Brain fitness leads to improvement for some HIV-positive people

8 November 2016

In Canada and other high-income countries the widespread availability of potent combination anti-HIV therapy (commonly called ART) has made severe HIV-related brain injury rare in the current era. Instead, researchers are finding milder forms of HIV-related brain injury. Such milder cases, particularly if they are symptom free, are often subtle and likely best uncovered through complex and time-consuming neuropsychological testing.

Scientists who study the brain today divide HIV-related brain injury into the following three categories:

- **asymptomatic neurocognitive impairment** (symptom-free neurocognitive impairment) – In such cases, testing detects subtle or mild degradation or decline in memory and thinking processes not seen in people of the same age who have similar levels of education. This decline is not sufficiently serious to affect a person’s ability to engage in everyday activities.
- **mild neurocognitive disorder** (MND) – Testing detects at least a modest decline in memory and thinking processes. This decline is below what would be seen in healthy people of the same age and educational level. In cases of MND, the ability to carry out everyday activities is usually only somewhat affected.
- **HIV-related dementia** - Testing reveals a severe decline in clear thinking and memory and a moderate-to-severe decrease in the ability to carry out activities of everyday living.

All three categories now make up what researchers call HAND—HIV-associated neurological disorder. Overall, some neuroscientists estimate that about 50% to 60% of HIV-positive people have some degree of HAND.

**Brain fitness**

Researchers are conducting studies of ways to reduce the effects of milder forms of HIV-related brain injury with so-called brain fitness exercises. These are computer-based exercises, usually in a game-like format, that are thought to help stimulate the brain so that over time as the exercises are repeated people’s memory, concentration, verbal fluency and other functions improve.

In experiments with HIV-negative people, different brain fitness programs have been found to help with rehabilitation of neurocognitive functions in people who have had strokes and trauma and in otherwise healthy seniors. Over the past several years, preliminary research from Canada and the U.S. has found some benefit from brain fitness exercises in people with HIV.

**A new study**

Recently, researchers at the University of Hawaii conducted a relatively large randomized study of adaptive vs. non-adaptive brain fitness training. In adaptive brain fitness programs, participants are required to complete tasks that gradually become more difficult as the software adapts to their abilities. In the study, researchers found that some HIV-positive participants developed improvement in several areas of neurocognitive functioning particularly when adaptive brain fitness exercises were used. Furthermore, MRI (magnetic resonance imaging) scans of participants’ brains suggested that improvement of information processing between and within different regions of the brain occurred. In some cases, the effects of the brain fitness program persisted for up to six months after participants had ceased the exercises.

**Study details**
Researchers ensured that prior to engaging in brain fitness participants underwent IQ testing, screening for HIV infection and other conditions, neuropsychological testing and other assessments. They then randomly assigned 173 participants (83 HIV positive and 90 HIV negative) to receive either adaptive or non-adaptive brain training with the goal of finding out their impact on working memory (explained below).

**About working memory**

The research team defined working memory as the “cognitive skill involved in retaining and manipulating information over short periods of time. Therefore, working memory is necessary for concentration, maintaining awareness and is crucial for learning and [activities that involve planning, organizing and problem solving].” They stated that deficits in working memory may lead to poorer adherence—a reduced ability to take ART every day exactly as directed.

**Back to the study**

Researchers used a brain fitness program called Cogmed. Clinical trials with this software have been found to help improve working memory in the following cases without HIV infection: some children with attention deficit hyperactivity disorder and adults with brain injury.

During the study, participants had to complete between 20 and 25 brain fitness sessions over a period of five to eight weeks. Each session lasted between 30 and 40 minutes.

The average profile of the HIV-positive participants upon entering the study was as follows:

- age – mid 50s
- 90% men, 10% women
- 96% were taking ART and 77% of ART users had an undetectable HIV viral load
- CD4+ count – greater than 500 cells/mm$^3$
- duration of HIV infection – 16 years

The distribution of factors such as race/ethnicity, socio-economic status and symptoms of depression was similar between HIV-positive and HIV-negative participants.

**Premature departure from the study**

Although researchers randomly assigned 173 participants to the study interventions—adaptive or non-adaptive brain fitness exercises—there were relatively high rates of participants who dropped out of the study: 35% in the adaptive and 29% in the non-adaptive brain fitness groups. The researchers suggested that brain fitness exercises may have been “too difficult” for the participants who dropped out, as such people tended to have statistically significantly lower IQ scores, more symptoms of depression, and, among the HIV-positive people, were more likely to have HIV-related neurocognitive impairment than participants who remained in the study. People who left the study were of similar age, gender, ethno-racial makeup and socio-economic status as people who remained in the study.

**Key findings**

- At the start of the study, researchers found that as a group HIV-positive people tended to have shorter attention spans and/or weaker working memory than healthy HIV-negative people of the same age and gender. However, the researchers stated that such findings are “typical” among HIV-positive people with symptom-free neurocognitive impairment.
- Adaptive brain fitness exercises significantly improved working memory in many participants one and six months after such training had ceased.
- Participants who underwent adaptive brain training subsequently reported fewer symptoms linked to problems associated with what neuropsychologists call “executive function.” These would involve tasks that required planning, organization and problem solving.
- Among HIV-positive people who underwent adaptive brain fitness training, researchers found that, overall, their neurocognitive abilities were able to reach levels “similar to or higher than the baseline performance of [healthy HIV-negative participants].”
- MRI scans showed changes suggesting improvement in the brains of participants who underwent adaptive brain fitness. Among HIV-positive participants, researchers noted that prior to starting brain fitness exercises,
MRI scans suggested that connections between different parts of the brain seemed to be initially somewhat abnormal. Over the course of the study, as more brain fitness exercises were done by HIV-positive participants, these connections reorganized and became similar to what was seen in healthy HIV-negative people of the same age and gender at the start of the study. Such changes likely underpinned their improvements in working memory.

For the future

The Hawaiian study has very promising results and should encourage more and larger clinical trials focused on brain rehabilitation among HIV-positive people. The need for such research is likely to intensify as more HIV-positive people reach their 60s and 70s. Such research should assess the different brain fitness programs available and find the ones that are most suitable for HIV-positive people who have neurocognitive impairment. Clinical trials also need to be done to test such software for its ability to prevent or delay the onset of HIV-related neurocognitive impairment in ART users. Just as HIV-positive people are now living for many years thanks to ART, studies that can assess and address HIV-related brain injury need to be conducted over longer time spans.

An important note

Readers should note that everyone, regardless of HIV status, can have episodes of forgetfulness from time to time. However, cases of persistent problems with memory and thinking clearly need to be reported to doctors so that they can be investigated and their underlying causes can be revealed. There are many factors other than HIV that could cause problems with memory and thinking clearly, including the following:

- untreated anxiety, depression and other mood issues
- untreated thyroid disease
- persistent sleep problems
- substance use
- co-morbidities - research suggests that some of the issues associated with aging (such as elevated blood pressure, pre-diabetes and diabetes, abnormal cholesterol levels, kidney disease, cardiovascular disease and so on) can indirectly or directly affect the health of the brain
- infections - research suggests that active co-infections such as syphilis and hepatitis C virus and perhaps even latent infection with the parasite *T. gondii*, among other germs, can affect the brain’s cognitive abilities
- a deficiency of some B-complex vitamins, particularly vitamin B₁₂

Resources

A Mind of Her Own - The Positive Side

Brain-related issues - TreatmentUpdate 203

HIV and brain-related issues - TreatmentUpdate 204

Brain Health - A Practical Guide to a Healthy Body for People Living with HIV

---Sean R. Hosein

REFERENCES:


Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.