

HIV-related memory loss linked to Alzheimer's protein

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More than half of HIV patients experience memory problems and other cognitive impairments as they age, and doctors know little about the underlying causes. New research from Washington University School of Medicine in St. Louis suggests HIV-related cognitive deficits share a common link with Alzheimer's-related dementia: low levels of the protein amyloid beta in the spinal fluid.

However, by analyzing biomarkers in the fluid surrounding the brain and spinal cord, the researchers report Dec. 8 in the journal *Neurology*, they could distinguish patients with HIV-related cognitive impairments from patients with mild Alzheimer's disease. This is important because as patients with HIV age, some will develop cognitive deficits related to HIV and others to Alzheimer's. New Alzheimer's treatments in the pipeline to improve memory and thinking may not work for both conditions.

"HIV patients with cognitive dysfunction don't have early Alzheimer's - although some of the symptoms may be similar," says lead author David Clifford, M.D., an authority on the neurological complications of HIV and director of Washington University's AIDS Clinical Trials Unit. "The underlying biology of both conditions may be related to amyloid, and we think this clue can help us find the cause of cognitive impairment in HIV patients.

Cognitive dysfunction is a major problem among the estimated 1 million Americans living with HIV. The impairments are often mild but can

affect a person's daily life, relationships and ability to hold a job. They include difficulties with memory, processing complex information and making decisions. These problems are expected to worsen as HIV patients live longer, due to potent drug cocktails that keep the virus in check.

In the new research, the scientists looked at the spinal fluid of 49 HIV patients with cognitive impairments, 21 HIV patients with normal cognitive function, 68 patients with mild Alzheimer's and 50 normal, healthy "controls." The Alzheimer's patients were older (average age 74) than the controls (average age 50), impaired HIV patients (average age 48) and cognitively normal HIV patients (average age 43).

They tested the spinal fluid for the presence of amyloid beta - the protein that folds and accumulates in the brains of Alzheimer's patients and is thought to play a key role in driving the brain damage that characterizes the disease. They also looked at other biomarkers associated with Alzheimer's, including tau, a protein found in tangled nerve fibers in Alzheimer's patients.

When amyloid beta accumulates in the brains of Alzheimer's patients, levels decrease in the spinal fluid, and Clifford and his colleagues expected to find low levels of the protein in samples of the Alzheimer's patients they studied.

But they were surprised to find the same low levels in the spinal fluid of HIV patients with cognitive dysfunction. Both groups of patients had significantly lower amyloid beta levels than HIV patients without cognitive impairments and the normal controls. The lower levels are an indicator that amyloid beta in the brain alters the normal turnover of the protein in the body.

Although Australian and European researchers had uncovered a link

between HIV-related cognitive deficits and amyloid beta in 2005 in a smaller study, Clifford thought that finding was an artifact and embarked on the current study largely to disprove it.

"I really did not expect the biology of HIV cognitive dysfunction to be related to Alzheimer's," Clifford says. "If you look at the brains of HIV patients with cognitive impairments, they don't look like Alzheimer's brains - they don't have the same atrophy or a plethora of plaques and tangles characteristic of Alzheimer's."

But low amyloid beta is where the similarity to Alzheimer's disease ends. The researchers found that patients with mild Alzheimer's had significantly higher levels of tau than either group of HIV patients or normal controls - a finding that strongly suggests Alzheimer's and HIV cognitive dysfunction are not one and the same, Clifford says.

He suspects the HIV-related [cognitive impairment](#) may be due to low levels of the virus that hide out in the brain, beyond the reach of drugs that can't easily cross the blood-brain barrier. Another cause may be low-grade inflammation in the brain that is driven by the virus.

Almost all HIV patients in the study were taking anti-retroviral therapy. "I am almost certain the dementia in AIDS patients is linked to HIV and not to anti-retroviral drugs - we see it even in patients who haven't received [HIV](#) therapy," Clifford says. "However, the more subtle impairment may be in some way associated with a change in the way the body processes amyloid beta. This will certainly be an important area of future research."

More information: Clifford DB, Fagan AM, Holtzman DM, Morris JC, Teshome M, Shah AR, Kauwe JSK. CSF biomarkers of Alzheimer disease in HIV-associated neurologic disease. *Neurology*. Dec. 8, 2009.

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