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

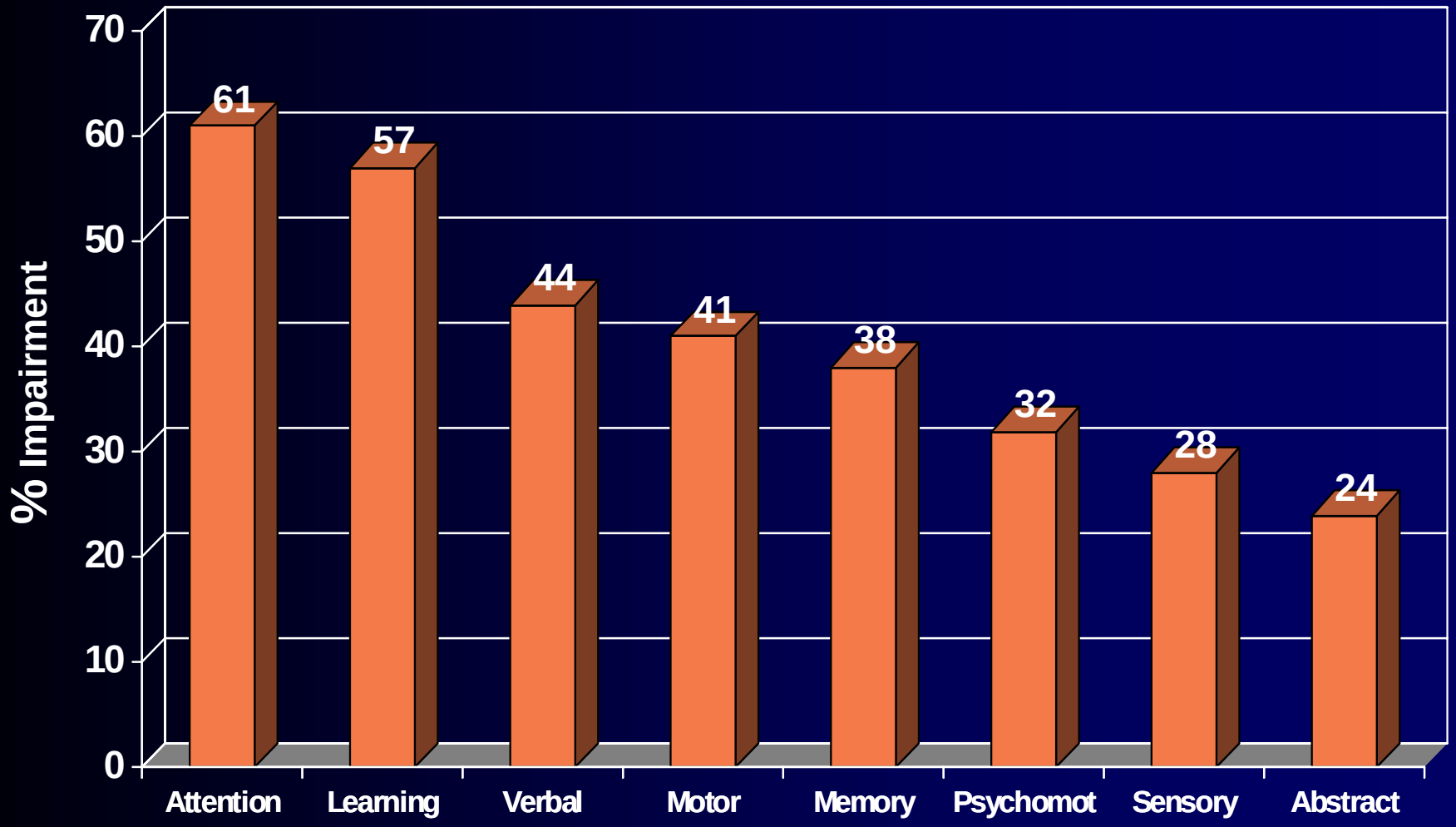
Cognitive impairments in HIV-infection: What changes can be experienced ?

- 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”



Heaton et al., 1995

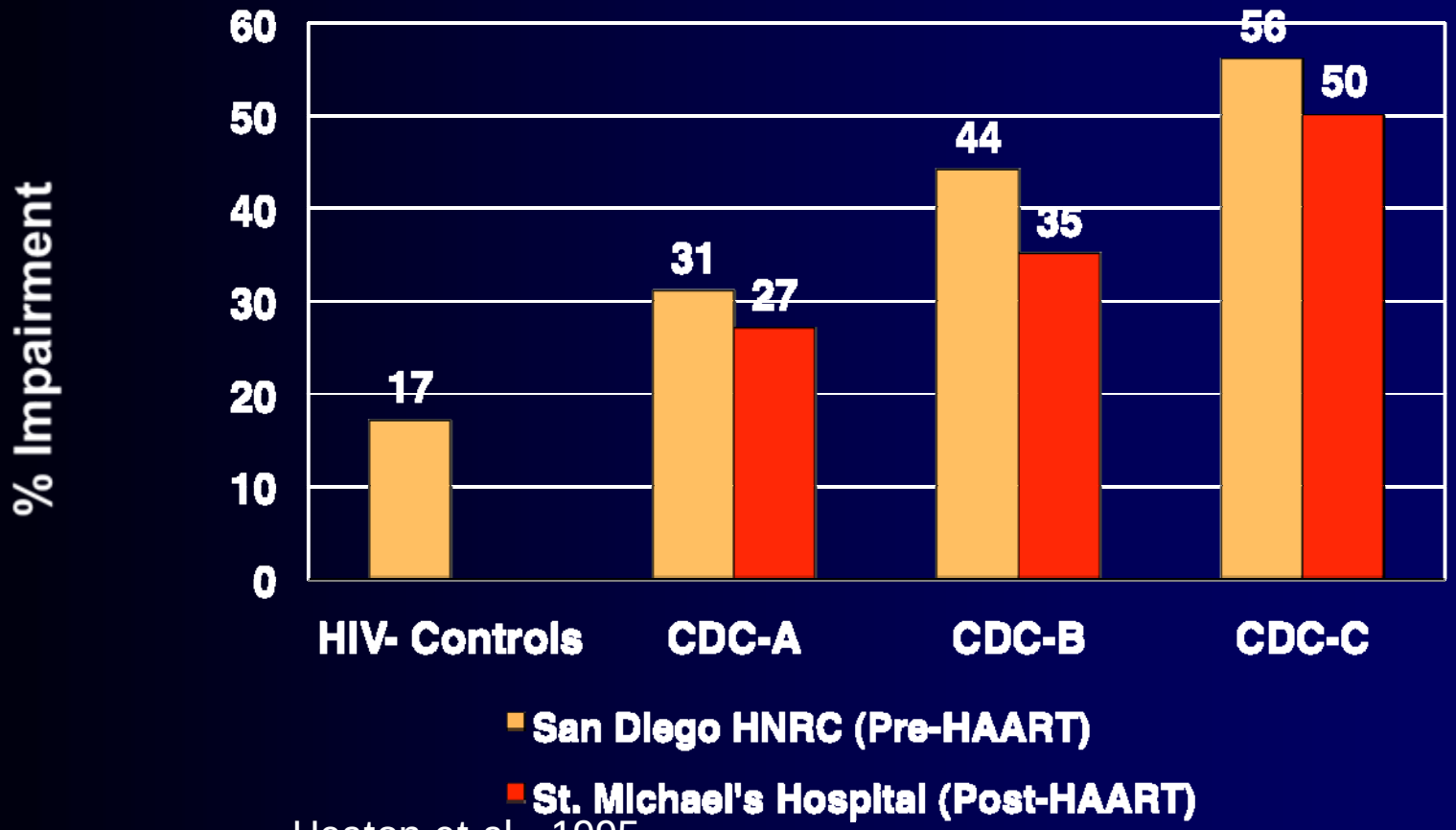
Are these cognitive changes and impairments similar to “normal” aging ?

Changes with HIV/AIDS	Changes with Aging
• Slowing	Yes
• Multi-tasking ability	Yes
• Word finding	Yes
• Short term memory	Yes
• Motor coordination	Yes

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

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
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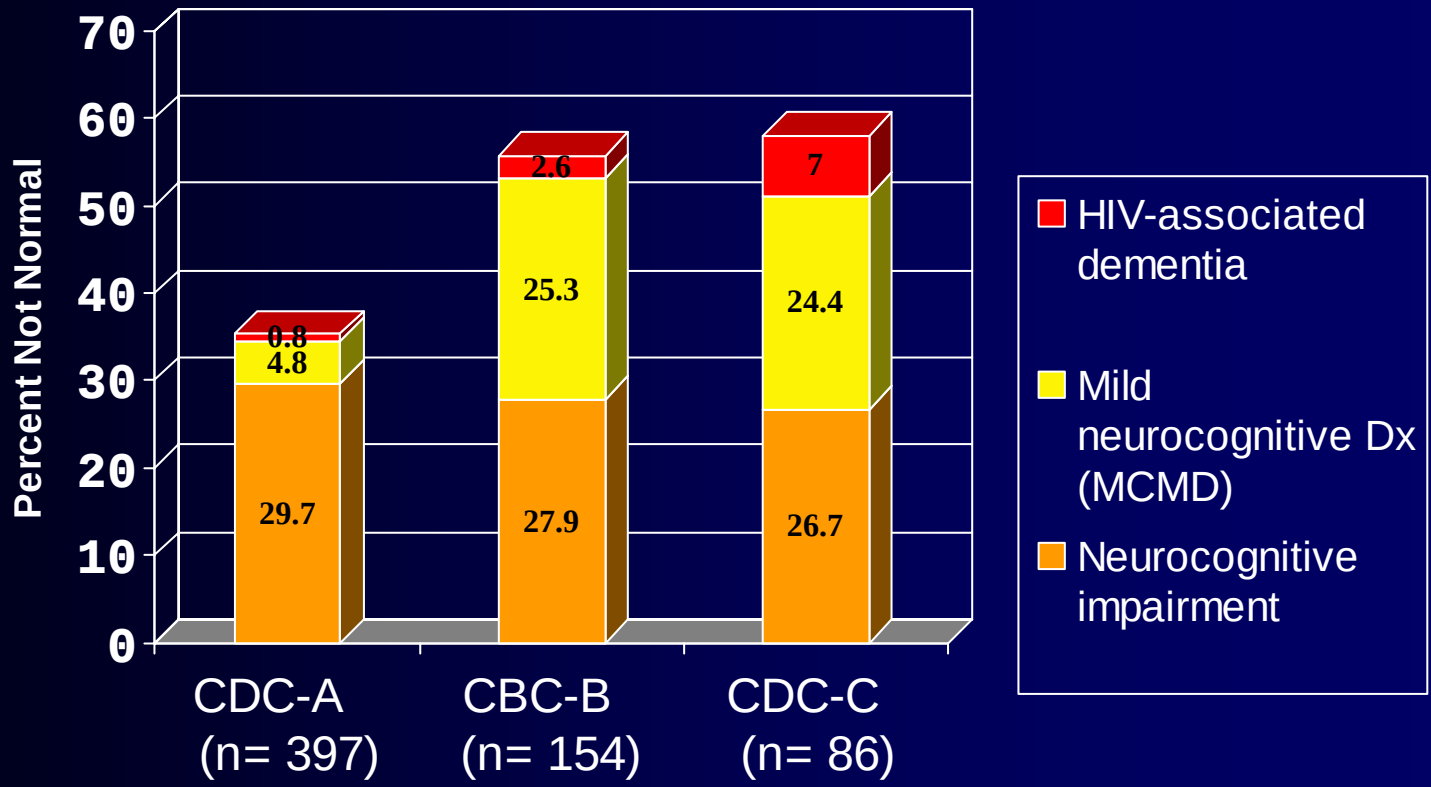
Pre-HAART

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 Neurognitive 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 ?

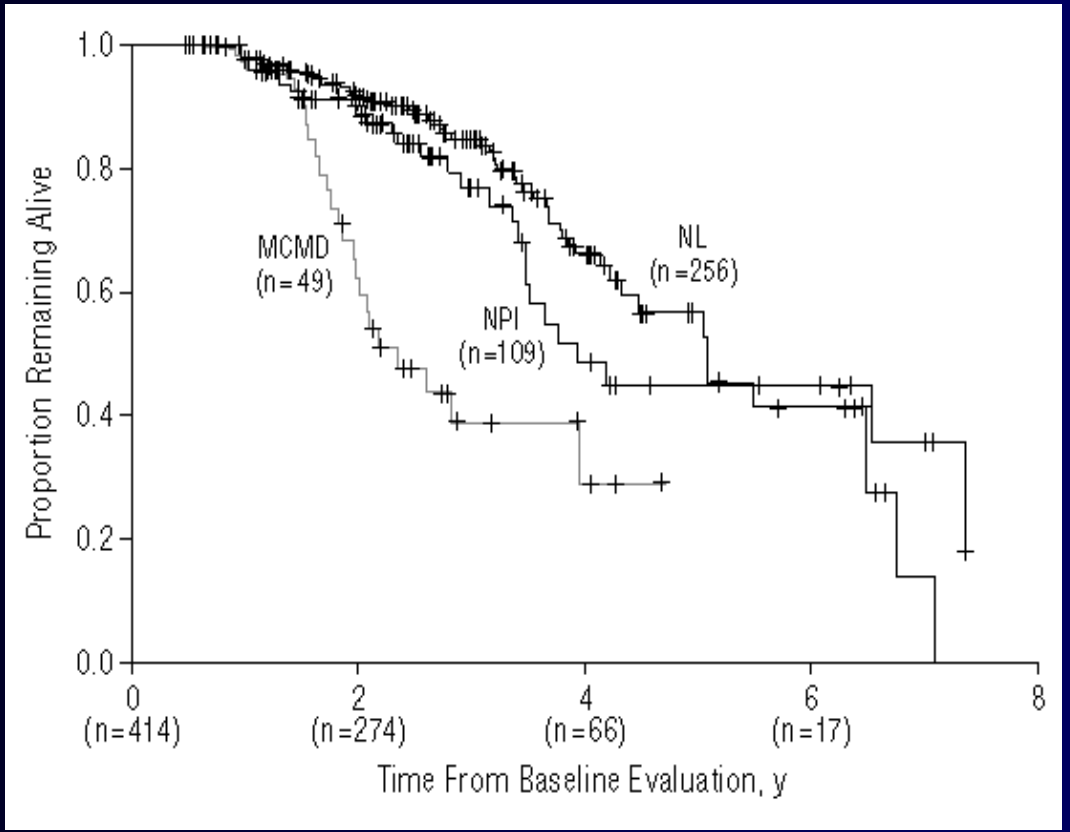
Can mild cognitive impairment affect everyday functioning? YES

- 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 of 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 you 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

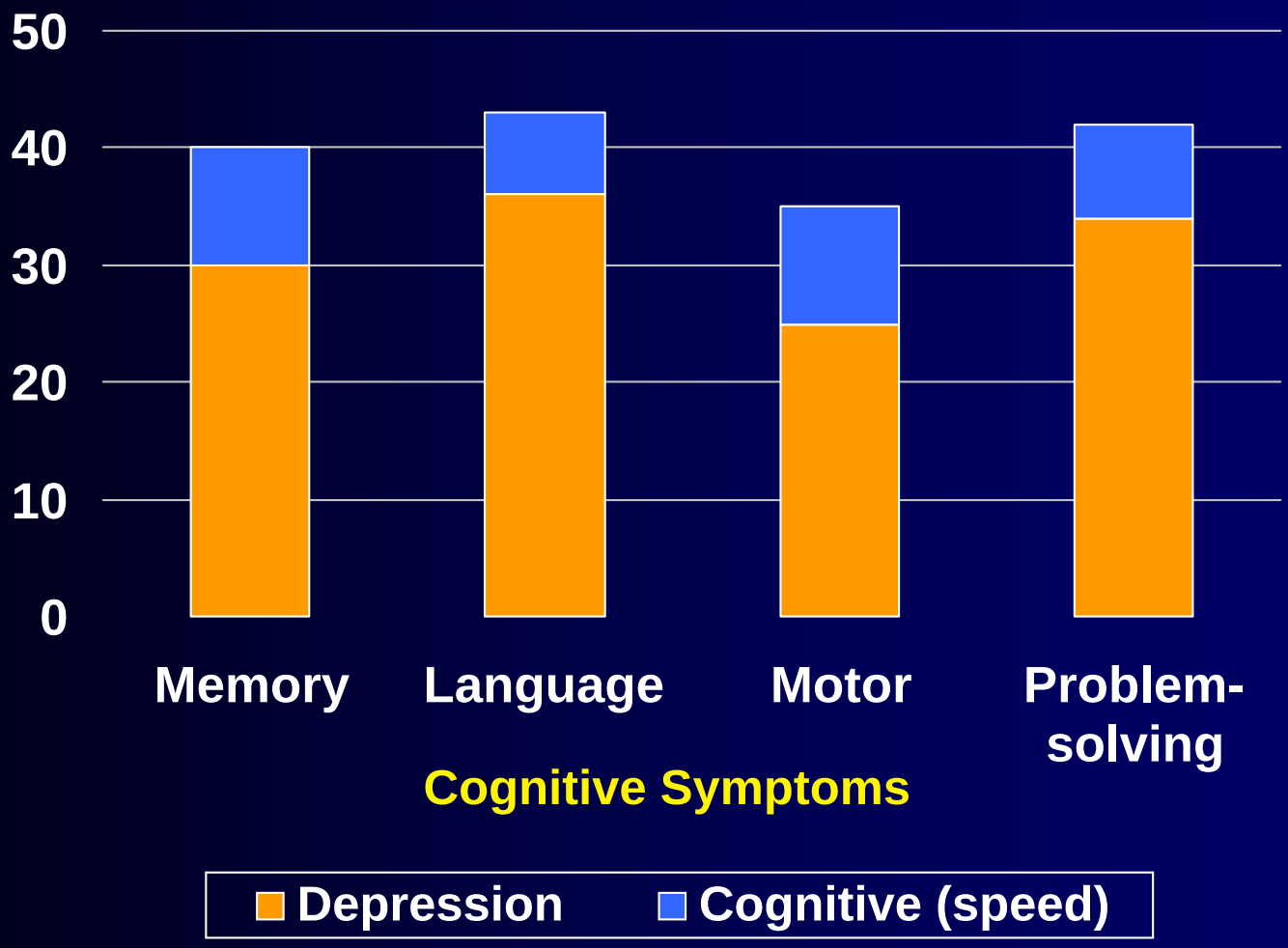
So what is the relationship between cognitive symptoms, mood and cognitive performance

	Cognitive Symptoms
Depression (mood)	+ 0.67* (strong effect)
Attention	- 0.25* (small effect)
Quickness and speed	- 0.30* (small effect)
Short-term memory	- 0.19* (small effect)
Conceptual skills	+ 0.02 (no relationship)

* $p < 0.05$; 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

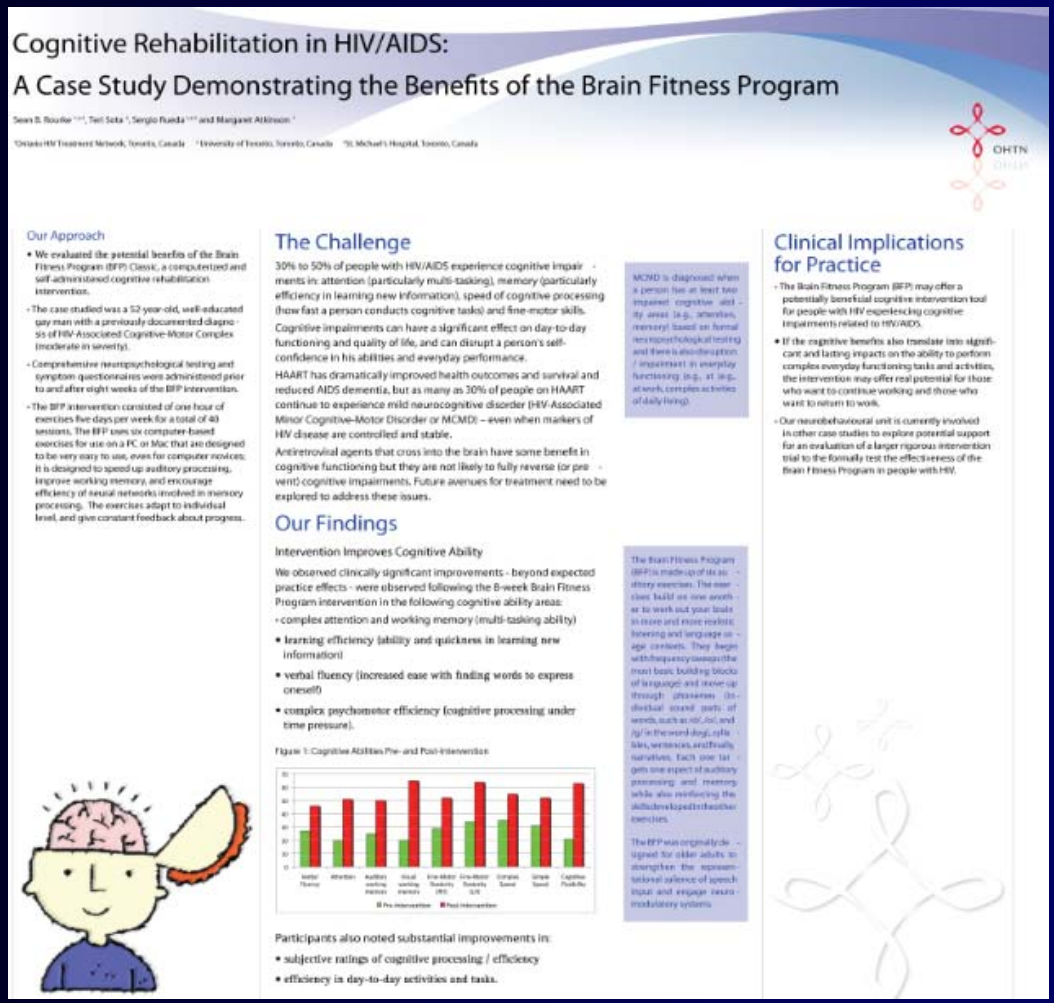
Part 4

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

Sean B. Rourke [1,2,3], Tori Sota [1], Sergio Rueda [1,2,3] and Margaret Atkinson [1]

[1]Ontario HIV Treatment Network, Toronto, Canada [2]University of Toronto, Toronto, Canada [3]St. Michael's Hospital, Toronto, Canada

OHTN

Our Approach

- 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 (moderate in severity).
- Comprehensive neuropsychological testing and symptom questionnaires were administered prior to and after eight weeks of the BFP intervention.
- The BFP intervention consisted of one hour of exercises five 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 Challenge

30% to 50% of people with HIV/AIDS experience cognitive impairments in: attention (particularly multi-tasking), memory (particularly efficiency in learning new information), speed of cognitive processing (how fast a person conducts cognitive tasks) and fine-motor skills.

Cognitive impairments can have a significant effect on day-to-day functioning and quality of life, and can disrupt a person's self-confidence in his abilities and everyday performance.

HAART has dramatically improved health outcomes and survival and reduced AIDS dementia, but as many as 30% of people on HAART continue to experience mild neurocognitive disorder (HIV-Associated Minor Cognitive-Motor Disorder or MCMD) – even when markers of HIV disease are controlled and stable.

Antiretroviral agents that cross into the brain have some benefit in cognitive functioning but they are not likely to fully reverse (or prevent) cognitive impairments. Future avenues for treatment need to be explored to address these issues.

MCMD is diagnosed when a person has at least two impaired cognitive abilities (e.g., attention, memory) based on formal neuropsychological testing and there is also disruption / impairment in everyday functioning (e.g., at work, complex activities of daily living).

Clinical Implications for Practice

- The Brain Fitness Program (BFP) may offer a potentially beneficial cognitive intervention tool for people with HIV experiencing cognitive impairments related to HIV/AIDS.
- 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 neurobehavioural 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 Brain Fitness Program in people with HIV.

Our Findings

Intervention Improves Cognitive Ability

We observed clinically significant improvements - beyond expected practice effects - were observed following the 8-week Brain Fitness Program intervention in the following cognitive ability areas:

- complex attention and working memory (multi-tasking ability)
- learning efficiency (ability and quickness in learning new information)
- verbal fluency (increased ease with finding words to express oneself)
- complex psychomotor efficiency (cognitive processing under time pressure).

Figure 1: Cognitive Abilities Pre- and Post-Intervention

The Brain Fitness Program (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.

The BFP was originally designed for older adults to strengthen the representational salience of speech input and engage neuromodulatory systems

Participants also noted substantial improvements in:

- subjective ratings of cognitive processing / efficiency
- efficiency in day-to-day activities and tasks.

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The Brain Fitness Program (BFP): More Details

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Our Findings: BFP Intervention Improves Cognitive Ability

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- complex psychomotor efficiency (cognitive speed)

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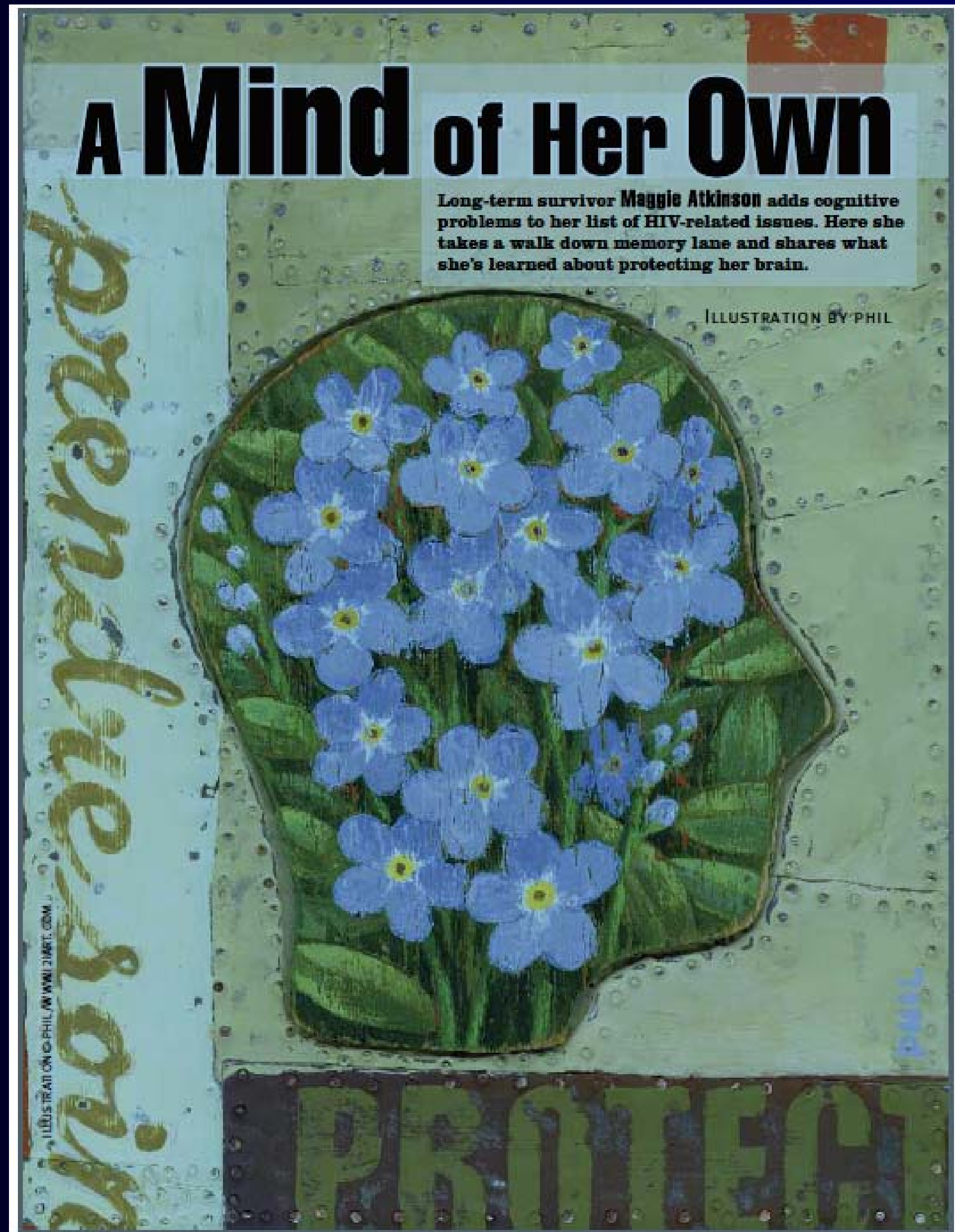

The Positive Side, Winter 2010 – A Lived Experience

Thank you

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