Impact of HIV on the Brain and Cognition

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Learning Objectives

At the conclusion of this presentation, participants should be able to:

• Identify risk factors for neurocognitive complications among HIV+ patients.

• Detect common neurocognitive deficits among HIV+ patients.

I will not discuss non-FDA approved uses of any products/devices or investigational devices.
HIV and the Brain

- Early penetration of the CNS
- Increased HIV RNA in dorsal striatum, hippocampus
- Cerebral white matter atrophy, prefrontal cortical neuron loss
- Both cortical and subcortical degeneration predict neurocognitive deficit
Pathogenesis of HIV Infection in the CNS

Bell, Histopathology, 2004
Importance of Neurocognitive Function in the Era of HAART

- Longer survival times but neurocognitive deficits persist

- Prevalence of dementia is lower, milder cognitive deficits unchanged

- Critically important for employment, driving, adherence, daily function

Heaton et al., 2004; Marcotte et al., 2006; Hinkin et al., 2002
Common Neuropsychological Test Findings

Motor and cognitive slowing

Poor memory and learning

Impaired executive functions
  Planning, judgment
  Actions based on future goals
  Impulse control

No longer a “subcortical dementia”
Model

Patient’s Copy

Time: 14 minutes
Trails B

Time to completion
Grooved Pegboard
Executive Functions: Working Memory

- Online and temporary information storage and processing

- Telephone # example

- Dorsolateral PFC, Striatum, PPC
Letter-Number Span Task

Patient Hears:

7X3M6C

Patient Says:

367CMX
Working Memory Performance

HIV-  HIV+  HIV-  HIV+

* p < .01

Martin et al, JINS, 1995, 2001
Executive Function: Stroop Task

BLUE
Executive Function: Stroop Task

TIGER
Executive Function: Stroop Task

BLUE
Risk factors for HIV-Associated Neurocognitive Disorder

- Not on ARV
- CD4 < 200
- Hepatitis C Coinfection
- Methamphetamine Dependence
- Aging

Martin & Paul, 2009; Gonzalez et al., 2009; Maki & Martin, 2009
Advances in ARV Therapy and Percentage of AIDS-Defining CNS Disorders at Autopsy

From Vago et al., AIDS, 2002
## Estimation of CNS Penetration-Effectiveness

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>0.5</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NRTIs</strong></td>
<td>Abacavir</td>
<td>Emtricitabine</td>
<td>Didanosine</td>
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<tr>
<td></td>
<td>Zidovudine</td>
<td>Lamivudine</td>
<td>Tenofovir</td>
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<td></td>
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<td>Stavudine</td>
<td>Zalcitabine</td>
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<tr>
<td><strong>NNRTIs</strong></td>
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<td>Efavirenz</td>
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<tr>
<td></td>
<td>Nevirapine</td>
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<td>Amprenavir-r</td>
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<td></td>
<td>Indinavir-r</td>
<td>Atazanavir</td>
<td>Ritonavir</td>
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<tr>
<td></td>
<td>Lopinavir-r</td>
<td>Atazanavir-r</td>
<td>Saquinavir</td>
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<td></td>
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<td></td>
<td>Tipranavir-r</td>
</tr>
<tr>
<td><strong>Fusion</strong></td>
<td></td>
<td></td>
<td>Enfuvirtide</td>
</tr>
<tr>
<td><strong>Inhibitor</strong></td>
<td></td>
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*Letendre S, et al. 13th CROI, 2006, Abstract 74*
Detectable CSF HIV RNA was significantly more common with low CPE rankings.

Antiretroviral Status and NP Performance
Women’s Interagency HIV Study

Richardson et al., JINS 2002
Risk factors for HIV-Associated Neurocognitive Disorder

- Not on ARV
- **CD4 < 200**
- Hepatitis C Coinfection
- Methamphetamine Dependence
- Aging
## CD4 Count and Neurocognitive Risk

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>CD4 cell count* &lt;200 vs &gt;350</td>
<td>1.74</td>
<td>1.12 , 2.70</td>
<td>0.01</td>
</tr>
<tr>
<td>Nadir CD4 cell count &lt;200 vs &gt;350</td>
<td>1.73</td>
<td>1.18, 2.55</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*cells/mm³

Adjusted for race, education, age, sex, and antiretroviral history

Risk factors for HIV-Associated Neurocognitive Disorder

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- CD4 < 200
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- Methamphetamine Dependence
- Aging
NP Abnormality and HCV Coinfection
Women’s Interagency HIV Study

Richardson et al., AIDS, 2006
Risk factors for HIV-Associated Neurocognitive Disorder

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- Nadir CD4 < 200
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- Aging
Neurocognitive Effects of HIV and Methamphetamine

Rippeth et al., 2004
Effects of HIV and Methamphetamine on Brain Structure

Jernigan et al., 2005
Risk factors for HIV-Associated Neurocognitive Disorder

Not on ARV
CD4 < 200
Hepatitis C Coinfection
Methamphetamine Dependence
Aging
HIV and Aging

- Increase from 1000 to 10000 in past decade of HIV/AIDS cases among persons > 50
- Estimated 50% of all cases by 2015
- HIV+ persons living longer, older persons seroconverting
- Greater non-HIV dementia risk (AD, VaD)

Hardy & Vance, Neuropsychology Review, 2009
Proportion of AIDS Cases Among Adults > 50

Summary

• Despite advances in antiretroviral therapy, HIV associated neurocognitive disorders (HAND) are a persisting problem.

• There are known risk factors for vulnerability to HAND.

• Milder but clinically significant cognitive problems with implications for driving, employment, daily functions.
• ARS Questions