmaceuticals, and products manufactured for hygiene and cosmetics (Crisponi, Fanni, Gerosa, Nemolato, Nerchi, Crespo-Alonso, Lachowitz, and Faa, 2012). While people with fAD might not be “more exposed” to aluminum in their everyday life than those without the disease, their genetic mutation is postulated to be responsible for the increased retention of the aluminum in their bodies. The association between the Amyloid-β proteins and aluminum deposits in the brain is one of the main focuses of the most recent studies being conducted in the field. Another key focus of these same studies is the amount of aluminum deposits in the brain, which may have a key role in the pathology of AD.

**Recent Progress**

In the early 2000s, researchers studying brain tissue that contains one of the above-mentioned mutations found a significant level of aluminum in the tissue, some of which had levels high enough to be considered pathologically concerning. In 2019 researchers Mould, Linhart, Gomez-Ramirez, Villegas-Lanau, and Exley conducted a study that built off of these findings to examine brain tissue for levels of aluminum and the locations of the accumulation compared to the location of the Amyloid-β plaque in the tissue. The study used brain tissue that had a mutation specifically in the PS1 gene (this is one of the three that affect the aluminum deposits and the Amyloid-β protein expression) (Mould et al. 2020). The results of the study found that the aluminum content on the studied brain tissues ranged from 0.30 to 33.48 micrograms per gram in dry weight. The majority of these 83 tissues had over 1.99 micrograms per gram dry weight. While there was no significant difference in the amount of aluminum content across the age range (48 years to 68 years), there was a significant difference in amount of aluminum deposits between men and women in the study, suggesting that women had the higher content than males. When compared to control brain tissues from the London Neurodegenerative Diseases Brain Bank that did not have the mutation, there was a significant difference in the aluminum content. In regard to the comparison of the location of aluminum deposits and the location of the Amyloid-β proteins, researchers found that the extracellular deposits of aluminum often were co-located with the Amyloid-β plaque. Some of the studied tissues showed of the aluminum deposits to be surrounded in a nest-like structure of the Amyloid-β protein. Researchers also made a new discovery that there are also deposits of aluminum found without the company of Amyloid-β protein (Mould et al. 2020).

**Discussion**

The research described above has brought much needed support to the hypothesis of the link between aluminum deposits and Alzheimer’s Disease. New questions rise from this breakthrough. What genetic predispositions are to be held responsible for the increased retention and deposition of aluminum in the brain tissue? Is the retention and deposition of aluminum a direct effect of the Amyloid-β protein clumping? The recent research has propelled the understanding of the neuropathy of familial Alzheimer’s Disease. The discovery of the co-location of the aluminum deposits and the Amyloid-β protein builds on and supports the long-standing hypothesis of the relationship between the two and their roles in the presence of AD, while the discovery of independently dwelling aluminum deposits leave many questions to be answered concerning the influence of the mutated genes. In new studies, researchers might look at brain tissues of patients who have a mutation in the PS1 and APP genes. This will help answer whether the independent deposits of aluminum are unique to the PS2 gene, or if this is seen in all cases. From a preventative aspect, research includes how to decrease the exposure of aluminum capable of entering the body (such as deodorants). There are some clinical issues that are unique to fAD. Those who have been diagnosed with fAD are widely excluded from clinical trials concerning AD because they are significantly younger than the ‘typical’ AD patient. Because of this, research specific to fAD is much less developed and established compared to research in AD. It is also unknown how many of the 10 million Americans living without healthcare are affected by fAD, which leads to projected statistics. While this is true for all disease studies, the effects are felt greater by those fields that are less developed, like fAD research.

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