



# Innovation at the Intersections of HIV and Brain Health

amfAR's Dr. Andrea Gramatica, VP of Research, and Dr. Kelsey Hopland, Program Officer, Research, discuss a new set of questions about cognitive conditions as people age with HIV and the possible answers found in scientific advances

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Advances in antiretroviral therapy have transformed HIV from a fatal infection into a manageable chronic condition. As a result, people living with HIV are living longer than ever before—a remarkable success story for science and medicine. But longevity also brings new questions, including how HIV may interact with the biology of aging.

One area drawing growing attention is brain health. How does HIV that has been treated long-term affect cognitive aging? Could it influence the development or progression of neurodegenerative diseases, such as Alzheimer's?

To explore these questions, Dr. Andrea Gramatica, an immunologist and VP of Research at amfAR, and Dr. Kelsey Hopland, a neuroscientist and new Program Officer, Research, at amfAR, sat down to discuss what scientists currently understand—and what remains unknown—about the intersection of HIV and neurodegeneration.

A good problem to have

Dr. Gramatica: We're having this conversation because of a good problem to have: people with HIV are living much longer lives. Antiretroviral therapy has been extraordinarily successful. For many individuals, HIV is now a chronic, manageable condition. That's a huge scientific and public health achievement. But as people with HIV live into their 50s, 60s, and beyond, we're encountering a new set of questions related to aging.

Dr. Hopland: Among those questions is what happens to the brain over time. In the general population, we know that the risk of neurodegenerative diseases increases with age. So naturally, researchers are asking whether similar or different patterns might emerge in people living long-term with HIV.

Dr. Gramatica: Clinicians who work with people living with HIV have long observed cognitive symptoms in some patients — things like 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 very different possibilities, both biologically and clinically.

Dr. 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. That makes it a unique biological context in which to study aging.

#### Understanding HIV-related neurocognitive disorders

Dr. Gramatica: Historically, the main neurological condition associated with HIV has been HIV-associated neurocognitive 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 in a subset of people living with HIV.

Dr. 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, an important question is whether those diseases look the same biologically in people with HIV as they do in the general population.

#### Possible biological mechanisms

Dr. 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.

Dr. Hopland: That's where the neuroscience 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.

Dr. 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.

Dr. Hopland: And then there's the question of classical Alzheimer's biology—proteins like amyloid and tau. We're still trying to understand whether those processes occur differently in people with HIV. At the moment, the honest answer is that we don't know.

#### What the field still lacks

Dr. Hopland: One of the biggest limitations is data. We simply don't yet have large, harmonized datasets specifically 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 findings across studies. Another challenge is that the relevant expertise is spread across multiple scientific communities—infectious disease specialists and HIV researchers,

neurologists and neuroscientists, imaging experts and computational scientists. Bringing those groups together is essential if we want to fully understand the problem.

### Opportunities for innovation

Dr. 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 computational approaches, especially machine learning, we can start to identify patterns across those complex datasets. But building the infrastructure to support that kind of research requires coordination and collaboration.

### A new initiative on the horizon

Dr. Hopland: That's why there is growing interest in developing a coordinated initiative focused on HIV and neurodegeneration. The vision would be to create a harmonized research resource—a cohort of people living with HIV and neurodegenerative diseases like Alzheimer's characterized with standardized clinical, cognitive, and biological data. Such a resource could help researchers answer fundamental questions about whether and how neurodegenerative diseases emerge in this population. Organizations like amfAR are well positioned to help bring together the necessary partners across disciplines to explore this kind of effort.

### Looking ahead

Dr. Gramatica: What makes this area exciting scientifically is that it sits at the intersection of several fields: immunology, virology, neuroscience, and aging research. And the questions we're asking today exist precisely because treatment for HIV has been so successful. People are living longer, healthier lives, and now we need to understand what healthy aging with HIV looks like. At the same time, studying HIV may also provide insights into neurodegenerative disease more broadly. Because sometimes the most important discoveries happen when different areas of science meet, where innovation happens at the intersections.

amfAR is a leading nonprofit dedicated to advancing scientific discovery and transforming global health with a primary and enduring commitment to ending the HIV/ AIDS epidemic. Serving as a catalyst for breakthrough science, amfAR supports innovative research in areas where viruses and the immune system play a defining role, including cancer, neurological conditions, autoimmune disorders, and other viral diseases. Through strategic investments, global research partnerships, and evidence-based policy leadership, amfAR helps accelerate discoveries that improve health and save lives. Since 1985, amfAR has raised more than \$950 million and awarded in excess of 3,900 grants to scientists worldwide. Learn more at [www.amfar.org](http://www.amfar.org).