Neurocognitive Impairments in HIV: Natural History, Impacts on Everyday Functioning and Promising Interventions

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Overview

1. Neurocognitive aspects of HIV: impairments and disorders
2. Impact of cognitive impairments on everyday functioning
3. Understanding the nature of cognitive symptoms
4. Rehabilitation and maintaining healthy cognitive function
Part 1

What are the neurocognitive changes / impairments / disorders associated with HIV/AIDS
Cognitive impairments in HIV-infection: What changes can be experienced?

- Slowing (cognitive operations)
- Concentration / paying attention
- Multi-tasking ability (“working memory”)
- Word finding
- Memory ability (particularly short-term)
- Motor coordination

Presentation is often variable / “spotty” – How so?

Are these similar to other medical conditions – YES - similar to TBI, MS, Schizophrenia, Parkinson’s Disease
Pattern of cognitive impairments: Most areas < 50-60% affected --> “spottiness”
Are these cognitive changes and impairments similar to “normal” aging?

<table>
<thead>
<tr>
<th>Changes with HIV/AIDS</th>
<th>Changes with Aging</th>
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<tbody>
<tr>
<td>Slowing</td>
<td>Yes</td>
</tr>
<tr>
<td>Multi-tasking ability</td>
<td>Yes</td>
</tr>
<tr>
<td>Word finding</td>
<td>Yes</td>
</tr>
<tr>
<td>Short term memory</td>
<td>Yes</td>
</tr>
<tr>
<td>Motor coordination</td>
<td>Yes</td>
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</tbody>
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**What changes do not occur with HIV/AIDS or aging:**
Most language functions, basic attentional skills, memory (retention / savings), implicit memory skills
How common is cognitive impairment in HIV (Pre- and Post-HAART)?

Heaton et al., 1995

- **San Diego HNRC (Pre-HAART)**
- **St. Michael's Hospital (Post-HAART)**

Heaton et al., 1995
Revised Criteria for HIV-Associated Neurological Disorders (HAND): Antinori et al., 2007 (AAN)*

1. HIV-associated asymptomatic neurocognitive impairment (ANI)
2. HIV-1-associated mild neurocognitive disorder (MND)
3. HIV-1-associated dementia (HAD)

* Modified from the HIV Neurobehavioural Research Centre Criteria
HIV-Associated Asymptomatic Neurocognitive Nmpairment (ANI)

1. Acquired cognitive impairment in at least 2 domains which are < 1SD from normative mean
2. Cognitive impairment does not interfere with everyday functioning
3. Does not meet criteria for delirium or dementia
4. There are no other pre-existing cause for ANI

* If there is a previous Dx of ANI but not currently – ANI Dx in remission
* If the person also meets criteria for a Mood or Substance Use Disorder than ANI should be deferred until MDE treated or 1 month after cessation from substance use
HIV-1-Associated Mild Neurocognitive Disorder (MND)

1. Acquired cognitive impairment in at least 2 domains which are < 1SD from normative mean
2. Cognitive impairment produces at least mild interference with everyday functioning (observed or by self-report – reduced mental acuity, inefficiency at work, homemaking or social functioning)
3. Does not meet criteria for delirium or dementia
4. There are no other pre-existing cause for MND

* If there is a previous Dx of ANI but not currently – ANI Dx in remission
* If the person also meets criteria for a Mood or Substance Use Disorder than ANI should be deferred until MDE treated or 1 month after cessation from substance use
HIV-1-Associated Dementia (HAD)

1. Marked acquired cognitive impairment in at least 2 domains < 2 SD or greater; typically impairment is in multiple domains, especially in learning of new info, slowed info processing and defective attention and concentration
2. Cognitive impairment produces marked interference with everyday functioning (work, home life, social functioning)
3. Does not meet criteria for delirium
4. There are no other pre-existing cause for other CNS infection, CNS neoplasm, CVD

* If there is a previous Dx of ANI but not currently – ANI Dx in remission
* If the person also meets criteria for a Mood or Substance Use Disorder than ANI should be deferred until MDE treated or 1 month after cessation from substance use
Pre-HAART
Rate and type of neurocognitive disorders

Grant, Heaton, & Marcotte (San Diego HNRC), 1997
HIV Neurobehavioural Research Centre
HAND Rates in Post-HAART era:
CDC A, B and C

Asymptomatic NPI – A: 27%; B: 26%; C: 18%

Mild Neurocognitive Dx – A: 5%; B: 18%; C: 28%

Dementia – A: 1%; B: 2%; C: 2%

Grant, et al. (San Diego HNRC), 2010
HNRC Changes in Impairment Rates

In 534 HIV-positive participants with rates of NP impairment of 27% CDC-A, 44% CDC-B and 53% CDC-C, over time:

- 47% remained cognitively normal
- 11% remained impaired
- 18% improved and remained stably improved
- 04% worsened and stayed so
- 20% fluctuated between impaired and normal
Part 2

What impacts do cognitive impairments in HIV/AIDS have on everyday functioning?
Can mild cognitive impairment affect everyday functioning? YES

- 2-3 fold increase in unemployment
- 5-times more likely to report difficulty managing with work demands if still working
- Can affect ability to manage medications (adherence of medications)
- Can affect various aspects of quality of life
- Minor Cognitive Motor disorder (MCMD) diagnosis is related to survival
- Increased cognitive difficulties significantly associated with reductions in quality of life
Can mild cognitive impairment affect everyday functioning beyond work? YES

- But what if person is not working – many people will report or notice problems with reading (having to read the same passage over 2-3 times)
- Or have trouble keeping track of conversations – particularly when there are other distractors
- May not be as quick to process new information or be able to keep track of a fast conversation with a lot of details
- May often forget names when person has just have met someone new and this can cause quite a bit of anxiety
MCMD Diagnosis Associated with Reduced Survival

Kaplan-Meier survival curves; NL = neurocognitively normal, NPI = neuropsychologically impaired, MCMD = minor cognitive/motor disorder. Crosshatches indicate censored observations; downward steps, deaths (Ellis et al., 1997)
Part 3

What are the kinds of cognitive symptoms in adults with HIV and what do they reflect?
Common cognitive symptoms
What do patients report?

What do they say about their memory, concentration, language skills, problem-solving ability, motor skill?

Are these indicative of neurocognitive impairments, depression, fatigue, substance use?
Common cognitive symptoms (in HIV and aging)

Memory:
I’m forgetful
My short-term memory is not as good
I keep misplacing things
I walk into a room and forget what I went to get

Word finding:
I have trouble remembering people’s names
I can’t seem to think of words as easily as before
It’s on the tip of my tongue
Common cognitive symptoms (in HIV and aging)

Concentration
- I am easily distracted
- I have trouble focusing
- I can’t do several things at once anymore
- I feel like I am in a fog

Slowing:
- I am a lot slower, both mentally and physically
- I can’t do things as fast as I once could
Do cognitive symptoms relate to the impairments detected on formal testing?

Yes:
- Stern et al., 1991
- Mapou et al., 1993
- Beason-Hazen et al., 1994
- Poutiainen et al., 1996
- Rourke et al., 1999a; 1999b

No Relationship:
- van Gorp et al., 1991
- Wilkins et al., 1991
- Burgess et al., 1993
- Hinkin et al., 1996
- Moore et al., 1997
- Rourke et al., 1999a; 1999b
So what is the relationship between cognitive symptoms, mood and cognitive performance

<table>
<thead>
<tr>
<th>Cognitive Symptoms</th>
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<tr>
<td>Depression (mood)</td>
<td>+ 0.67* (strong effect)</td>
</tr>
<tr>
<td>Attention</td>
<td>- 0.25* (small effect)</td>
</tr>
<tr>
<td>Quickness and speed</td>
<td>- 0.30* (small effect)</td>
</tr>
<tr>
<td>Short-term memory</td>
<td>- 0.19* (small effect)</td>
</tr>
<tr>
<td>Conceptual skills</td>
<td>+ 0.02 (no relationship)</td>
</tr>
</tbody>
</table>

* p < 0.05; Rourke et al., 1999a
Does depression affect different kinds of cognitive symptoms?

“Yes and about the same amount”
• Multiple factors contribute to cognitive symptoms in HIV:
  1) Psychological (e.g., negative thinking - depression)
  2) Somatic and functional symptoms (fatigue)
  3) Quickness in thinking (processing speed)
  4) Multi-tasking ability (working memory)

• Each of the contributors have potentially different therapeutic avenues for intervention – depression (medication / CBT), cognition (ARVs / cognitive rehabilitation / combination)

• Studies needed to identify if there is a sequence of interventions to achieve maximal benefit
Part 4

Cognitive Rehabilitation Approaches
What can people do to maintain their best cognitive health with HIV and aging?

• Generally speaking, what is good for your heart (vasculature) is good for your brain – (eat well, get lots of rest, get physical exercise, don’t drink too much or smoke, lower stress level)

• Exercise your brains – Case Study
A Case Study Demonstrating The Benefits of Brain Fitness Program

Cognitive Rehabilitation in HIV/AIDS: A Case Study Demonstrating the Benefits of the Brain Fitness Program

Our Approach
- We evaluated the potential benefits of the Brain Fitness Program (BFP) during a computer- and self-administered cognitive rehabilitation intervention.
- The intervention was a 12-week, well-structured program with supplementary brain fitness exercises designed to enhance cognitive performance and brain plasticity (Boston University, Complex Thinking Inventory).
- Participants completed a follow-up assessment to assess improvements in cognitive function and brain fitness outcomes.
- The BFP intervention consisted of at least one hour of brain fitness training for 60 minutes per session. Participants also received personalized feedback on their progress and were encouraged to practice brain fitness exercises outside of sessions.

The Challenge
30% to 50% of people with HIV/AIDS experience cognitive impairments related to attention, particularly trailing, memory, and organizational efficiency. This cognitive impairment can lead to difficulties in daily life, such as difficulty paying bills, remembering appointments, and maintaining interpersonal relationships.

Smart (HIV/AIDS Rehabilitation and Treatment) has been successful in improving outcomes and reducing HIV-related complications. SMART is designed to improve executive function, elevate mood, and decrease fatigue.

Our Findings
- Intervention improves Cognitive Ability
- We observed significant improvements in key cognitive function areas following the Brain Fitness Program intervention.
- Participants improved in the following cognitive ability areas:
  - Complex attention and working memory
  - Multiple tasking ability
- Improved efficiency and accuracy in completing tasks
- Better ability to process new information
- Improved ability to maintain focus and attention

Clinical Implications for Practice
- The Brain Fitness Program (BFP) may be a useful tool for individuals living with HIV/AIDS and those at risk for cognitive impairment.
- The program can be adapted to fit the needs of individuals with varying levels of cognitive impairment.
- The BFP can be delivered in group or individual sessions, making it accessible to a wide range of individuals.

Participants also reported substantial improvements in:
- Overall cognitive processing and efficiency
- Ability to perform daily activities and tasks
Our Approach: Brain Fitness Program

• We evaluated the potential benefits of the Brain Fitness Program (BFP) Classic, a computerized and self-administered cognitive rehabilitation intervention.

• The case studied was a 52 year-old well-educated gay man with a previously documented diagnosis of HIV-Associated Cognitive-Motor Complex.

• Comprehensive neuropsychological testing and symptom questionnaires were administered prior to and after 8 weeks of the BFP intervention.
Our Approach: Brain Fitness Program

- The BFP intervention consisted of 1 hour of exercises 5 days per week for a total of 40 sessions.
- The BFP uses six computer-based exercises for use on a PC or Mac that are designed to be very easy to use, even for computer novices; it is designed to speed up auditory processing, improve working memory, and encourage efficiency of neural networks involved in memory processing.
- The exercises adapt to individual level, and give constant feedback about progress.
The Brain Fitness Program (BFP): More Details

• BFP is made up of six auditory exercises.
• The exercises build on one another to work out your brain in more and more realistic listening and language usage contexts. They begin with frequency sweeps (the most basic building blocks of language) and move up through phonemes (individual sound parts of words, such as /d/, /o/, and /g/ in the word dog), syllables, sentences, and finally, narratives. Each one targets one aspect of auditory processing and memory, while also reinforcing the skills developed in the other exercises.
• BFP was originally designed for older adults to strengthen speech input and engage neuromodulatory systems involved in learning and memory.
Our Findings: BFP Intervention Improves Cognitive Ability

We observed clinically significant improvements -- beyond expected practice effects -- following 8-weeks of BFP in following NP ability areas:

- complex attention / working memory (multi-tasking ability)
- learning (ability and quickness in learning new information)
- verbal fluency (increased ease finding words to express)
- complex psychomotor efficiency (cognitive speed)

Participants also noted substantial improvements in:

- subjective ratings of cognitive processing / efficiency
- efficiency in day-to-day activities and tasks.
Clinical Implications for Practice

• The Brain Fitness Program may offer a potentially beneficial cognitive intervention tool for people with HIV experiencing cognitive impairments related to HIV.

• If the cognitive benefits also translate into significant and lasting impacts on the ability to perform complex everyday functioning tasks and activities, the intervention may offer real potential for those who want to continue working and those who want to return to work.

• Our research unit is currently involved in other case studies to explore potential support for an evaluation of a larger rigorous intervention trial to the formally test the effectiveness of the BFP in people with HIV.
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.

ILLUSTRATION BY PHIL
Thank you
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