

# Alzheimer's Disease Form Linked To Chromosome 3 by Researchers

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Dr. Shirley E. Poduslo and research staff have identified a form of late onset Alzheimer's disease that may be linked with markers on chromosome 3. A patient with the clinical signs enrolled into the DNA Bank. The clinical signs included a loss of memory that became progressively worse. The routine blood studies were normal, indicating that there were no thyroid or vitamin B12 problems. The CT scan showed shrinkage of the brain, but there were no signs of strokes or tumors. The patient had three siblings who were also affected. The mother who died at a young age had several siblings with severe memory problems.

The patient lived for 13 years with the disease. When the patient died, an autopsy was performed. The patient's brain in this study only had plaques, but no tangles. (As a reminder, the classical signs of Alzheimer's disease in an autopsy brain are the loss of neurons and the presence of plaques and tangles. The plaques must be of a certain number, which is dependent upon the age of the patient, in order to even make the diagnosis of Alzheimer's disease. Thus an older patient with the disease will have more plaques than a younger person will have.)

The researchers were puzzled by the autopsy report. We thought that this patient might possibly have one of the frontotemporal dementias rather than Alzheimer's disease. (The frontotemporal dementia refers to the front and side of the brain being affected first. This results in clinical signs of behavioral and language problems appearing before memory is affected.) Some of the frontotemporal dementias are genetically linked with markers on chromosome 17, especially with the gene called tau. (Tau is a protein normally found in brain in tiny scaffolding structures called microtubules. They help the neuron to keep its shape. Abnormal tau accumulates in the tangles found in Alzheimer's brains.) We analyzed 9 markers on chromosome 3 and found that the disease in this family was highly linked with several of these markers.

A report by a group from California suggested that 30 percent of elderly Alzheimer's patients may not have tangles in their brains at autopsy. The plaques were present as expected in these elderly patients. The California researchers concluded that the patients without the neurofibrillary tangles also had Alzheimer's disease. They believe that the present of tangles may be associated with a greater severity of the disease.

The family studied fits into this category of Alzheimer's disease of having plaques but not the tangles found in the autopsy brain. From our studies, this form of Alzheimer's disease with plaques, but no tangles, is linked with markers on chromosome 3. We are now looking for the gene in this area of chromosome 3 that may be mutated in this form of the disease

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