HIV-Associated Neurocognitive Disorders in Older Adults: 
Prevalence, Profile, and Functional Implications

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Friday, November 17th, 2017
• No conflicts of interest
• NIH support
  – R01-MH073419
  – R21-MH098607
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    – P30-MH062512
cART Reduced Mortality and Dementia, Yet Milder Forms of HAND Persist

CDC; Heaton et al., 2010; 2011; Tierney et al., 2017
Myriad Clinico-demographic Factors Can Influence the Expression of HAND
Aging May Modify the Development and Expression of HAND

Cognition

Functional threshold

Chronological age

Low

High

20 30 40 50 60 70 80 90 100
Are the CNS Effects of HIV and Aging Additive or Synergistic?

**Additive Model**

- None
- Mild
- Moderate
- Severe

**Synergistic Model**

- None
- Mild
- Moderate
- Severe
The Prevalence of “Older” Adults Living with HIV Continues to Rise
Older HIV+ Adults Carry Numerous Risk Factors for Neurocognitive Impairment

- HIV disease severity
  - Lower nadir CD4
- Cardiovascular disease
- Metabolic syndrome
- Polypharmacy
- Older age

![Diagram showing various health conditions and their prevalence in different groups: Younger HIV- (n=56), Younger HIV+ (n=50), Older HIV- (n=65), Older HIV+ (n=91).]
HIV and Aging Both Adversely Affect the Central Nervous System

- HIV and aging are independently associated with:
  - **Neuropathological changes**
    - Reduced synaptodentritic complexity
    - Altered structure and function of frontal systems
      - Medial temporal cortex also affected
  - **Neurocognitive impairment**
    - Executive dysfunction
    - Episodic memory deficits
    - Psychomotor slowing
  - **Functional Problems**
    - Activities of daily living
Additive Effects of HIV and Aging on Brain Structure and Function

• Structural MRI
• Functional MRI
• Resting State
• Diffusion tensor imaging*
• MR spectroscopy*
Higher Apathy Among Older HIV+ Adults
HIV and Age Confer Additive Risk of Neurocognitive Impairment
Accelerated and Accentuated Neurocognitive Aging in HIV Disease

Sheppard et al., 2017
Synergistic Adverse Effects of HIV and Age on Activities of Daily Living (ADL)

Morgan et al., 2012
Lower Rates of Gainful Employment in Older HIV+ Adults
Lower Quality of Life Among Older HIV+ Adults

Morgan et al., 2012
HAND Exacerbates Age-Associated Deficits in Medication Management Capacity
HAND Influences Retention Care in Older HIV+ Adults

Jacks et al., 2015
HIV and Aging: Possible Mechanisms of CNS Injury

- **HIV factors**
  - Cumulative HIV-induced neural injury
    - Increasing immunosuppression
  - Direct and indirect
  - Inflammation
  - Increased exposure to ARVs
    - Toxicity from ART
    - Metabolic syndrome

- **Age factors**
  - Hormonal changes
  - Diabetes
  - Cerebrovascular disease
  - Other organ systems
    - Kidney, liver
  - Progressive dementias
The Alzheimer’s Disease Hypothesis of Aging and HAND

- **Alzheimer’s disease**
  - Most common cause of dementia among older adults
  - Progressive dementia
    - Amyloid plaques and neurofibrillary tangles
      - Especially in the medial temporal lobes
  - Neurocognitive profile
    - Rapid forgetting, semantic memory failures, aphasia, dyspraxia

- **Shared HAND-AD risk factors**
  - Age*
  - APOE-e4*
  - Lipid

- **Neuroanatomy**
  - Hippocampus and MTL*

- **Biomarkers**
  - Amyloid beta*
  - Tau*

- **Neuropathology**
  - Amyloid plaques *
No Evidence for an AD Memory Profile in Older HIV+ Adults

Scott et al., 2011
Reason for Cautious Interpretation: Base Rates of AD Across the Lifespan

- **<65**
- **65-74**
- **75-84**
- **85+**

**Graph Details:**
- Vertical axis: Rates per 100,000
- Horizontal axis: Age groups (<65, 65-74, 75-84, 85+)
- The graph shows a significant increase in rates for the 85+ age group compared to the other age groups.
Risk of Mild Cognitive Impairment (MCI) in HIV Disease Increases with Age

* $p < 0.01$, OR = 6.7
Verbal Memory Declines More Rapidly with Age in HIV Disease

Seider et al., 2014
Where Do We Go From Here?
Interventions for HAND in Older HIV+ Adults

- Currently no effective pharmacological options
  - Smaller improvements with cART in O+ (Al Khindi et al., 2011)
- Emerging evidence for standard neurorehab approaches
  - Speed of processing training improves timed IADLs in O+ (Vance et al., 2012)
- Cognitive neuropsychology
  - Self-generation, cueing, errorless learning, spaced retrieval, etc.
    - “Snow_Window”
    - Intervening items
    - “Snow_W_____”

![Graph showing comparison between Control, Spacing, and Testing groups for Words Recalled in HIV-50+ and HAND 50+ populations.](image-url)
Where Do We Go From Here?
Modernizing Our Assessment Armamentarium
HIV infection is associated with a 3-fold decrease in successful aging among older adults (Moore et al., 2013)

Age and HIV have additive effects specifically on successful cognitive aging (Moore et al., 2014)

Successful cognitive aging is associated with better mental QoL, adherence, healthcare provider relationships (Malaspina et al., 2011)
Summary of Age Effects on HIV-associated Neurocognitive Disorders (HAND)

- Age and HIV show generally additive effects on brain structure and function
- Age and HIV show synergistic effects on functional outcomes (e.g., ADLs)
- Older adults with HAND are at risk for poor functional and health outcomes
- Rising prevalence of HIV+ adults 65+ may change the landscape of neuroAIDS
- Effective pharmacological, cognitive, and behavioral interventions are needed
Questions?
One-Year Incidence Neurocognitive Disorders in HIV Across the Lifespan

Sheppard et al., 2015

* $p < .05$
In Vivo Amyloid Imaging in HAND Is Not Consistent with the AD Hypothesis

Ances et al., 2012