

## HIV Infection Prematurely Ages The Brain

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HIV infection or the treatments used to control it are prematurely aging the brain, researchers at Washington University School of Medicine in St. Louis and the University of California-San Diego have found.

Blood flow in the brains of HIV patients is reduced to levels normally seen in uninfected patients 15 to 20 years older, scientists report online in *The Journal of Infectious Diseases*.

"The graying of the AIDS patient community makes this infection's effects on the brain a significant source of concern," says first author Beau Ances, M.D., Ph.D., assistant professor of neurology at Washington University. "Patients are surviving into their senior years, and a number of them are coming forward to express concerns about problems they're having with memory and other cognitive functions."

Epidemiologists estimate that 14 percent to 18 percent of all AIDS patients in the United States are more than 50 years old. This age group also has one of the highest rates of new infection. If current trends continue, by the year 2015, their number will grow to more than 50 percent of the overall patient population.

Prior studies of HIV infection's long-term health effects have found the virus may adversely affect the heart, liver, endocrine system, skeleton and kidney. A recent study of the overall health of the body found that HIV infection advances the body's age by about 10 years. HIV can lead to dementia in some patients, but scientifically quantifying the effects of HIV and aging in the brain has been challenging, according to Ances.

"We believe the virus crosses into the brain using infected immune cells," Ances says. "Once in the brain, HIV doesn't directly infect neurons but instead affects supporting cells that can release immune factors that harm neurons."

Researchers including Washington University's David Clifford have detected similarities between HIV-associated dementia and Alzheimer's disease. However, adapting the cognitive tests used in diagnosis of Alzheimer's disease to HIV research has been difficult. Problems have included the time burdens the tests place on patients, socioeconomic factors prevalent in the AIDS patient population that make standardizing test results challenging and the lack of centers that have the capability to perform such tests.

In an attempt to find a quicker alternative available at many hospitals, Ances and his colleagues turned to magnetic resonance imaging scanners and a new technique known as arterial spin labeling that allows precise, non

invasive blood flow measurement.

Ances used this approach to assess brain blood flow in 26 subjects with HIV and 25 uninfected controls. Both groups were comparable in mean age range and education, and researchers screened participants for confounding factors such as head injuries, neuropsychiatric disorders and substance abuse.

When individuals were resting in the scanner, brain blood flow values were significantly reduced in subjects with HIV compared to uninfected controls. These reductions decreased brain blood flow to levels roughly equivalent to readings seen for uninfected individuals 15 to 20 years older.

When scientists asked participants to perform a visual task, which normally triggers an increase in blood flow to particular regions of the brain involved in the task, participants with HIV had greater blood flow increases, suggesting the brain and its support systems had to work harder to get the task done.

Researchers also found that HIV reduced brain blood flow even among young, recently infected patients, reinforcing earlier results that they previously published.

"Brain blood flow levels decline naturally as we age, but HIV, the medications we use to control it or some combination of the two appear to be accelerating this process independent of aging," Ances says.

Alzheimer's researchers have long recognized that the disease can do damage to the brain for years before clinical symptoms appear. The brain appears to be able to adapt to ongoing damage up to a threshold, and at that point symptoms become apparent. It is not clear if a similar phenomenon is taking place in HIV patients as they age.

Typically physicians use blood tests that quantify the levels of HIV in a patient's blood to determine when to start medications. Ances says the new results suggest that the virus' effects on the brain may be another factor to consider.

"Could we reduce the harmful effects of the virus if we started treatment earlier, or does treatment significantly contribute to the harm that's being done?," Ances asks. "These are the kinds of issues we urgently need to start examining as the AIDS patient population ages."

Ances BM, Vaida F, Yeh MJ, Liang CL, Buxton RB, Letendre S, McCutchan JA, Ellis RJ, and the HIV Neurobehavioral Research Center. HIV infection and aging independently affect brain function as measured by magnetic resonance imaging. *Journal of Infectious Diseases*, Feb. 1, 2010. 201(3):336-40

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