NeuroAIDS and Cognitive Aging: Updates on Current Trends and Interventions

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**PRESENTER DISCLOSURES**

- **GRANTS/RESEARCH SUPPORT:** NIH and University of Alabama at Birmingham – Grant support (e.g., 1R01MH106366-01A1; 1R21 NR16632-01; Women’s Interagency HIV Study; etc…)

- **SPEAKER’S HONORARIA:** Multidisciplinary Approaches across the Palliative Care Continuum Conference – Lecture Honorarium; Association of Nurses in AIDS Conference – Lecture Honorarium; International Antiretroviral Society – Lecture Honorarium; ect...

- **CONSULTING FEES:** POSIT Science Inc. – Presenting their software as part of presentation; Department of Defense – Grant Reviewer; HIVERA Grant Reviewer, Berlin & Frankfort, Germany.

- **OTHER:** Employee of the University of Alabama at Birmingham
Keep in Mind

- Do you purposely do things to keep your brain sharp?
  - We think about sodium intake, exercise, stress reduction, but do we think about brain health?

- Do you expect to have your same level of mental functioning 20 years from now?

- Do you ask your patients about what they do to help their brain to age? (and if you do, do you know what to tell them?)

  4 Focus Groups → 30 Older Adults with HIV
  - Gross understanding that keeping active is important for brain health.
  - Passive acceptance of decreased brain function (*Nothing we can do!*).
Learning Objectives

1. COGNITIVE RESERVE
2. NEUROAIDS & INTERVENTIONS
3. CONCLUSIONS
1. COGNITIVE RESERVE

Cognitive Reserve Hypothesis

- The ability of the brain to compensate for damage and yet continue to function. Ideally, the greater, stronger, and more sophisticated the synaptic connections are, the greater the cognitive reserve.

- An enormous number of studies suggest that more/better education, exposure to novel stimuli over the lifespan, and optimal health facilitates better cognitive reserve.

- By what process does cognitive reserve increase?
  - NEUROPLASTICITY
Positive and Negative Neuroplasticity

- **Enriched Environmental Paradigm**
  - **Enriched Environment**
  - **Standard Environment**
  - **Impoverished Environment**

**Positive Neuroplasticity**
- The brain builds more sophisticated and more connections between neurons.
- Better Cognitive Reserve

**Negative Neuroplasticity**
- Studies in the aging and HIV literature show that increased cognitive activity, which reflects an enriched environment, promotes optimal cognitive functioning.
- The brain atrophies quicker with less sophisticated and less connections between neurons.
- Poorer Cognitive Reserve

Placed in isolation, with no toys
Placed 3 to a cage, with no toys
2. NEUROAIDS AND INTERVENTIONS

There is a ~20% Bi-directional Fluctuation over Time of HIV-Associated Neurocognitive Disorder
(Antinori et al., 2007. Neurology, 59, 1789-1799.)

So someone can be diagnosed with HAD one year and the following year could be classified as having MND. Why?

Some gender difference are sometimes observed. Women tend to display more impairments in verbal memory and learning.

Does HIV infect neurons in the brain? NO

*It is both monocytes and particularly macrophages.
Age: 56

AIDS Diagnosis: 2007
- CD4 Count – 6 cells/mm³
- Viral Load – 800,000 copies/mL

HAD Diagnosis: 2009

2010 Neuropsychological Assessment – Mixed Results

BSW 2011 – Jackson State University (summa cum laude)

MSW 2012 – December 2012

2010 Neuropsychological Assessment

“Mr. Nicholas’ overall intelligence functioning fell in the average range. His composite scores were in the average to high average range, with the exception of Processing Speed performance across the various subscales.

“Mr. Nicholas’ self-report during the clinical interview as well as his performance on the neuropsychological and achievement tests revealed cognitive dysfunction consistent with dementia of the subcortical type associated with HIV infection, including impairments in memory, motor speed and control, word finding, and generalized slowing of information processing speed. His language functions were relatively preserved, also consistent with dementia due to HIV infection.
2010 Neuropsychological Assessment: Mixed Results

“I would often have trouble finding the word (dysnomia) I wanted to use. This was very unusual for me because I am extremely, almost frighteningly, articulate. Words would just flow out of my mouth. Not any more.”

“The results of the neuropsychological evaluation were so unexpected, so devastating ....”
I had also noticed a demonstrable slowing in how I did *everything*.”

“I used to spend hours devouring books. Now I had a hard time finishing a page. I’ve always been a little absent-minded… But it had become ridiculous. I don’t know where it came from, except that it popped into my head one day: ‘If it is not in my hands, it’s lost!’ That phrase is now almost a mantra! It is not an exaggeration to say I spend *hours* daily looking for items I’ve misplaced.”
Nick.ms

Cognition/Cognitive Reserve

High School

High

Hi

IQ
128
(90%)

GRE
Verbal: 790
Math: 740

IQ
98

HAD?

BSW
MSW

Actively Pursing Interests

AIDS Dx

HAD

1992
2007
2008
2009
2010
2011
2012
TODAY

Time
In our previous study, as a group, older adults with HIV performed worse on all cognitive performance measures compared to younger adults with HIV and younger and older adults without HIV.

Older adults also performed worse on a laboratory measure of everyday functioning. This measure was timed; other activities that are speed or time dependent may also be compromised.

Figure 1. Z-scores for Cognitive Test Performance for Clusters 1 and 2, and the HIV-Negative Group. 
Note. FTT = Finger Tapping Test; WCST = Wisconsin Card Sorting Test; UFOV® = Useful Field of View; CRT = Complex Reaction Time; HVLT = Hopkins Verbal Learning Test; LP = Letter and Patter Comparison. For the purpose of clarity, higher z-scores reflect higher performance for all variables.
Predictors of Neurocognition in Adults with HIV

Other predictors of neurocognitive functioning are reported in adults with HIV.

- Stress, Depression, Anxiety, Post-traumatic Stress
- Age
- Income
- Educational Level/Attainment
- Reading/Reading Quality
- Insulin Resistance
- Hepatitis C/Liver Fibrosis
- Cognitive Activity & Employment
- Treatment Status (viral load, CD4 count)
- Substance Use
- Head Injury
- APOE-4
Everyday Functions Compromised by Poor Cognition in HIV

- Instrumental Activities of Daily Living (Heaton et al., 2004).
- Financial and medical management (Heaton et al., 2004).
- Medication adherence (Woods et al., 2009).
- Prone to risky decision-making (Hardy, Hinkin et al., 2006) & cognitive impulsivity (Martin et al., 2004).
- Lower health-related quality of life (Doyle et al., 2012).
- Higher risk of mortality (Ellis et al., 1997; Wilkie et al., 1998).
Useful Field of View®

- The Useful Field of View® is defined as the area from which one can extract visual information in a single glance without eye or head movement. While it is a test of visual attention, it is also sensitive to visual impairment.

- A measure of visual speed of processing.

Welcome to UFOV Test 1

This exercise will measure how fast you can identify a single object.

Touch continue for a demonstration

Which object was inside the white box?
Welcome to UFOV Test 2

This exercise will measure how fast you can divide your attention between two objects.

Touch continue for a demonstration.

After each presentation you will be asked two questions. Which object was inside the white box?

On which spoke was the outside object located?

Indicate your answer by clicking the button which corresponds to the location of the target.
Welcome to UFOV Test 3

This exercise will measure how fast you can divide your attention between two objects when the outside object is surrounded by clutter.

Touch continue for a demonstration.
Welcome to UFOV Test 4

This exercise will be like the previous exercise except the center task will be more difficult.

Touch continue for a demonstration
GOOD UFOV – Can see more information at a moment’s glance.

Wider view is better! This means more of the visual field is being cognitively processed.

POOR UFOV – Can see little information at a moment’s glance. Could compromise driving?

Only a tiny fraction of the visual field is being cognitively processed.
DRIVING SIMULATOR used in this study.
EXAMPLE OF INTERSTATE DRIVING
EXAMPLE OF SUBURBAN DRIVING
In Our Previous Driving Simulator Study

- Older age was associated with lower divided attention reaction time in the simulator.
- Poor UFOV performance was predictive of slower reaction time, number of pedestrians hit, and driving outside of the lane.
- Poor UFOV test performance was related to higher self-reported accidents in the past year.

Speed of Processing Training

- This **speed of processing training** protocol has been used to improve the rate at which normal, community-dwelling older adults process information (Vance, Dawson, Wadley, Edwards, Roenker, Rizzo, & Ball, 2007).

- It has been shown to improve driving performance and measures of everyday functioning (i.e., The ACTIVE Study; The Accelerate Study).

- Because of its efficacy in older adults, speed of processing training may improve such performance in adults with HIV.

Methods

Baseline

Speed of Processing Training

No-Contact Control

Posttest

R03

Neuropsychological & Everyday Functioning Measures (5-6 weeks apart)

CCTS Study
Methods

- Speed of Processing Training

Methods

• Speed of Processing Training (continued)

UFOV performance improved in those who received the speed of processing training.

Those in the speed of processing training group became faster in taking in more information and processing it at a moment's glance.

**ACTIVE Studies**

<table>
<thead>
<tr>
<th>HIV ISSUES</th>
<th>SOP TRAINING BENEFITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased Speed of Processing</td>
<td>Improved Speed of Processing</td>
</tr>
<tr>
<td>Poorer Driving</td>
<td>Improved Driving</td>
</tr>
<tr>
<td>Poorer IADL Performance</td>
<td>Improved IADL Performance</td>
</tr>
<tr>
<td>Decreased Locus of Control</td>
<td>Improved Locus of Control</td>
</tr>
<tr>
<td>Risk for Depression</td>
<td>Protection against Depression</td>
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<tr>
<td>Poorer Self-rated Health</td>
<td>Improved Self-rated Health</td>
</tr>
<tr>
<td>Poorer Health-related Quality of Life</td>
<td>Improved Health-related Quality of Life</td>
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This recently funded study may improve speed of processing in middle-aged and older adults with HIV which may improve driving safety as well as reduce the incidence of HIV-Associated Neurocognitive Disorder (HAND).

NIH/NIMH – “An RCT of Speed of Processing Training in Middle-Aged and Older Adults with HIV” (1R01MH106366-01A1 – VANCE, PI)
A simple qualitative comparison was completed between baseline and post-test.

<table>
<thead>
<tr>
<th>Frascati Criteria CR</th>
<th>Case A 10 hrs of Internet Training</th>
<th>Case B 10 hours of SOP Training</th>
<th>Case C 20 hours of SOP Training</th>
<th>Comparisons/Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR Baseline</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>Case C no longer has HAND.</td>
</tr>
<tr>
<td>CR Posttest</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>CR Improvement</td>
<td>0</td>
<td>0</td>
<td>-1</td>
<td></td>
</tr>
<tr>
<td>UFOV® Baseline</td>
<td>667</td>
<td>1,084</td>
<td>1,031</td>
<td>Cases B &amp; C improved the most.</td>
</tr>
<tr>
<td>UFOV® Posttest</td>
<td>480</td>
<td>634</td>
<td>248</td>
<td></td>
</tr>
<tr>
<td>UFOV® Improvement</td>
<td>-177</td>
<td>-450</td>
<td>-783</td>
<td></td>
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</table>

Note. CR = Clinical Rating; HAND = HIV-Associated Neurocognitive Disorder; hrs = hours; SOP = Speed of Processing; UFOV® = Useful Field of View.
ENGAGEMENT

Engagement -- Physical Exercise, Social, Mental Activity
- 139 Adults with HIV ($M_{age} = 48.7$ years; 48% 50+)
- Cross-sectional $\rightarrow$ Active Lifestyle & Neuropsychological Testing
- Physical Exercise – Any strenuous exercise in the past 72 hours?
  - No (0)/Yes (1)
- Social Engagement – Lawton and Brody ADL Questionnaire
  - “Frequently engage in or initiate social activity”
  - No (0)/Yes (1)
- Mental Activity – Working full- or part-time?
  - No (0)/Yes (1)
- Active Lifestyle Factors ranged from 0 to 3
- “Increasing number of ALFs was associated with a lower prevalence of HAND [$df = 1$, $X^2 = 5.1$, $p = .02$].”
  - ALF 0 – $63\%$ HAND (34% ANI, 18% MND, 11% HAD)
  - ALF 1 – 51% HAND (35% ANI, 14% MND, 2% HAD)
  - ALF 2 – 33% HAND (27% ANI, 3% MND, 3% HAD)
  - ALF 3 – $20\%$ HAND (15% ANI, 5% MND, 0% HAD)

Nick.ms

Suggests and Compensation Strategies by Nick

- **Low-Tech Suggestions**
  - **Medication Adherence** – Weekly pill box
  - **Redundancies** – Keys, medications, etc.
  - **Journaling** – Keeping track of events.

- **Driving Down the Road** – “I would be driving down the highway and suddenly be unable to remember where I was going or why. I still knew who I was and where I was and what I was doing, but clueless as to why….it is a frightening experience.”
  - Involved in 4 accidents in the two year prior to diagnosis which he was at-fault
  - SOLUTION 1 → Post-It goes on the Dashboard Stating. ..Destination
  - SOLUTION 2 → Slow down, plan A to B, be more careful.

- **High-Tech Suggestions**
  - **Evernote** (evernote.com) & **Wunderlist** (wunderlist.com) – For keeping track of lists and reminders.
  - **iCal** – The calendar that comes with the iPad.
  - **30/30 App** – “Sense of timing is off.” It allows one to set a certain amount of time on a task, and then gives you an alert when time is up.
  - **Check App** – Helps him keep up with bills, credit cards, and bank accounts.
3. CONCLUSION

TAKE HOME POINTS

✓ Use it or loose it!

✓ That which is good for the body is good for the brain.

✓ Comorbidities, both physical and psychiatric, can impair cognition and cognitive reserve.

✓ Thus, it is important to adhere to treatments to protect cognitive reserve.
TAKE HOME POINTS

- Encourage patients to continue to pursue interests, especially if they are cognitively challenging.
  - Ask patients what they are doing to protect brain health.
  - Empower patients to be proactive about brain health.
  - The activity needs to make the brain sweat!!!
  - Start early to protect and preserve brain function.

- Compensation strategies are available.
Neuroplasticity