



Cognitive Conditions

The Foundation for AIDS Research shared a conversation about possible answers found in scientific advances. Below is an excerpt.

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People with HIV are living longer than ever before, but longevity brings new questions. One area drawing growing attention is brain health. How does HIV that has been treated long term affect cognitive aging?

To explore this question, Andrea Gramatica, PhD, an immunologist and vice president of research at amfAR, and Kelsey Hopland, PhD, a neuroscientist and new program officer of research at amfAR, discuss what scientists understand—and what remains unknown—about HIV and neurodegeneration.

Gramatica: Clinicians who work with people living with HIV have long observed memory difficulties, slower processing speed or problems with attention. The challenge is understanding what's driving those symptoms. Are they related to HIV itself? Are they part of normal aging? Or could they reflect early stages of neurodegenerative disease? Those are different possibilities, both biologically and clinically.

Hopland: And the complexity is that HIV interacts with the immune system in ways that can persist even when the virus is well controlled by therapy.

Gramatica: Historically, the main neurological condition associated with HIV has been HIV-associated neuro-cognitive disorder, or HAND. In the early years of the epidemic, before effective treatment was available, severe forms of cognitive impairment were unfortunately common. Today, thanks to treatment, the severe forms are much rarer. But milder cognitive symptoms still occur.

Hopland: What's changed now is that the population with HIV is aging. Researchers are asking whether some individuals might also develop more typical neurodegenerative diseases, such as Alzheimer's. If that's happening, do those diseases look the same biologically in people with HIV as

they do in the general population?

Gramatica: From the immunology perspective, one of the key drivers may be chronic immune activation. Even when antiretroviral therapy suppresses the virus effectively, the immune system can remain in a state of low-level activation. Chronic inflammation has been implicated in many age-related diseases, including neurodegenerative conditions.

Hopland: That's where the neuro-science perspective intersects. Inflammation is increasingly recognized as an important contributor to diseases like Alzheimer's. So one hypothesis is that the immune environment created by long-term HIV infection might influence how neurodegenerative processes develop in the brain.

Gramatica: Another possibility involves viral persistence. HIV reservoirs remain in the body even during effective treatment, including in immune cells that exist within and interact with the brain. Understanding how those reservoirs might influence brain biology over decades is an active area of research.

Hopland: One of the biggest limitations is data. We don't yet have large, harmonized datasets designed to study HIV and neurodegeneration together. Many existing studies were designed to answer different questions. That means researchers often work with fragmented datasets collected using different clinical measures, cognitive tests or biological samples. It's difficult to compare.

Gramatica: There are several areas where innovation could make a major difference. One is the creation of longitudinal cohorts—following people with HIV over time to understand how cognitive and biological changes evolve. Another is integrating multiple types of data: clinical assessments, neuroimaging, biomarkers and molecular data. With modern approaches, especially machine learning, we can identify patterns across those complex datasets. But building the infrastructure to support that kind of research requires coordination and collaboration.

Hopland: That's why there is growing interest in developing a coordinated initiative focused on HIV and neuro-degeneration. Organizations like amfAR are well positioned to help bring together the necessary partners across disciplines to explore this kind of effort.