CATIE News

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Cardiovascular issues can affect brain health

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In the time before the availability of potent anti-HIV combination therapy (commonly called ART or HAART) one of the feared consequences of HIV infection was dementia. In cases of AIDS-related dementia, people could gradually lose control of their muscles and memory, have difficulty thinking clearly and their personality could undergo drastic changes.

However, the widespread availability of ART today has made AIDS-related dementia relatively uncommon in Canada and other high-income countries. Instead, multiple research studies have found that subtle deficits in thinking and memory persist in ART users. The reasons for these generally mild abnormalities are not clear but may be related to the following or other issues:

- aging with a chronic viral infection
- potential side effects from ART or other medicines
- persistent inflammation caused by long-term HIV infection
- poor penetration of some anti-HIV drugs into the brain
- having other health conditions (co-morbidities)

Inside the brain

Brain cells are very active and require fresh blood rich in oxygen and nutrients, particularly a stable level of glucose, which is used as a source of energy. In HIV-negative people, neurocognitive decline—problems with thinking clearly and remembering—has in some cases been linked to the following co-morbidities:

- diabetes
- abnormal levels of cholesterol in the blood
- higher-than-normal blood pressure
- narrowed arteries (due to formation of plaque)
- problems with the heart

Researchers in Italy have conducted a neurocognitive assessment of 245 HIV-positive people and evaluated them for conditions that could affect the important functions of their brain. They found that co-morbidities such as diabetes and other risk factors for poor cardiovascular health did weaken the neurocognitive abilities of participants. It is possible that these metabolic problems could perhaps intensify subtle HIV-related effects on the brain. The research team suggests that by focusing on the diagnosis and treatment of co-morbidities in HIV-positive people, doctors might be able to effect improvements in mild neurocognitive dysfunction.

Study details

Researchers in Rome and Galatina, Italy, evaluated 245 HIV-positive participants between July and October 2010. All participants underwent a comprehensive series of neurocognitive tests and also ultrasound scans of the arteries in their neck. These arteries are called the carotid arteries and they supply fresh oxygen-rich blood to the brain. In addition, participants gave blood for tests and were interviewed by the research team.

The average profile of participants upon entering the study was as follows:
- 76% men, 24% women
- age – 46 years
- HCV co-infection – 58%
- duration of HIV infection – 11 years
- lowest-ever CD4+ cell count – 230 cells
- current CD4+ cell count – 527 cells
- proportion with HIV viral load less than 50 copies/ml – 84%

The proportion of participants with different cardiovascular risk factors was as follows:

- abnormal levels of cholesterol in the blood – 61%
- smoking tobacco – 54%
- higher-than-normal blood pressure – 15%
- family history of premature cardiovascular disease – 13%
- obesity – 6%
- diabetes – 5%

Results

On average, participants had two risk factors for a future heart attack or stroke.

About 31% of participants had narrowed carotid arteries.

Neurocognitive functioning

A total of 53% of participants had mild neurocognitive impairment detectable only with testing. No participants had any greater degree of this problem and so their ability to carry out daily tasks or work was not affected.

Interestingly, neurocognitive impairment was most common (61%) among participants who had two or more risk factors for cardiovascular disease (CVD).

Taking many factors into account, the researchers found that having narrowed arteries was linked to mild neurocognitive decline. Among people with diabetes, a statistical trend emerged toward poor neurologic functioning.

Among a sub-set of people (206 participants) whose viral loads were less than 50 copies/ml, findings were similar to the larger group.

The research team also assessed the effect of different anti-HIV drugs on neurocognitive abilities and found that participants who used abacavir (Ziagen and in Kivexa and Trizivir) seemed to have better neurocognitive function.

Factors such as lowest-ever CD4+ cell count, current CD4+ count and length of time with HIV infection were not linked to performance on neurocognitive tests.

As an aside, although most of our report focuses on co-morbidities and their effect on neurocognitive function, other researchers have found that, in general, the more educated a person is, the more likely that a decline in neurocognitive function is delayed compared to people who have less education. One study in the U.S. found that a high degree of education might help delay the loss of neurocognitive function in HIV-positive people.

Not surprisingly, in the present study, researchers found that participants who had more than 11 years of schooling performed better on neurocognitive testing.

Bear in mind

The design of this study was cross sectional; this is analogous to a snapshot in time. It can only provide a glimpse of the state of health of participants. There was no control or comparison group in the Italian study. Findings from a cross-sectional study are not definitive.

A more useful study would have been to recruit a larger number of participants, both HIV positive and HIV negative, to monitor and test them repeatedly over several years. This would be a study of a different design called a
longitudinal study. However, longitudinal studies are expensive and sometimes difficult to recruit for and maintain. Cross-sectional studies can, however, provide limited findings that can be used to make the case for funding a longitudinal study.

Perhaps the most important finding from the Italian study is that cardiovascular disease risk can affect the workings of the brain, particularly the parts involved in memory and thinking in HIV-positive people. A similar effect has been observed in HIV-negative people. As ART enables HIV-positive people to live near-normal life spans, the focus of care may need to shift to monitoring for and treating the diseases of aging.

Other studies have also found an increased risk for CVD among HIV-positive people. In part, this may be a consequence of HIV infection and the persistent inflammation that this virus triggers. In experiments with monkeys infected with simian immunodeficiency virus (SIV, which can cause an AIDS-like disease in susceptible monkeys), researchers have found signs of premature cardiovascular disease. And another study by a team experienced in HIV brain research used MRIs and found a connection between problems controlling blood sugar and damage to structures deep within the brain.

All of this research underscores the need for longitudinal studies to assess the risk of CVD in HIV-positive people. It also highlights the necessity of potential interventions for people at risk for CVD with combinations of therapy (exercise, medicine, changes to the diet, help for smoking cessation, stress reduction and so on) so that health can be maintained or improved. Moreover, by preventing and treating co-morbidities, the research team suggests that, in theory, doctors may be able to reverse the mild neurocognitive impairment that seems to be relatively common in studies with HIV-positive people in the present era.

Resources:

- A mind of her own – understanding HIV and how to deal with neurocognitive issues
- HIV and cardiovascular disease – CATIE Fact Sheet on tips for a healthy heart

REFERENCES:


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