

Impact of HIV on the Brain and Cognition

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Supported by HHS R01 DA12828

Learning Objectives

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

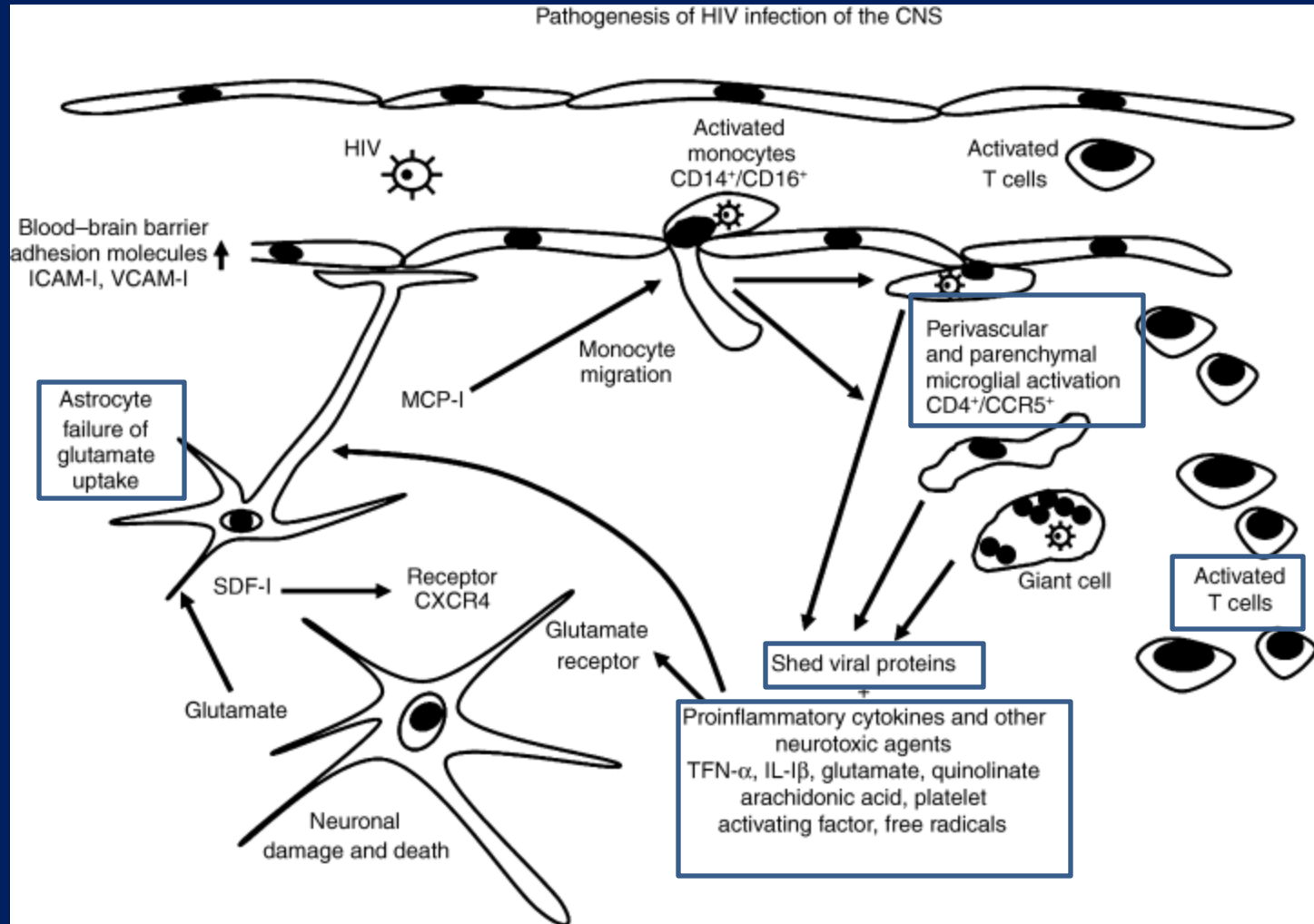
- Identify risk factors for neurocognitive complications among HIV+ patients.
- Detect common neurocognitive deficits among HIV+ patients

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

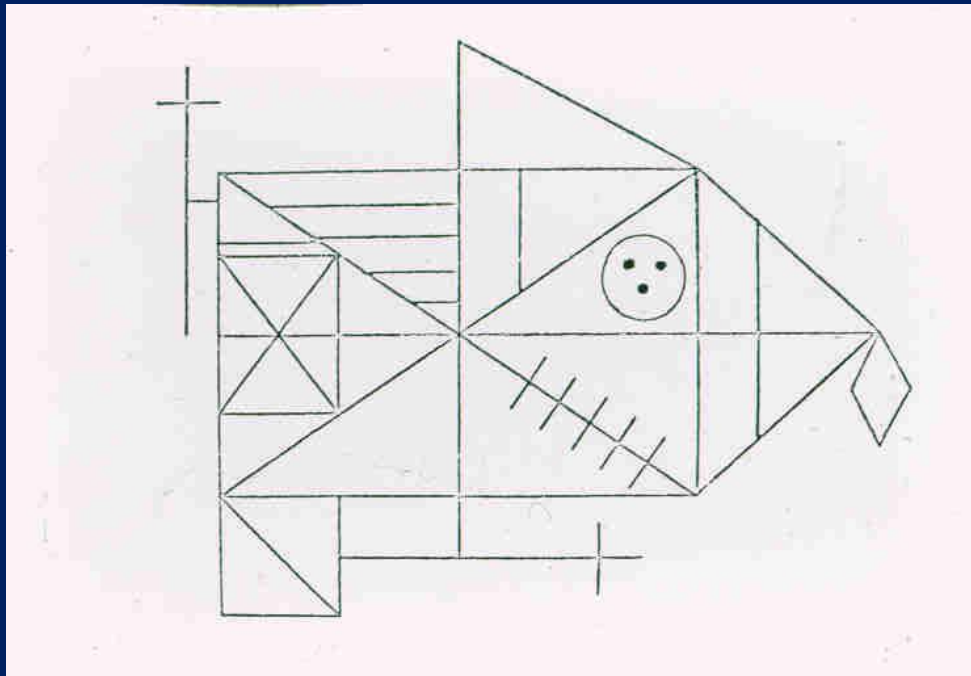
Impaired executive functions

Planning, judgment

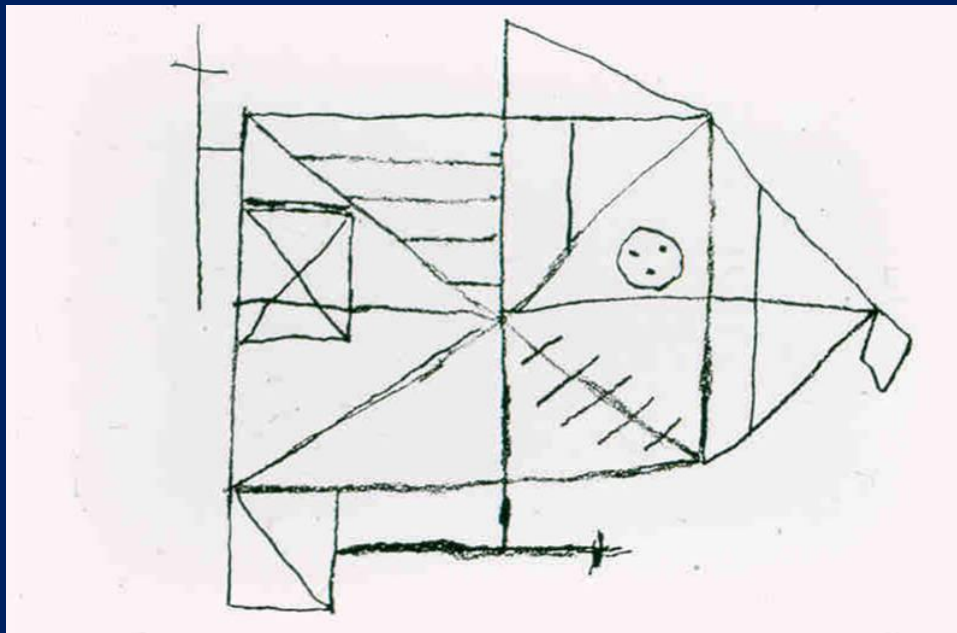
Actions based on future goals

Impulse control

No longer a “subcortical dementia”



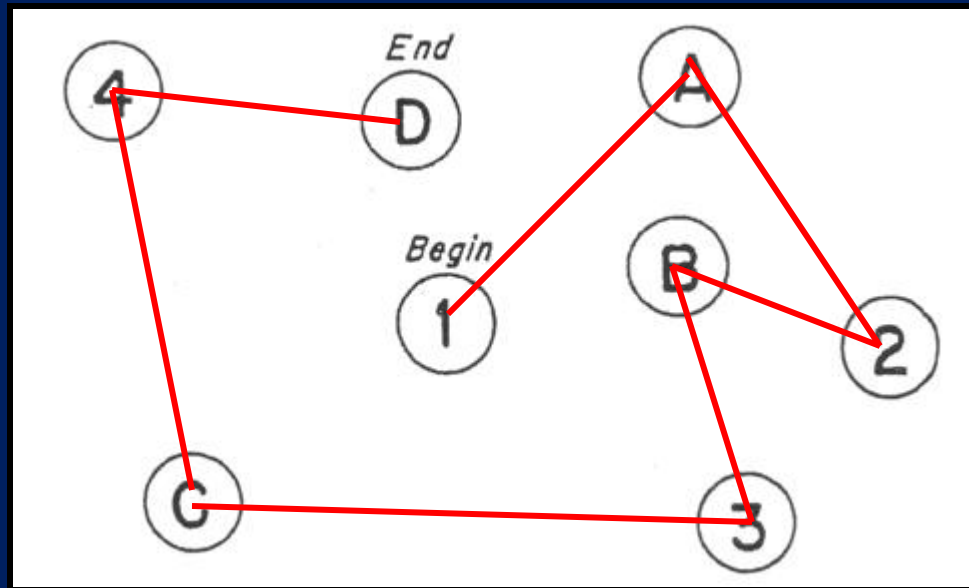
Model



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

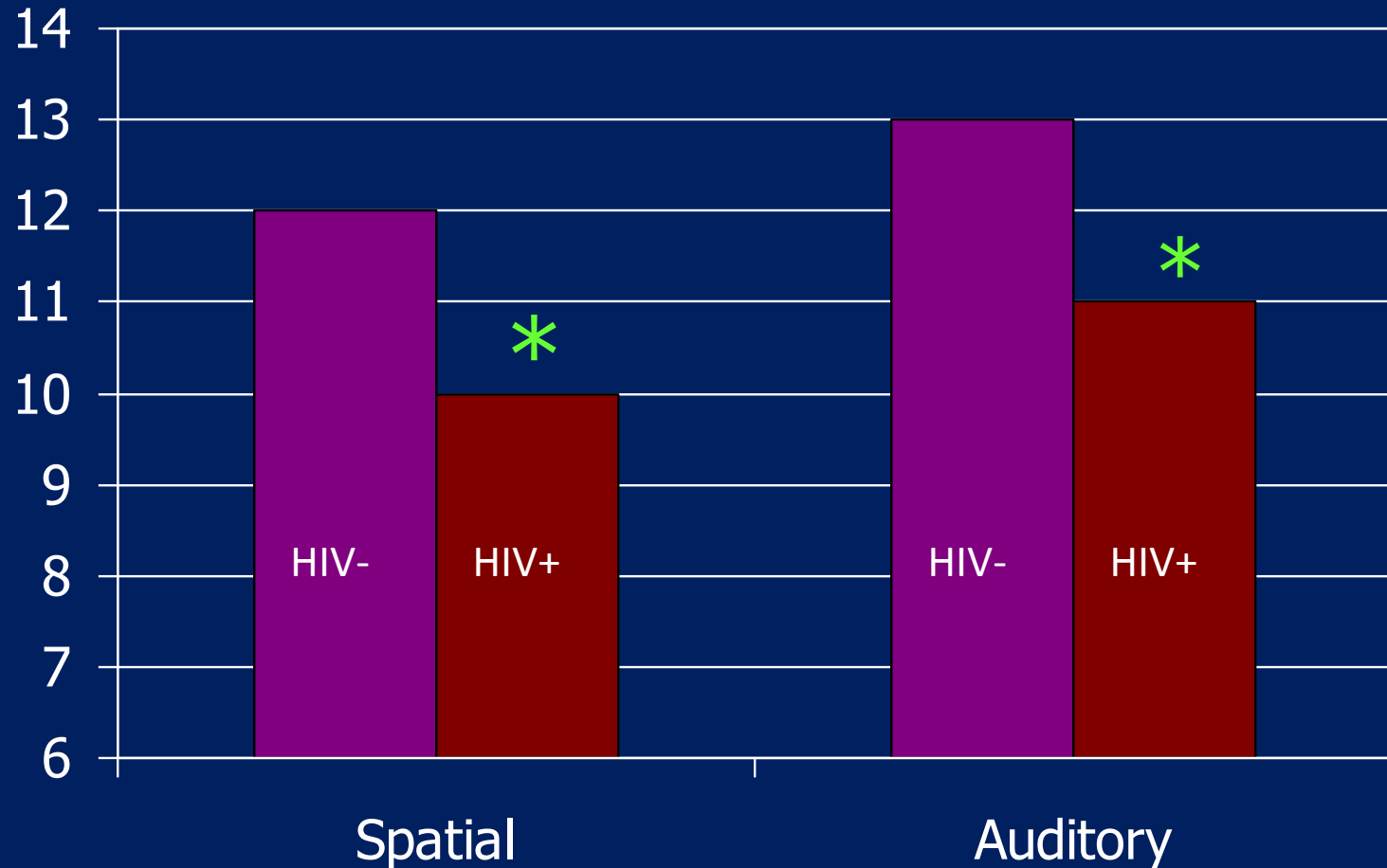
Patient Hears:

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

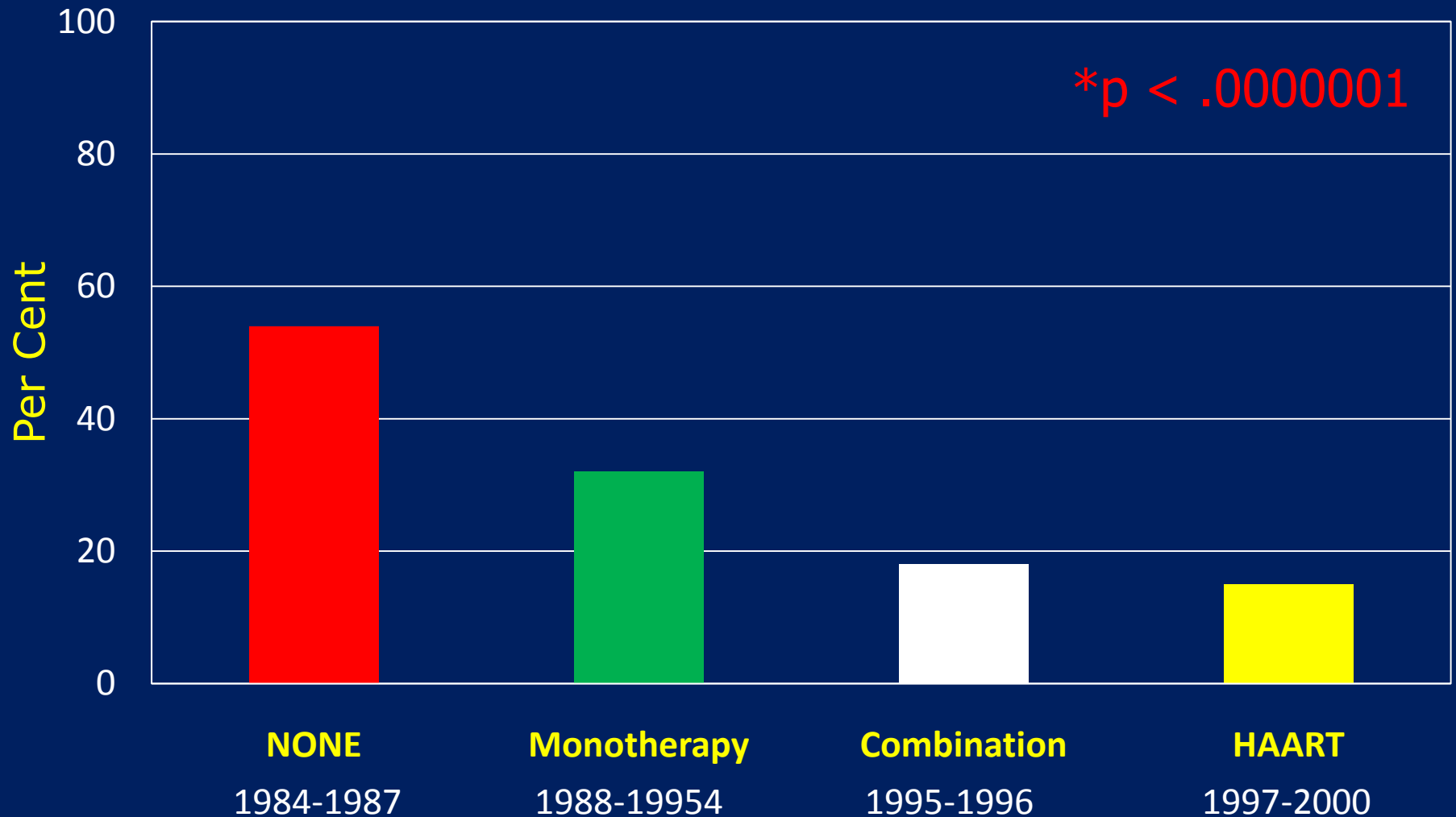
CD4 < 200

Hepatitis C Coinfection

Methamphetamine Dependence

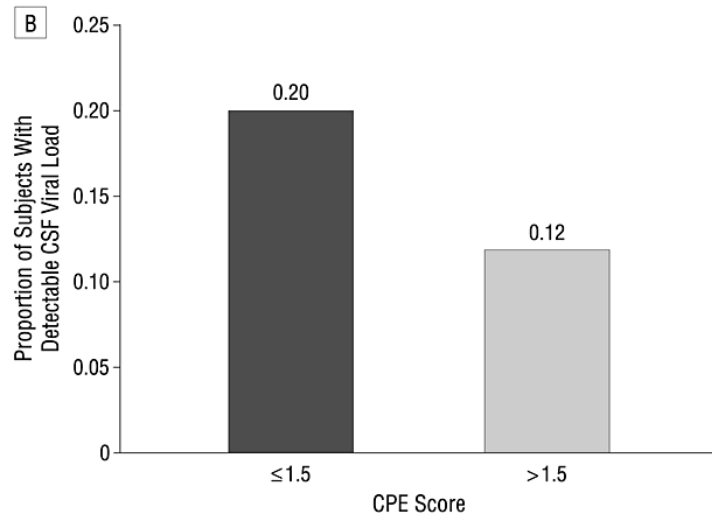
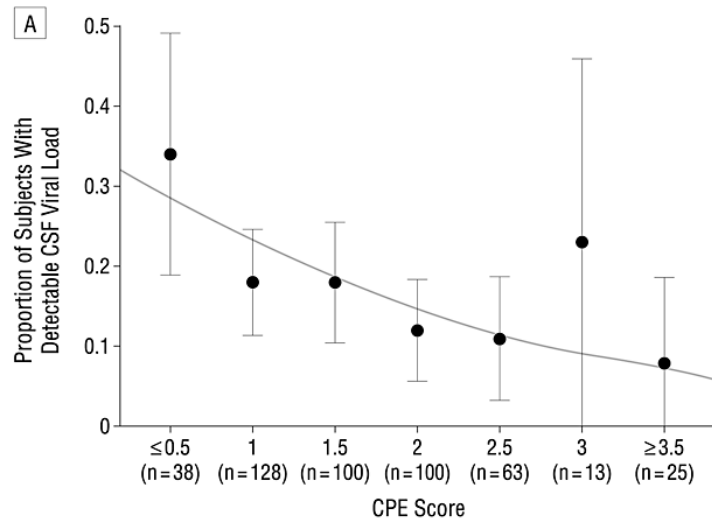
Aging

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



Estimation of CNS Penetration-Effectiveness

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

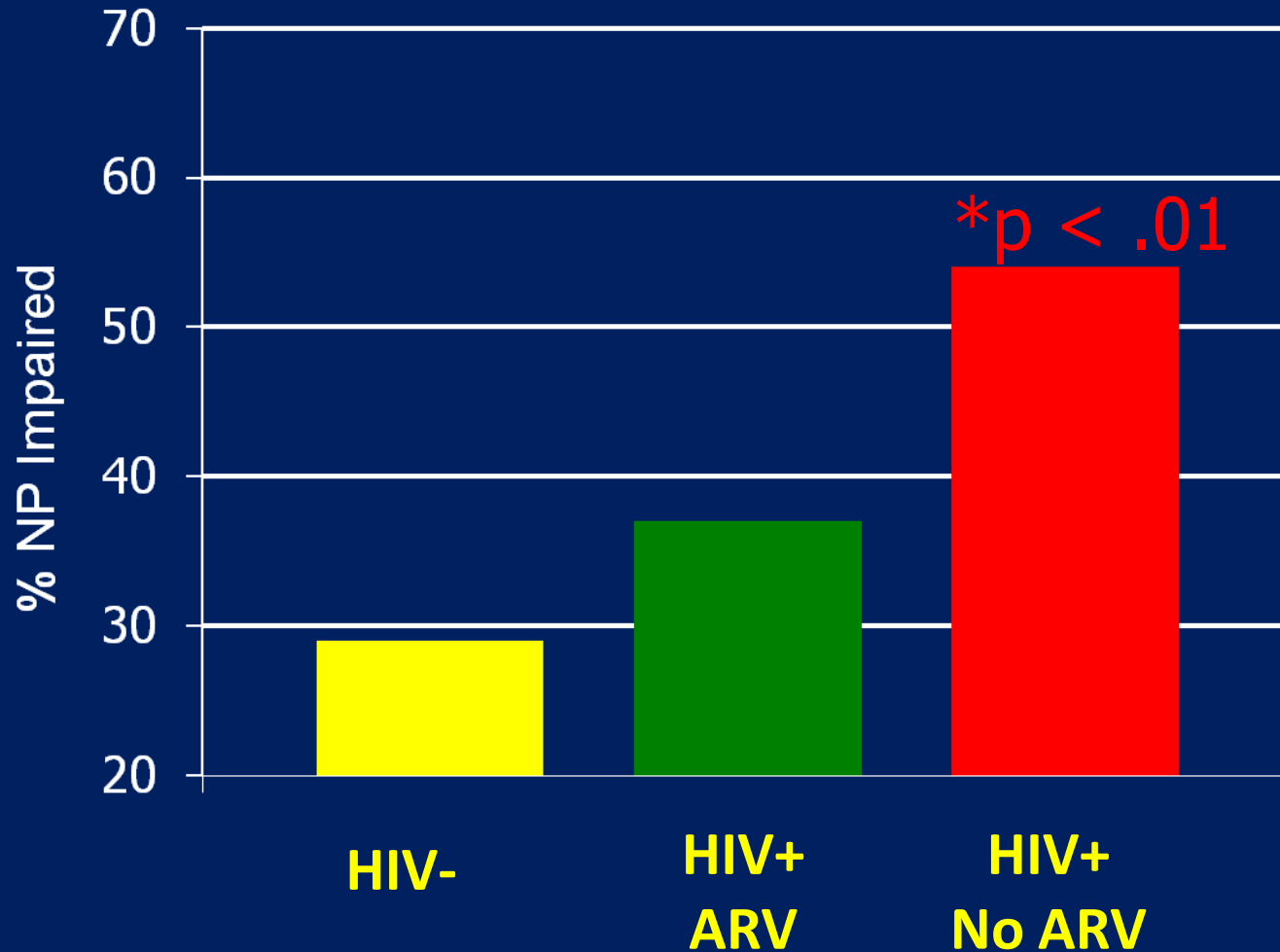


Detectable CSF HIV RNA was significantly more common with low CPE rankings

. 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

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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/mm³

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

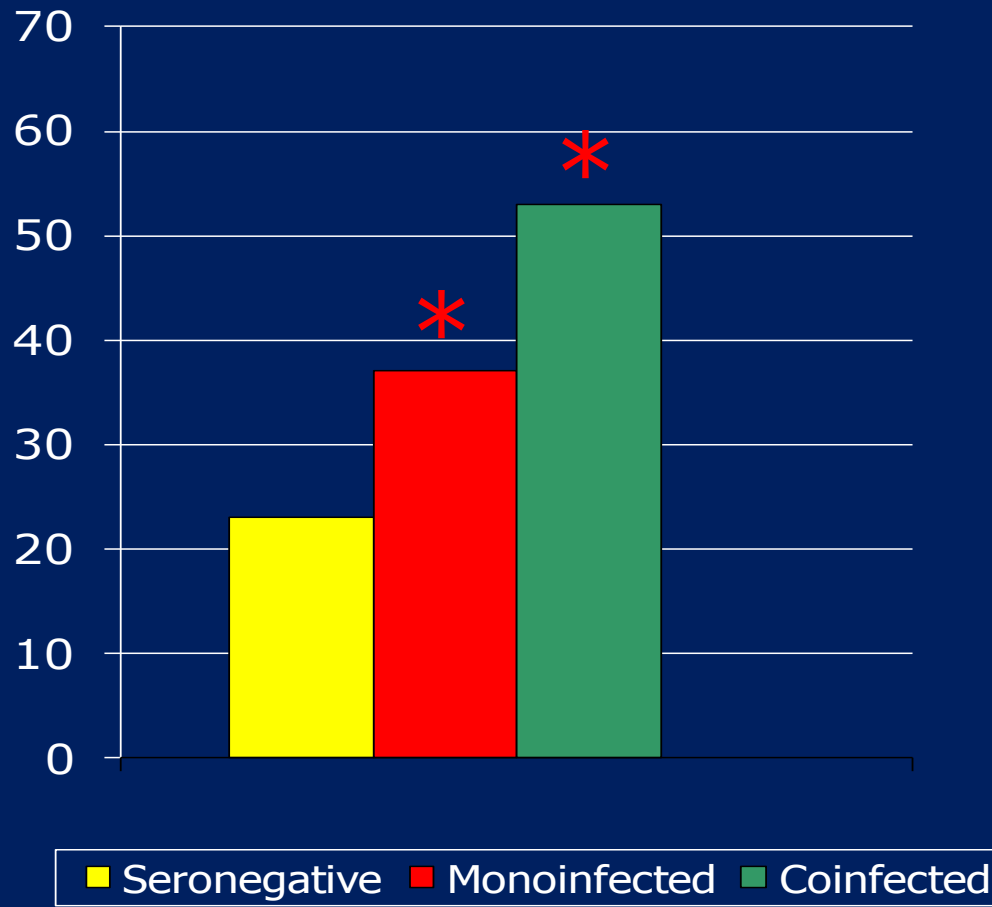
CD4 < 200

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NP Abnormality and HCV Coinfection Women's Interagency HIV Study



Risk factors for HIV-Associated Neurocognitive Disorder

Not on ARV

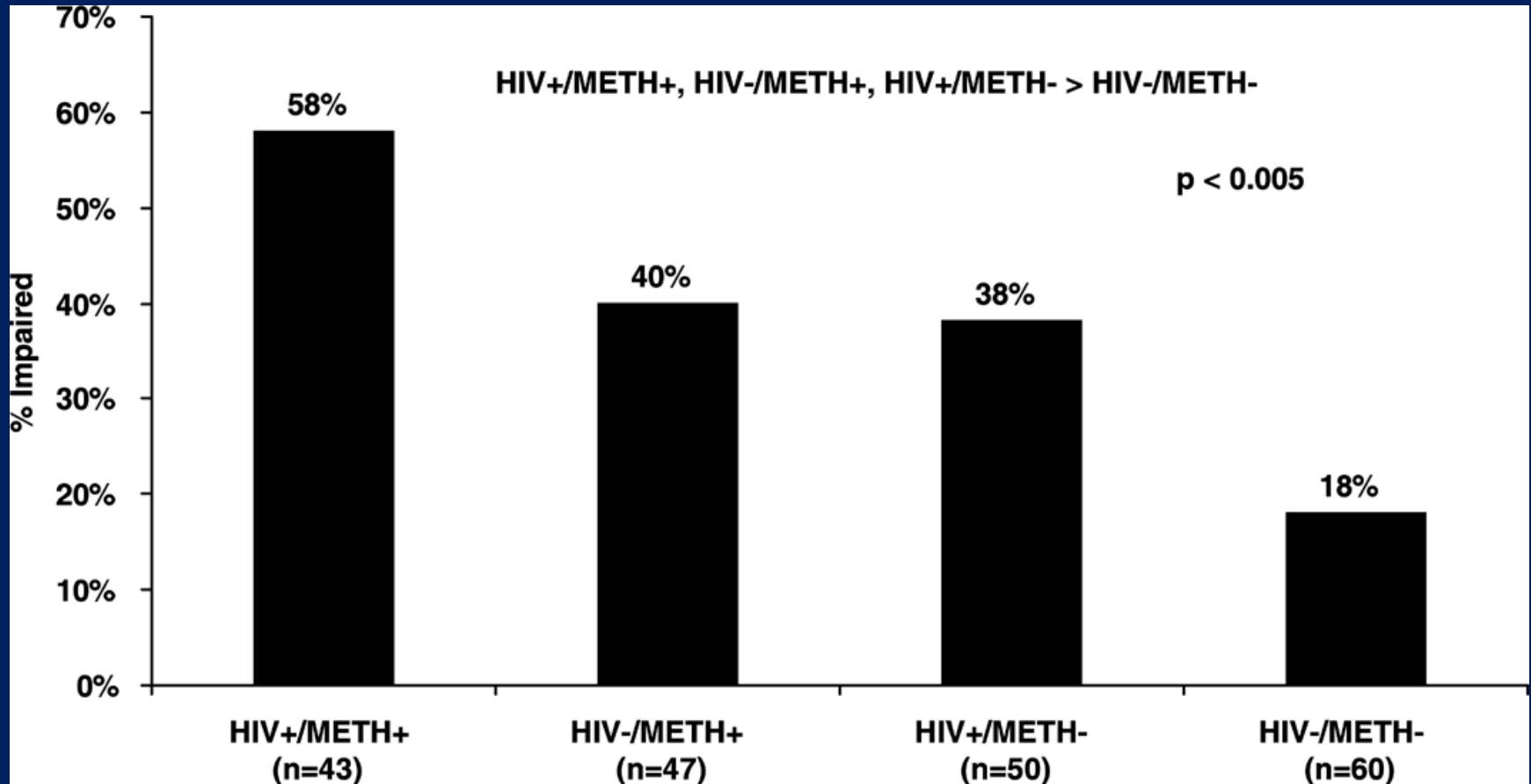
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Hepatitis C Coinfection

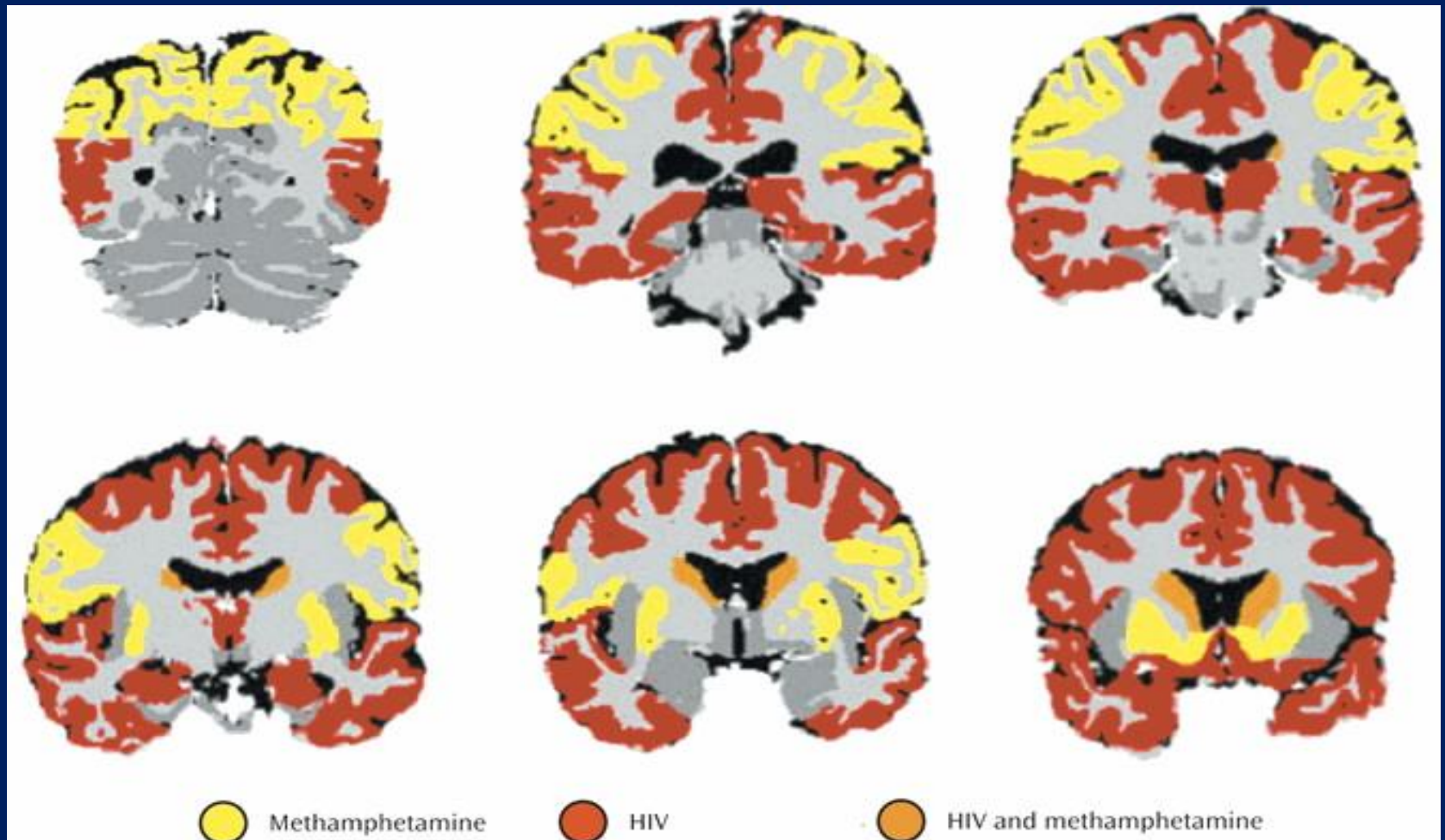
Methamphetamine Dependence

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

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Hepatitis C Coinfection

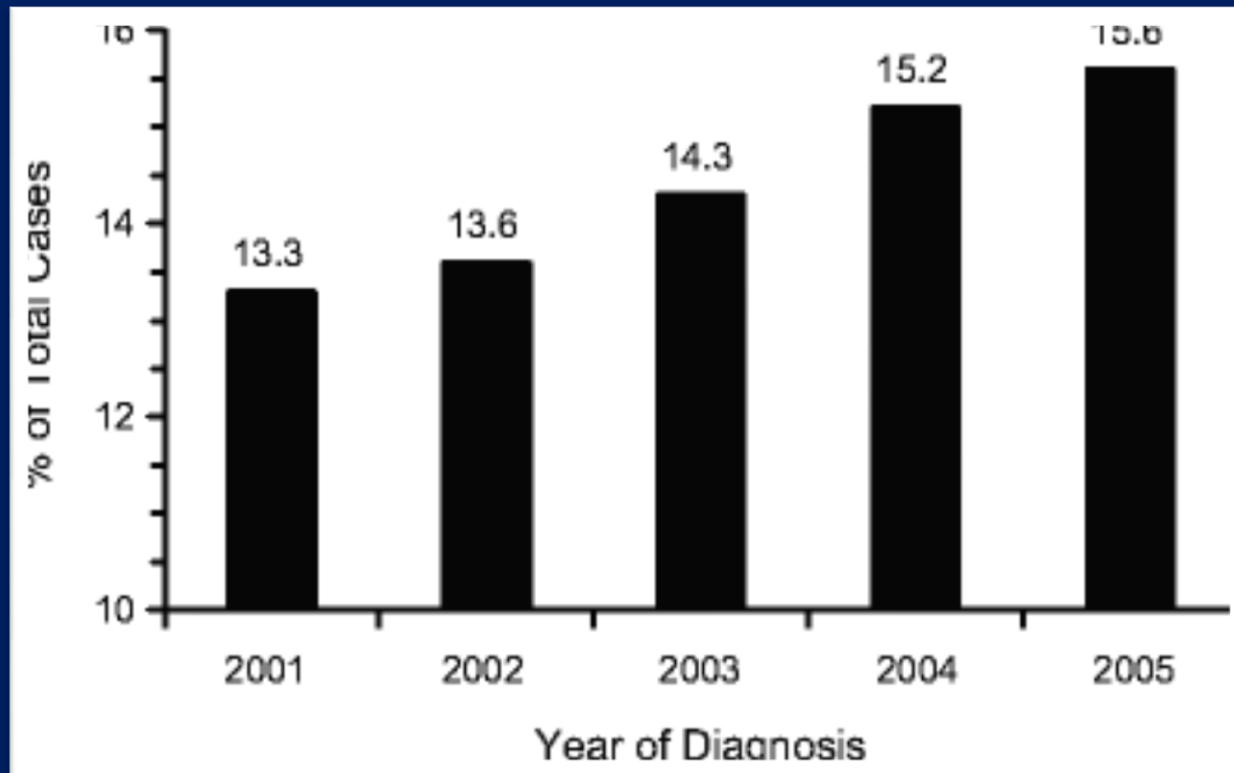
Methamphetamine Dependence

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