

# 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:

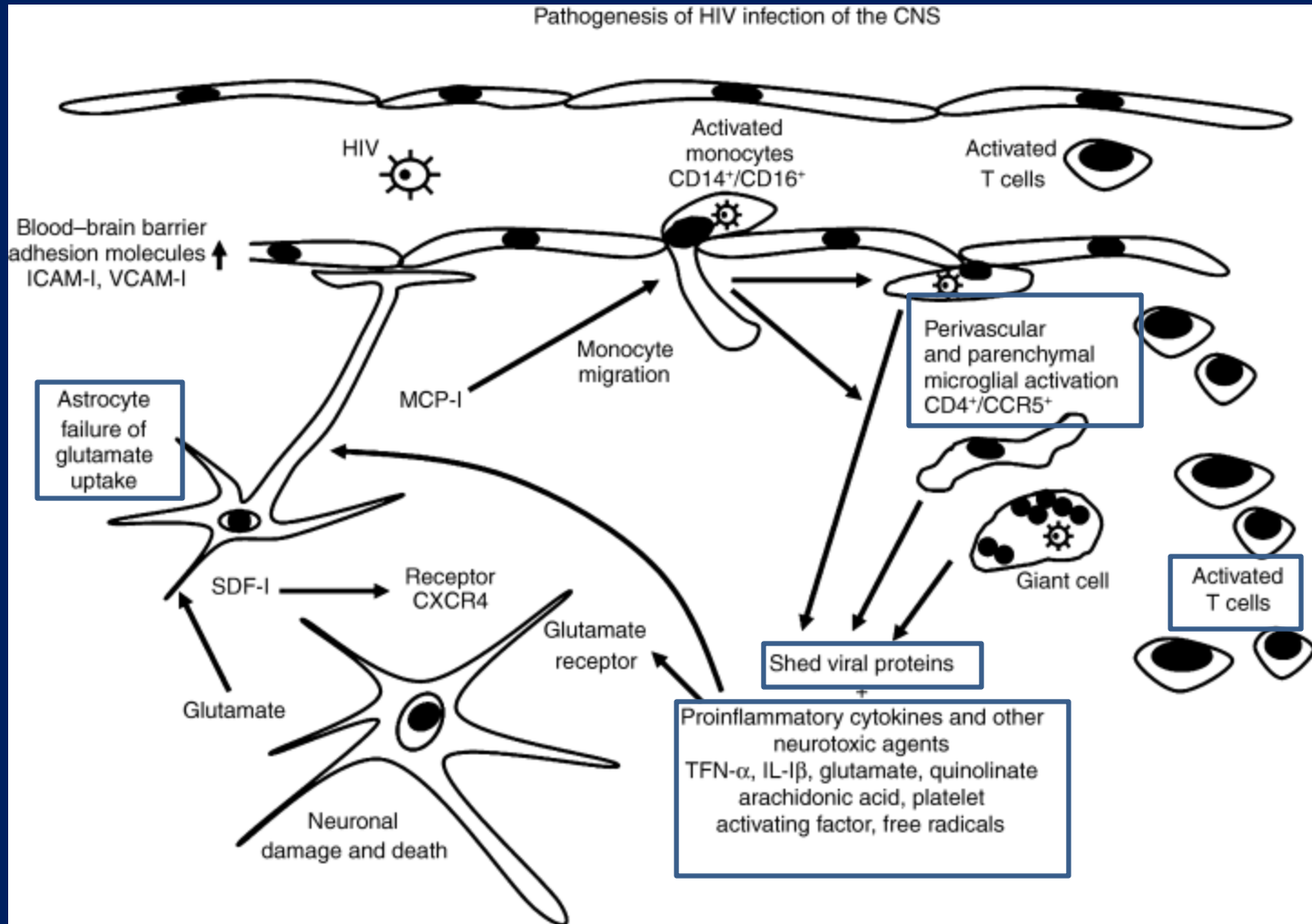
- Identify risk factors for neurocognitive complications among HIV+ patients.
- Detect common neurocognitive deficits among HIV+ patients

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



# 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

# Common Neuropsychological Test Findings

Motor and cognitive slowing

Poor memory and learning

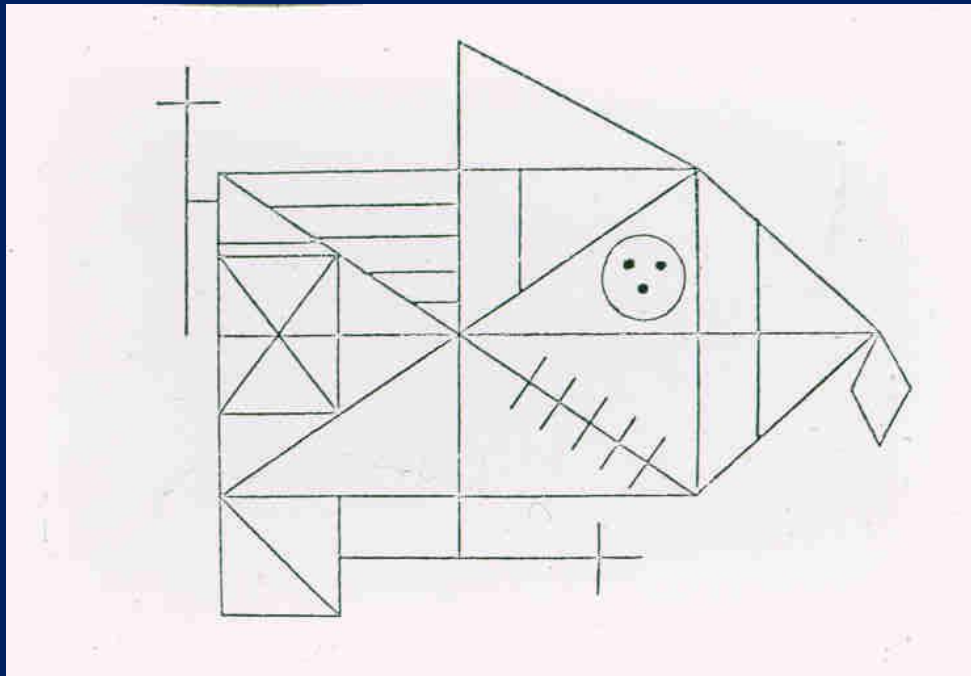
Impaired executive functions

Planning, judgment

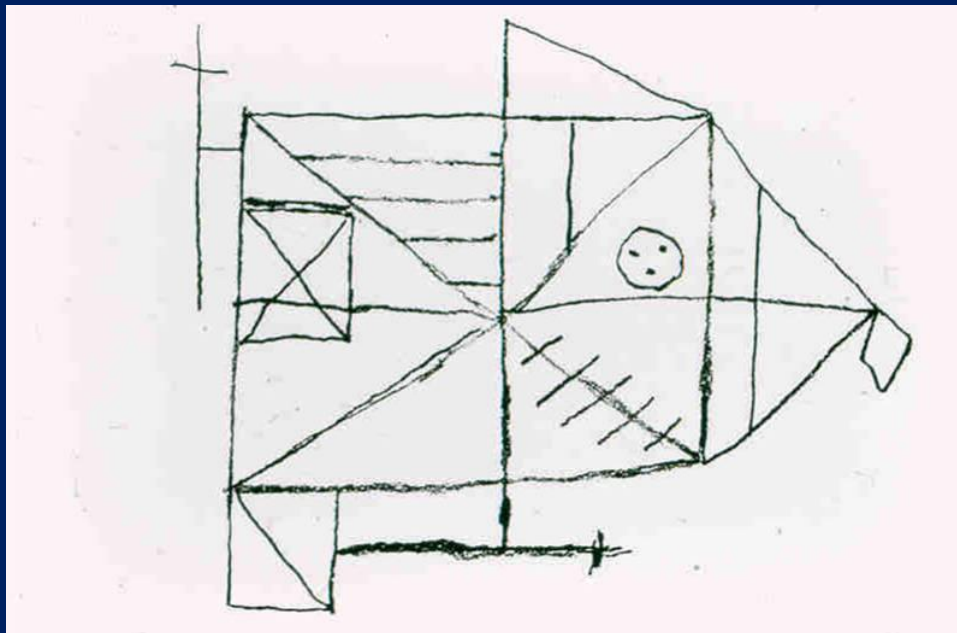
Actions based on future goals

Impulse control

No longer a “subcortical dementia”



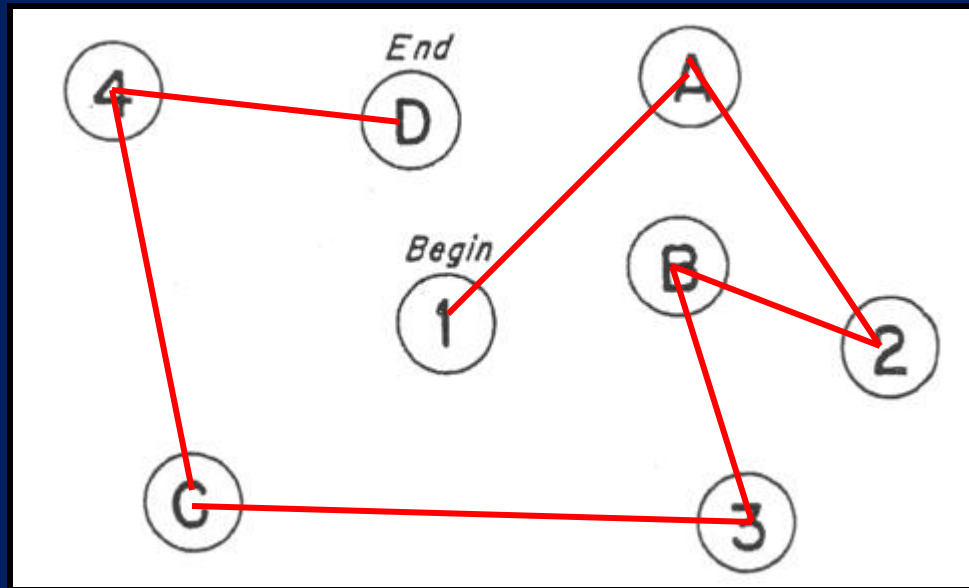
Model



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

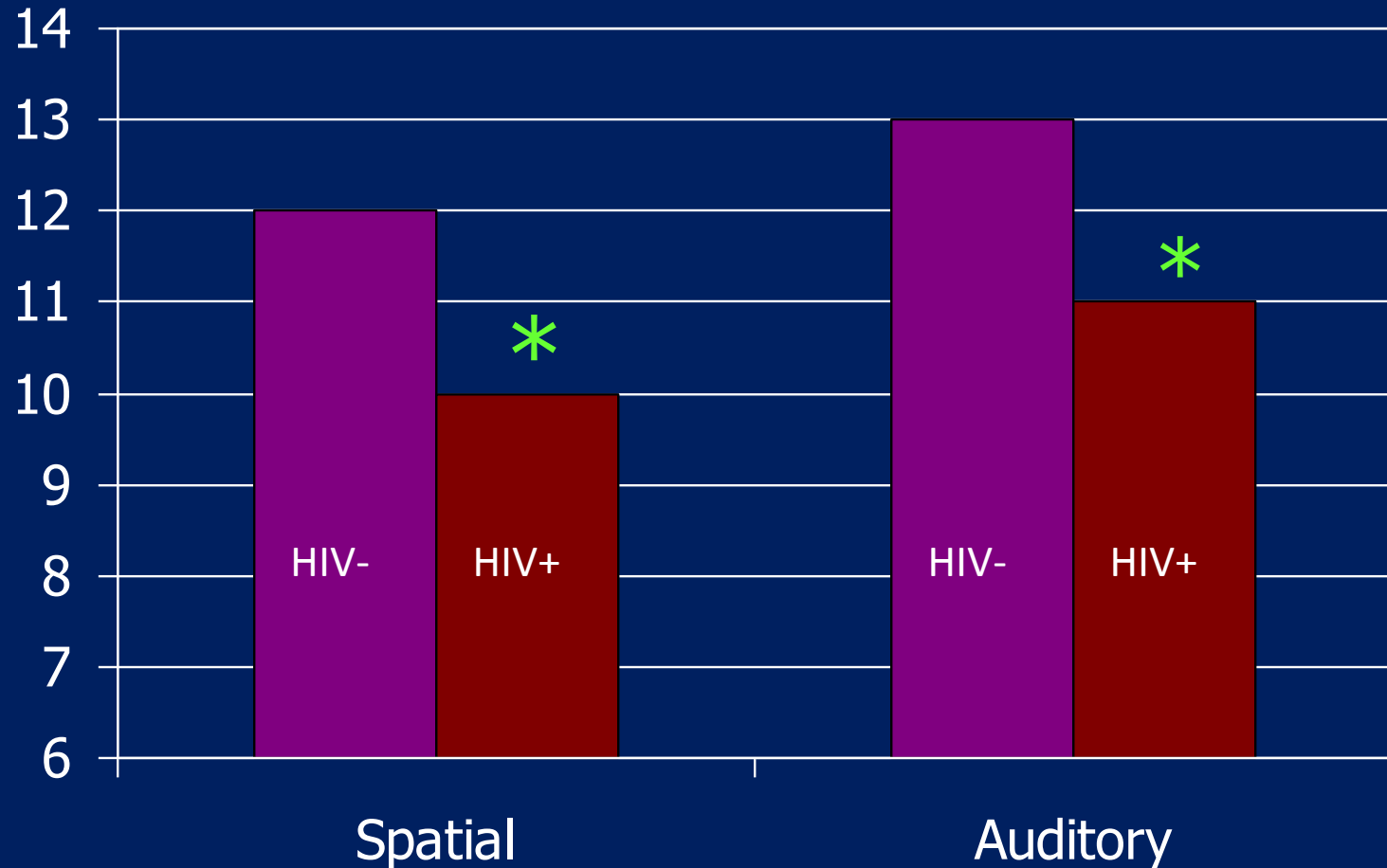
Patient Hears:

7X3M6C

Patient Says:

367CMX

# Working Memory Performance



\*  $p < .01$

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**

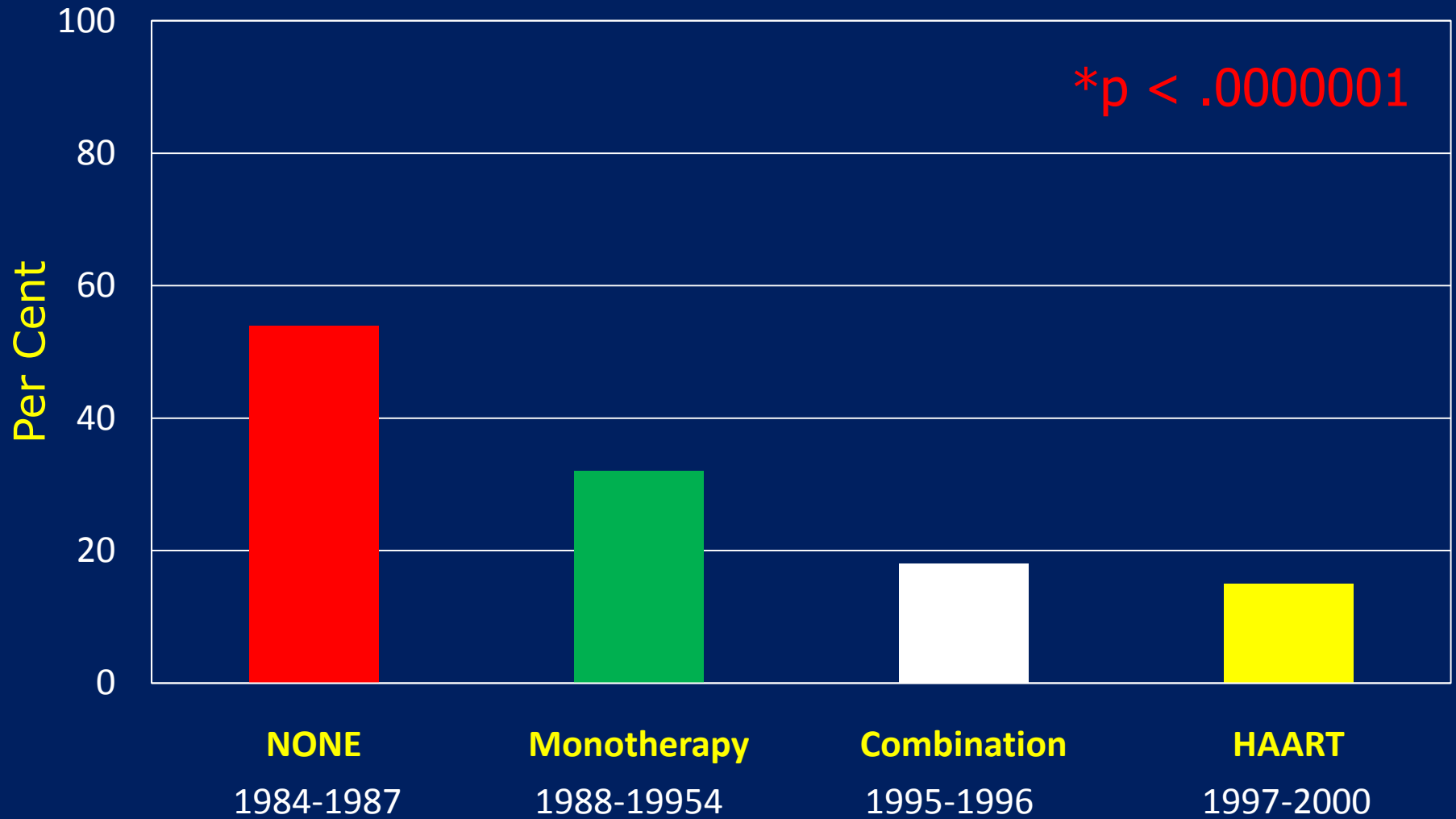
CD4 < 200

Hepatitis C Coinfection

Methamphetamine Dependence

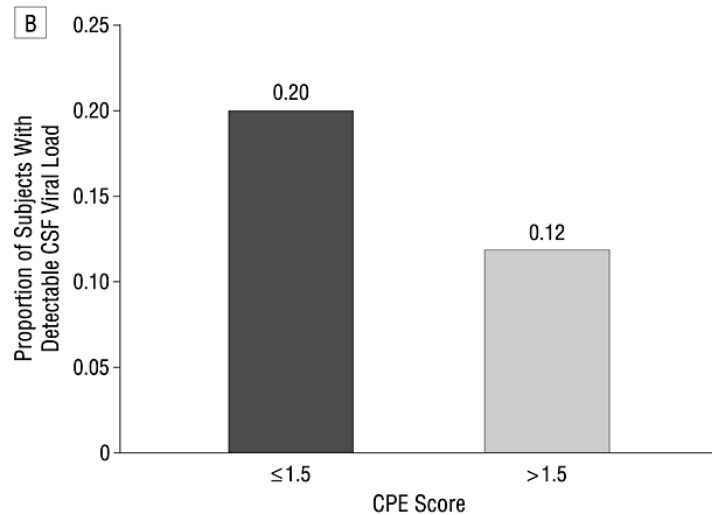
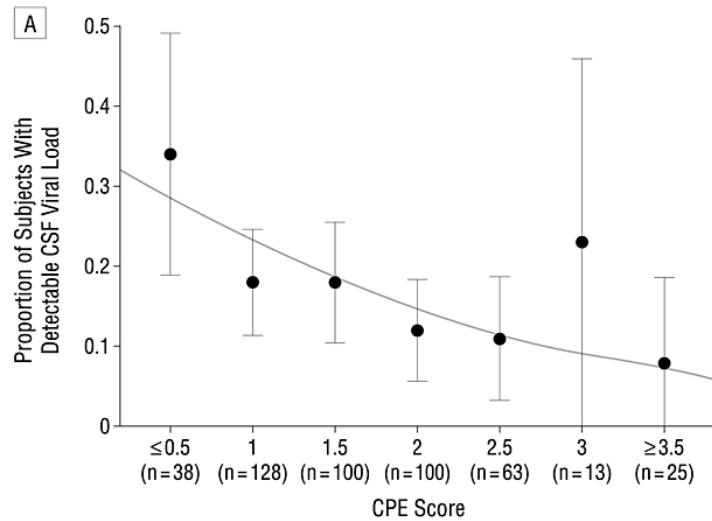
Aging

# Advances in ARV Therapy and Percentage of AIDS-Defining CNS Disorders at Autopsy



# Estimation of CNS Penetration-Effectiveness

	1	0.5	0
<b>NRTIs</b>	Abacavir	Emtricitabine	Didanosine
	Zidovudine	Lamivudine	Tenofovir
		Stavudine	Zalcitabine
<b>NNRTIs</b>	Delavirdine	Efavirenz	
	Nevirapine		
<b>PIs</b>	Amprenavir-r	Amprenavir	Nelfinavir
	Indinavir-r	Atazanavir	Ritonavir
	Lopinavir-r	Atazanavir-r	Saquinavir
		Indinavir	Saquinavir-r
			Tipranavir-r
<b>Fusion Inhibitor</b>			Enfuvirtide

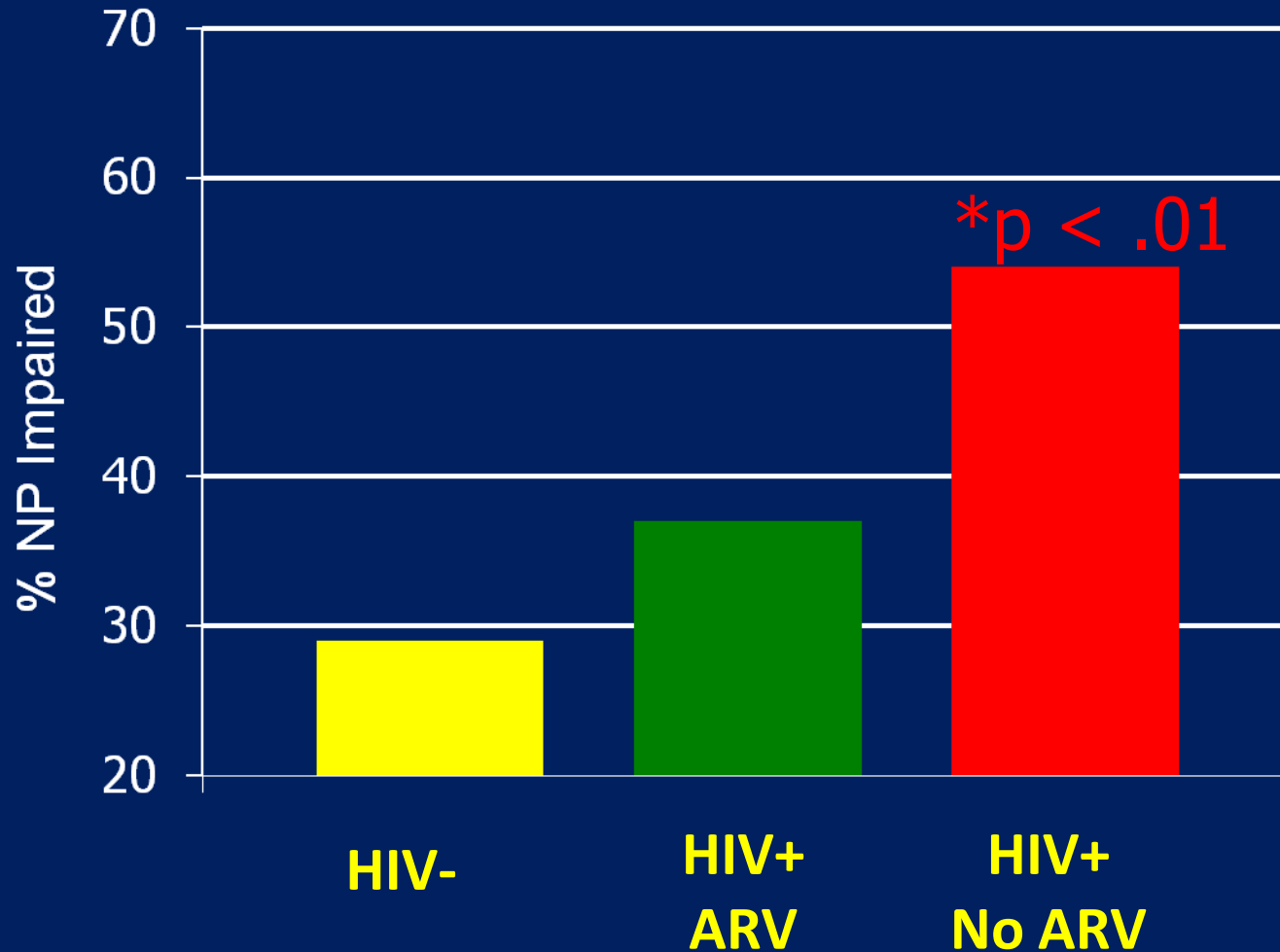


Detectable CSF HIV RNA was significantly more common with low CPE rankings

. Letendre, S. et al. Arch Neurol 2008;65:65-70

# Antiretroviral Status and NP Performance

## Women's Interagency HIV Study



# Risk factors for HIV-Associated Neurocognitive Disorder

Not on ARV

**CD4 < 200**

Hepatitis C Coinfection

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Aging

# CD4 Count and Neurocognitive Risk

Variable	Odds Ratio	95% CI	p-value
CD4 cell count* <200 vs >350	1.74	1.12 , 2.70	0.01
Nadir CD4 cell count <200 vs >350	1.73	1.18, 2.55	<0.01

\*cells/mm<sup>3</sup>

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

Robertson K, et al. *AIDS*. 2007;21:1915-1921.

# Risk factors for HIV-Associated Neurocognitive Disorder

Not on ARV

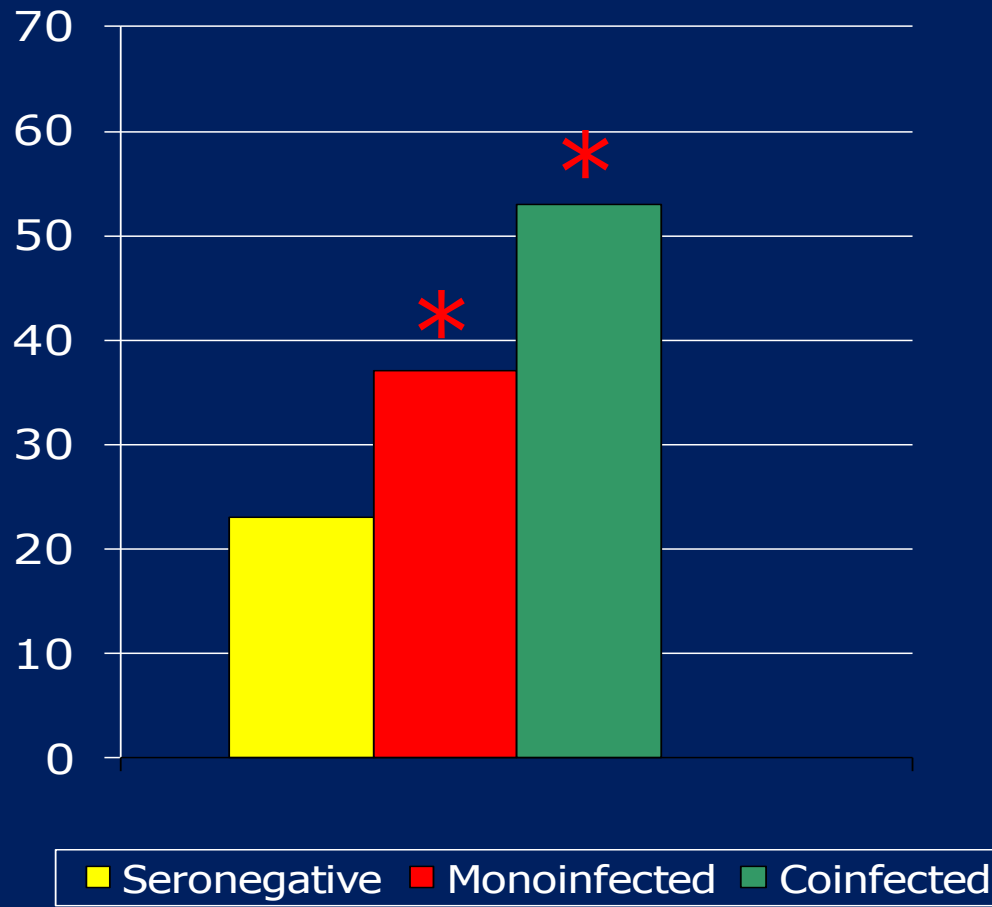
CD4 < 200

**Hepatitis C Coinfection**

Methamphetamine Dependence

Aging

# NP Abnormality and HCV Coinfection Women's Interagency HIV Study



# Risk factors for HIV-Associated Neurocognitive Disorder

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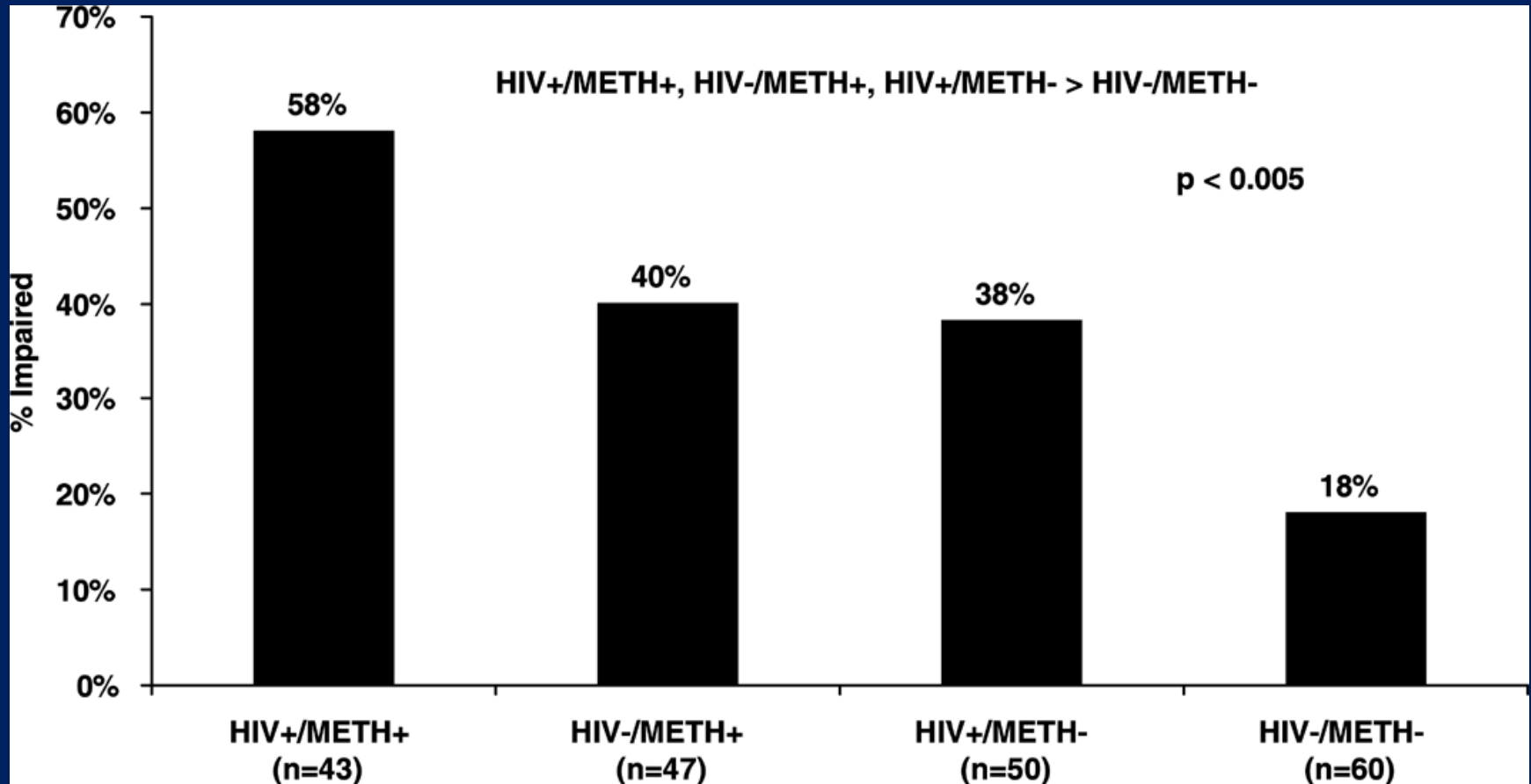
Nadir CD4 < 200

Hepatitis C Coinfection

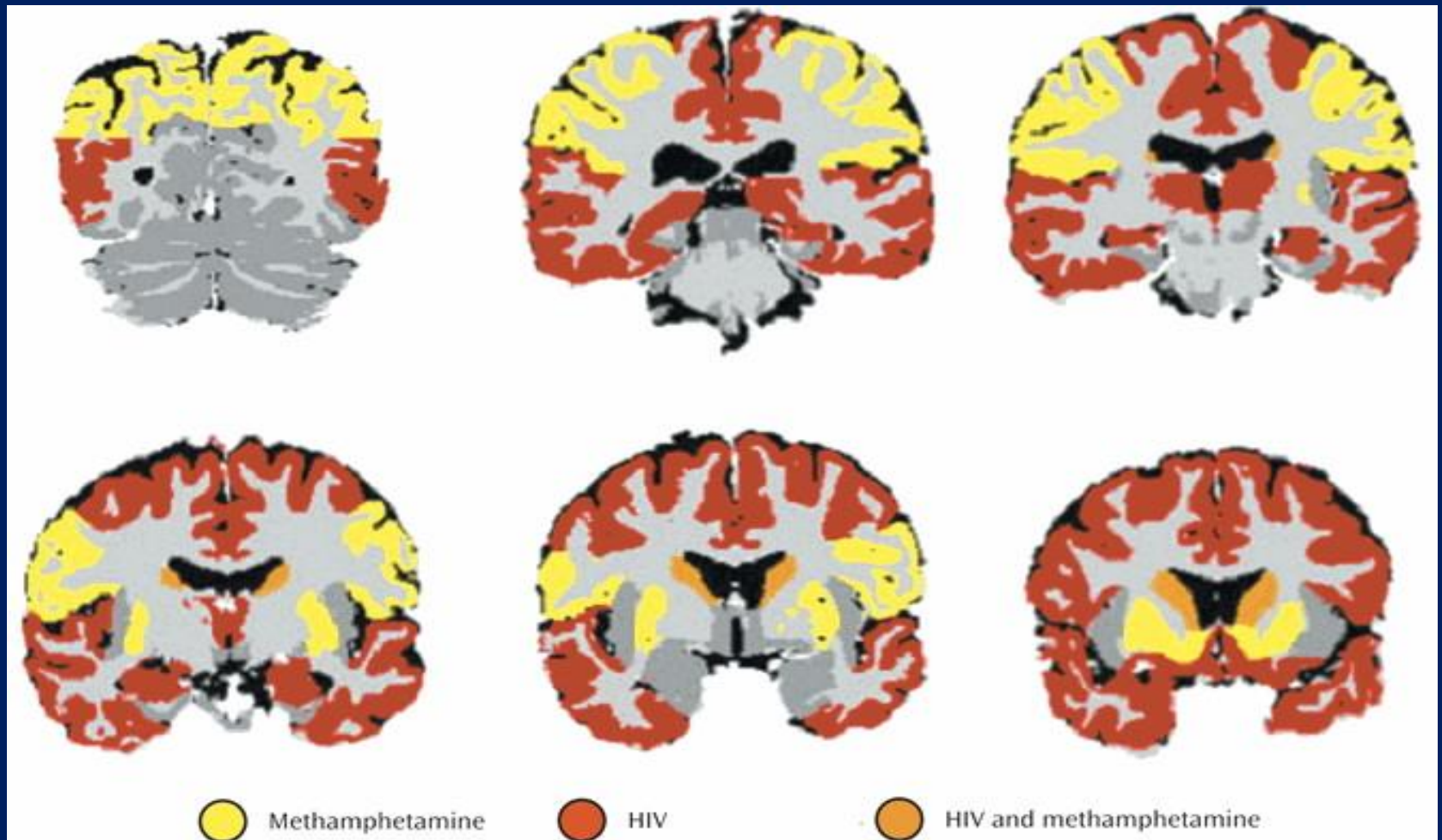
**Methamphetamine Dependence**

Aging

# Neurocognitive Effects of HIV and Methamphetamine



# Effects of HIV and Methamphetamine on Brain Structure



# Risk factors for HIV-Associated Neurocognitive Disorder

Not on ARV

CD4 < 200

Hepatitis C Coinfection

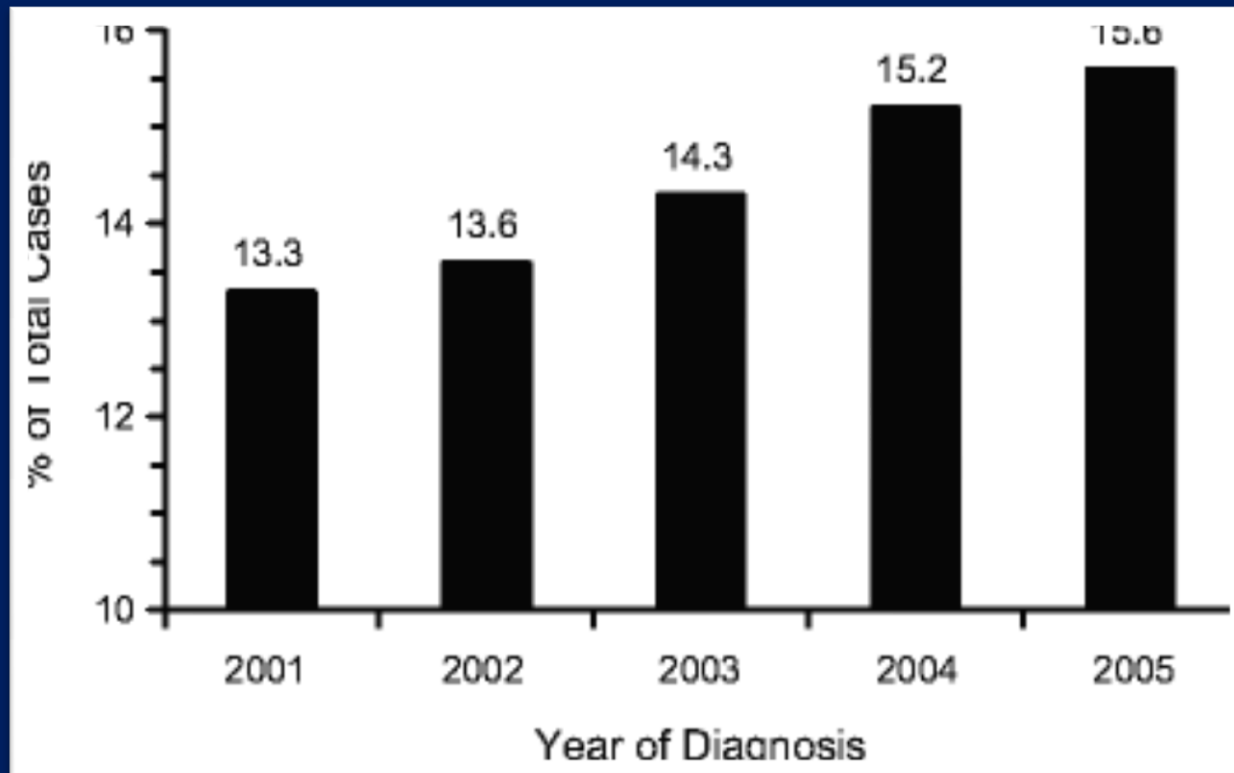
Methamphetamine Dependence

**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)

# 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