

# A Mind of Her Own

Long-term survivor Maggie Atkinson adds cognitive problems to her list of HIV-related issues. Here she takes a walk down memory lane and shares what she's learned about protecting her brain.

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I first noticed a slight reduction in my ability to think clearly in 1993, when my CD4+ cell count fell below 200. I just didn't feel as sharp.

A year later, when I got PCP, the life-threatening pneumonia that is a hallmark of AIDS, my handwriting deteriorated so much that I had to concentrate to write legibly. About five years ago, I started having trouble remembering names of famous people. Over the next couple of years, these memory lapses progressed to the names of colleagues and then friends, which was awkward, to say the least.

I also began to have difficulty finding words. It started with complex words. My brain would substitute another similar-sounding or simpler word. My sentences began to be filled with "thing" or "stuff" or "you know." As it got worse, I forgot everyday words. As an AIDS activist, I used to speak in public regularly. Gradually, I began to shy away from those activities because it was embarrassing to be fumbling for words. I was acting like a stereotypical geriatric, not a 40-something lawyer.

Fortunately, about two years ago, I found some strategies that helped and I've gotten much, but not all, of my functioning back. Based on my personal experience and some additional research, here is what I learned about protecting the brain.

### First, some terminology

The term *cognition* refers to the high-level functions of the brain, such as speaking, seeing, calculating, processing information, remembering, planning and problem-solving. When these processes are reduced, experts use the term *neurocognitive impairment*, or *NCI*.

When reading about NCI, you find very similar-sounding terminology. *Dementia*, for example, is a general term that refers to a severe decline in cognitive function that interferes with daily activities. It is not a disease itself but a group of symptoms that may accompany a disease or condition. *AIDS dementia complex* is a term introduced in 1986 to refer to the severe cognitive deficits and motor and behavioral changes associated with advanced HIV disease.

With advances in HIV research, our understanding of the effects of HIV on the brain has become more nuanced. Now, experts often speak of *HIV-associated neurocognitive disorders (HAND)*. This umbrella term covers a range of disorders of increasing severity—from asymptomatic (signs of impairment on neuropsychological tests but no loss of function in day-to-day life) to mild (signs of impairment in both tests and daily living) to the most severe form, *HIV-associated dementia (HAD)*.

### How common is NCI among PHAs?

Experts are still not sure how common NCI is. Since the advent of highly active antiretroviral therapy (HAART), rates of the severe form—HAD—have declined dramatically in the developed world, from about 50 percent down to as low as 2 percent. University of Alberta's Dr. Chris Power, one of North America's leading neurologists, has estimated that about 7 percent of the more than 3,000 patients in the HIV clinics in Calgary and Edmonton have HAD.

Milder forms of NCI may be more common, and researchers in the United States are taking an in-depth look at this issue in the CHARTER (CNS HIV Antiretroviral Therapy Effects Research) study. Their results, released this past summer, indicate that the rate of NCI was 52 percent among



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1,555 middle-aged HIV-positive volunteers—with 21 percent having mild impairment, 29 percent moderate and 2 percent severe.

Similar findings have been made by Dr. Sean B. Rourke, a neuropsychologist, scientist and the director of research in the Mental Health Service at St. Michael's Hospital in Toronto. Having done neuropsychological testing on more than 500 people with HIV/AIDS (PHAs), he found NCI prevalence ranging from about one-quarter to one-third among people with HIV and up to 50 percent in people with AIDS, excluding those with conditions that can also cause NCI (such as depression or a history of traumatic brain injury). Dr. Rourke notes that his data are slightly biased because he sees patients who have been referred for cognitive problems.

There is not yet a general consensus on these data, but it is clear that NCI—especially its milder, subtler forms—may be touching a large proportion of PHAs.

### What causes NCI?

HIV enters the brain early on in the course of infection. Although it doesn't infect brain nerve cells (neurons), HIV damages them both directly and indirectly. Proteins from HIV-infected cells cause the release of certain chemical

## Acronyms

- HAD** – HIV-associated dementia
- HAND** – HIV-associated neurocognitive disorders
- NCI** – Neurocognitive impairment

messengers (neurotransmitters), which, in turn, cause inflammation, excitation and even cell death. In a less direct fashion, HIV infects other cells in the brain that cause a release of toxins that damage that organ.

HAD is associated with advanced HIV disease, and although rates of HAD are declining, the milder forms of NCI are not necessarily following suit, says Dr. Ian Everall, a professor of psychiatry at the University of California, San Diego. He speculates that while HAD may be caused by the direct toxicity of HIV in the brain, milder forms of NCI are caused by secondary processes brought on by low-level presence of the virus: “HAD is a product of uncontrolled viral replication and immune suppression, so when we control replication with HAART, we get less HAD. But perhaps we are still living with low-grade infection and inflammation, which is subtly affecting the neurons and causing mild neurocognitive disorder.”

Along with HIV and aging (see next section), there are many other factors that can cause or contribute to NCI, depending on their severity, including: depression, concussion, learning disabilities, alcohol or other substance-use disorders, non-HIV-related neurologic conditions (such as epilepsy and multiple sclerosis), systemic diseases (such as high blood pressure, diabetes, asthma and thyroid disease), hepatitis C virus and vitamin B<sub>1</sub> and B<sub>12</sub> deficiencies.

### Aging and NCI

Aging affects the structure and function of the brain, slowing it down, making it less accurate and reducing its capacity to store and retrieve memories. Again, scientists have a range of terms for the severity of this decline, beginning with *age-related cognitive decline*, which is associated with normal aging. *Mild cognitive impairment*, evidenced by poorer memory and performance on neuropsychological testing, is seen in about 20 percent of those over 70. The

most severe impairment is dementia, one common cause of which is *Alzheimer’s disease*. This irreversible illness severely and progressively affects cognition, behavior and motor functions and day-to-day living. Most often found in people over 65, its incidence doubles about every five years from then. Approx-

mately 50 percent of HIV-negative people over 80 have Alzheimer’s.

“It is a concern that with the aging of the HIV population we may be seeing additional effects of age [on NCI],” says Dr. Power. He hasn’t seen much Alzheimer’s in HIV-positive patients until they’re in their 70s, but some studies have shown signs of Alzheimer’s disease in the brains of PHAs much earlier. In a small substudy of brain samples from HIV-positive people over 55, Dr. Everall and his colleagues from the National NeuroAIDS Tissue Consortium found beta amyloid plaques, a characteristic of Alzheimer’s disease, in 35 out of 36 brains.

For years, doctors and PHAs have suspected that HIV causes accelerated aging of the body. It wouldn’t be surprising if the virus had this effect on the brain, too. In a recent small study, the blood flow in the brains of PHAs appeared similar to that of HIV-negative people who are 15 to 20 years older. Dr. Rourke says that with neuropsychological testing “in those [HIV-positive people] with mild neurocognitive disorder, I am seeing an accelerated aging, like 10, 15 or even 20 years older.”

### Do you have HAND?

If you suspect that you have a problem with your cognition, the first step is to see your doctor. He or she may refer you to a specialist for further testing. Diagnosis of HAND involves neuropsychological testing that evaluates different parts of brain functioning. If you have signs of mild neurocognitive disorder, your doctor will take a full history

### Penetration of anti-HIV drugs through the blood-brain barrier

	Higher	Intermediate	Lower
Nukes (NRTIs)	abacavir AZT	FTC 3TC d4T	ddl tenofovir ddC
Non-nukes (NNRTIs)	delavirdine nevirapine	efavirenz	
Protease inhibitors (PIs)	boosted amprenavir boosted darunavir boosted indinavir boosted lopinavir	amprenavir atazanavir boosted atazanavir indinavir	nelfinavir ritonavir saquinavir boosted saquinavir boosted tipranavir
Integrase inhibitor	raltegravir		
Fusion inhibitor			T-20

Adapted from Letendre S, et al, 13th CROI, 2006, Abstract 74

and perform tests to determine the conditions that might be causing the impairment.

## HAART for HAND

“HAART is the cornerstone of treatment for HAND,” Dr. Power says. Early intervention with HAART can reduce the risk of HAND and decrease symptoms. From a number of recent studies, it appears crucial to begin HAART before the CD4+ count falls below 200—how much earlier is not certain. It may well be that HAND, even if it is not affecting daily functioning, should be an indicator for treatment.

Which combination of drugs to take is another question. Some antiretrovirals are better than others at passing through the blood–brain barrier, which keeps many toxins out of the brain and spinal cord. Recent studies, including CHARTER, indicate that having a regimen with more drugs that can penetrate the barrier leads to reduced rates of NCI.

Some researchers have developed a system of ranking the ability of antiretrovirals to penetrate the blood–brain barrier (see chart on p. 23). However, there are no official guidelines as to whether or not to change a HAART regimen if you have an undetectable viral load but are showing signs of NCI. That is an individual decision between you and your doctor.

## Forget Me Nots: Dealing with the symptoms of NCI

Your doctor can refer you to rehabilitation experts, such as physical and occupational therapists, who can help you to deal with the effects of NCI on your daily functioning. I asked two professionals for their tips.

**Sheila Thomas, occupational therapist at the Sherbourne Health Centre in Toronto, works one-on-one with PHAs:** “It all depends on your needs and goals. Sometimes it’s a matter of creating a routine—always put keys in the same place, associate taking meds with certain things like getting up in the morning, plan to do recurring things on the same day of the week. It depends on how you take in information best. Some people do better with visual cues like Post-it notes, others with an auditory alarm such as a timer. Minimize distractions by not having the TV and radio on when you’re trying to talk to someone. Pace yourself throughout the week: Try to spread things out so you’re not doing everything at once. Leave yourself extra time. Electronic calendars and a cell phone or personal organizer with phone numbers in it can make life easier.”

**Dr. Sean Rourke, a neuropsychologist, scientist and the director of research in the Mental Health Service at St. Michael’s Hospital in Toronto,** notes that a diagnosis of mild neurocognitive disorder, though initially stressful, can be therapeutic. “In a way, it can be a relief to find out that you really do have a problem and it isn’t all in your imagination.” He suggests some compensatory strategies: “Lists, date books, use them strategically. You may need to write things down to crystallize them better. If you have short-term memory problems, take more time to prepare things, practice a few more times, write it down. Retrieval is often a problem with HIV. Don’t overdo it, but have the main concepts written down in front of you to rely on, to get back on track. You may need more time, and you may have to build in these pieces to compensate, but you can still do it well.”

## Nutrition and more

When I first did neuropsychological testing with Dr. Rourke 10 years ago, I asked what I could do to preserve my memory. He told me: “Whatever helps the heart, helps the brain.”

I found two fairly similar approaches—the Pritikin Program for Diet and Exercise created by Nathan Pritikin ([www.pritikin.com](http://www.pritikin.com)) and The Spectrum Lifestyle Program founded by Dr. Dean Ornish ([www.pmri.org/lifestyle\\_program.html](http://www.pmri.org/lifestyle_program.html))—that have proven results in reducing heart disease, cancer, diabetes and their contributing factors. (You can also read more about these programs in *The Pritikin Edge* by Robert E. Vogel, 2008, and *The Spectrum* by Dr. Dean Ornish, 2007.)

Last August I went to the Pritikin Longevity Center in Florida for two weeks and saw a 30 percent drop in my cholesterol and a 50 percent reduction in my insulin levels. I also felt 15 years younger, physically and mentally. In a nutshell, this is the recommended lifestyle at the Pritikin Center:

- diet: fruits, vegetables, beans, soy, fish, whole grains, no added fat, nonfat dairy, no added salt, little or no coffee and alcohol
- vitamin D<sub>3</sub>: 1,000 to 2,000 IU/day, depending on test results
- exercise (aerobic, resistance, flexibility): 6 to 7 days per week
- stress management: meditation, yoga
- no smoking
- sufficient sleep

With respect to diet, Lark Lands, a medical journalist, editor and longtime AIDS treatment educator and advocate ([www.larklands.net](http://www.larklands.net)), suggests taking plenty of natural anti-inflammatories, as inflammation plays a key role in the processes that block and damage arteries. Avoid fats that promote inflammation, such as partially hydrogenated oils (“trans fats”) and polyunsaturated vegetable oils. Some examples of naturally anti-inflammatory foods and seasonings are: ginger, turmeric, bioflavonoid-rich fruits (such as colourful berries, grapes and citrus fruits), omega-3 fatty-acid-rich foods (such as wild, fatty fish, flaxseed and walnuts) and garlic (eating more than a couple cloves of raw garlic may interact with some drugs, so speak with your doctor and pharmacist about possible interactions with your meds).

According to Lands, many of the mental changes experienced in HIV disease may be the result of advanced vitamin B<sub>12</sub> deficiency. This deficiency can cause memory loss, confusion, chronic fatigue, decreased reflexes, unsteady gait, weakness, neuropathy and depression. B<sub>12</sub> deficiency is common in PHAs and older adults. Unfortunately, the tests commonly used to assess B<sub>12</sub> status may not be reliable, often indicating that a person has “normal” levels when, in fact, there is a deficiency. Consequently, vitamin B<sub>12</sub> therapy based on symptoms, rather than test results, is recommended.

To maintain general health and protect mental functioning, Lands recommends taking a high-quality multivitamin, an antioxidant formula, fish oil (try to find mercury-free

## Work Those Brain Cells!

Learning new things is highly valuable when it comes to your brain health. The best activities are progressively challenging, mentally rewarding, novel or surprising and demanding of focused attention. Here are some ways to exercise your brain:

- learn to play music
- learn a language
- do crossword puzzles (must be challenging) or jigsaw puzzles (more than 500 pieces)
- play ball or juggle
- crochet or knit
- use your “other” hand
- take dance lessons
- play bridge

kinds), vitamin B<sub>12</sub>, folic acid and N-acetyl-cysteine (NAC).

### Exercise

A number of studies in sedentary seniors who took part in fitness programs have shown that exercise improved their cognition. Exercise may promote the growth of brain cells and increase human growth hormone, which can help cognition.

Exercise is important, especially when you're HIV positive, because it may prevent or help a slew of conditions (including diabetes, high blood pressure, chronic kidney disease and depression) that might adversely affect cognition.

Learning ballroom dancing, particularly tango, may be good not only because of the physical exercise and social interaction but also because of the mental benefits. “There are trends that suggest that tango is good for working memory and divided attention,” says Patricia McKinley, associate professor at the McGill School of Physical and Occupational Therapy. “I think that any challenging dance would be good for you.”



*“Whatever helps the heart, helps the brain,” says Dr. Sean Rourke.*

### Fitness for the brain

A couple of years ago, I saw Dr. Norman Doidge, Toronto psychiatrist and researcher, speak about his book, *The Brain that Changes Itself*. He explained how the brain is plastic and therefore can change based on what you do and think. He also mentioned the success of the Brain Fitness Program (BFP) in improving the memory of healthy seniors. I went online and read about the early impressive results of the IMPACT study (Improvements in Memory with Plasticity-based Adaptive Cognitive Training), a randomized, double-blinded prospective study of the Brain Fitness Program by researchers from the Mayo Clinic and the University of California, San Francisco. Among 524 HIV-negative seniors, those using the BFP had a 131 percent increase in brain processing speed. Their memory improved to that of individuals 10 years younger on average. Their neuropsychological test performance was significantly better than the active controls. And 75 percent of participants self-reported positive changes.

I purchased the computer program. Although there was no evidence that it could help people with HIV, I thought, what do I have to lose? I did the 40 one-hour sessions—one hour per day, five days a week, for eight weeks. As a result of the sometimes-grueling exercises, I had a 54 percent increase in brain processing speed, plus I noticed I had much better word recall and short-term memory. I wasn't fumbling for words anymore. I could remember names of people I met. My hearing, handwriting and especially my self-confidence improved.

I recommended the program to a friend, who went to Dr. Rourke for neuropsychological testing before and after doing the BFP. He had a 34 percent increase in brain processing speed. More importantly, he went from testing below normal in all areas to normal, and in one-third of the domains to above average compared to his peers. “Before the BFP I would forget what I was talking about,” he told me. “I was perpetually making lists. I knew there wasn't anything I could do except watch it happen. I felt a mix of sadness, loss and grief. After the BFP, I noticed I wasn't having trouble carrying on a coherent conversation. I wasn't making as many lists. It was easier to get my key in the door, I wasn't fumbling anymore. Now I feel more confident, I feel better.”

“The results are quite amazing,” Dr. Rourke says. “This kind of improvement is unprecedented. We are doing more case studies at our neurobehavioral unit with a view to an eventual trial.”

### A work in progress

It's been two years since I completed the BFP and my memory has started slipping a bit, so I've decided to do the program again. Although the results have been shown to last at least five years, some people choose to repeat it to keep themselves sharp. This time I did neuropsychological testing before starting, and it turns out that I am functioning much as I did seven years ago when I was last tested, before my memory started failing. I am looking forward to seeing how I perform after a refresher.

Besides that, I've started to do more things that stretch my brain, such as going to the museum, relearning a language and learning to play a musical instrument. I'm doing jigsaw puzzles and knitting and even brushing my teeth with my left hand. And I'm still trying to follow the Pritikin program as much as possible. Next up? I'm signing up for ballroom dancing, maybe the tango! +

Maggie Atkinson is an AIDS activist, lawyer and long-term survivor with HIV/AIDS. Her motto in life is not “Why me?” but “What can I do about it?”