

NeuroAIDS and Cognitive Aging: Updates on Current Trends and Interventions



David E. Vance, Ph.D., MGS

**Professor & Director of Research and Scholarly Development
Office of Research and Scholarship, School of Nursing
University of Alabama at Birmingham (UAB)**

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

Studies in the aging and HIV literature show that increased cognitive activity, which reflects an enriched environment, promotes optimal cognitive functioning.

Negative Neuroplasticity

- The brain atrophies quicker with less sophisticated and less connections between neurons.
- Poorer Cognitive Reserve

2. NEUROAIDS AND INTERVENTIONS

There is a ~20% Bi-directional Fluctuation over Time of HIV-Associated Neurocognitive Disorder

(Antinori et al., 2007. *Neurology*, 69, 1789-1799.)

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

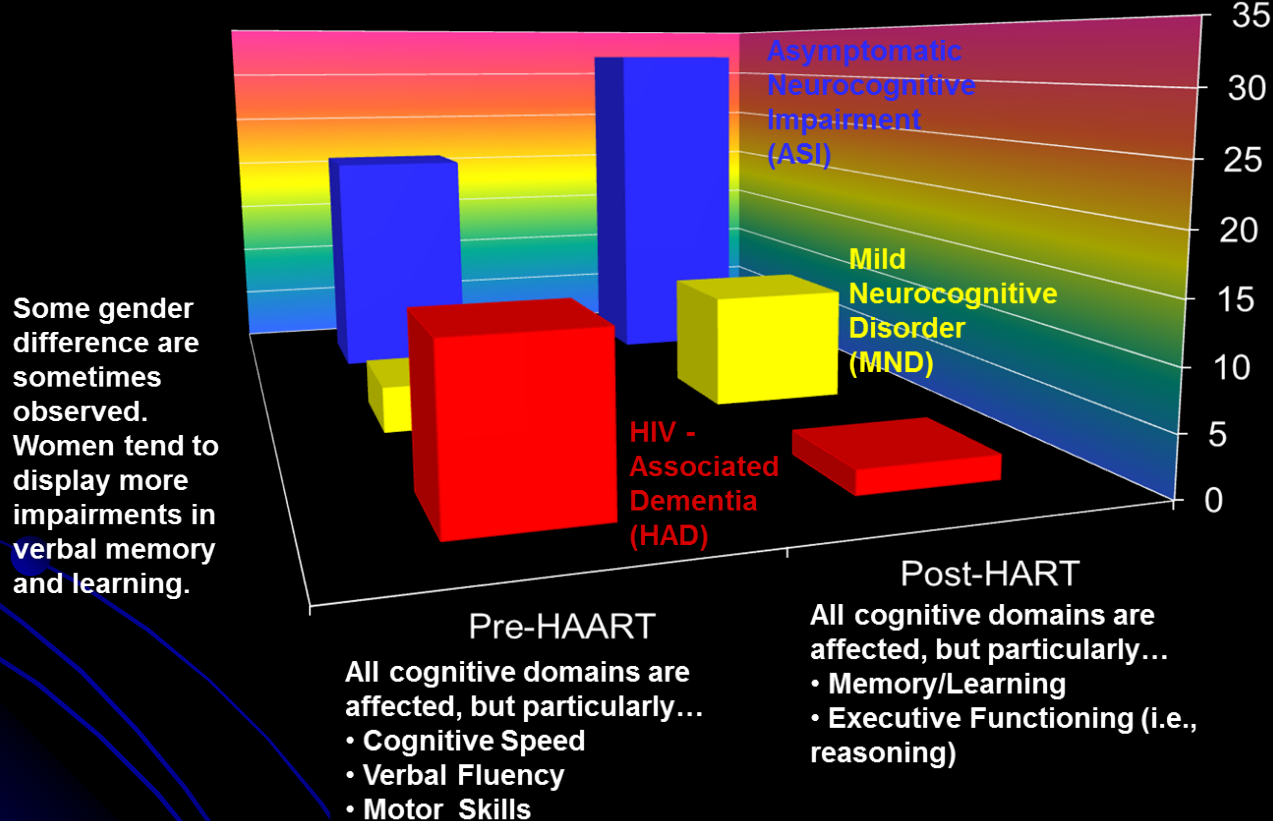
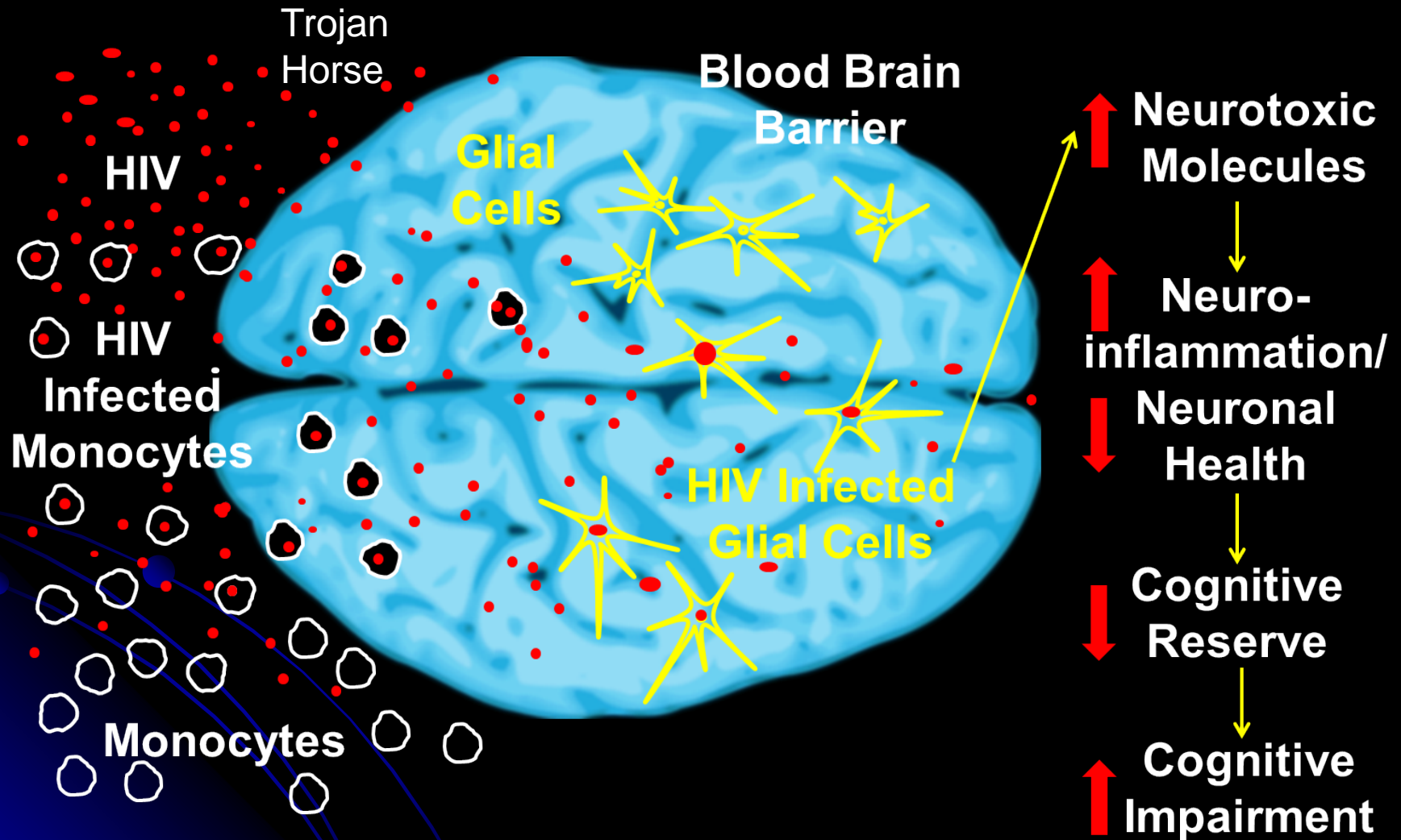


Figure 1. Note. Croteau, D. Pharmacologic interventions for HIV-associated neurocognitive disorders. *Psychology and AIDS Exchange Newsletter*. Retrieved from <http://www.apa.org/pi/aids/resources/exchange/2013/01/pharmacologic-interventions.aspx>

Vance, D. E., Cody, S. L., & Moneyham, L. (2017). Remediating HIV-associated neurocognitive disorders via cognitive training: A perspective on neurocognitive aging. *Interdisciplinary Topics in Gerontology and Geriatrics*, 42, 173-186. DOI: 10.1159/000448562

Does HIV infect neurons in the brain? **NO**



* It is both monocytes and particularly macrophages.
Vance, D. E., Humphrey, S. C., & Batey, D. S. (2015). HIV-related cognitive dysfunction: Implications for aging and social work. *Social Work in Mental Health*, 13, 553-570.

Nick.ms



- **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**
- **26th Annual Social Work and HIV/AIDS Conference in 2013 – “Help! I’ve Lost My Mind! There’s an App for That!”**

Nick.ms

- 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.

Nick.ms

- 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”

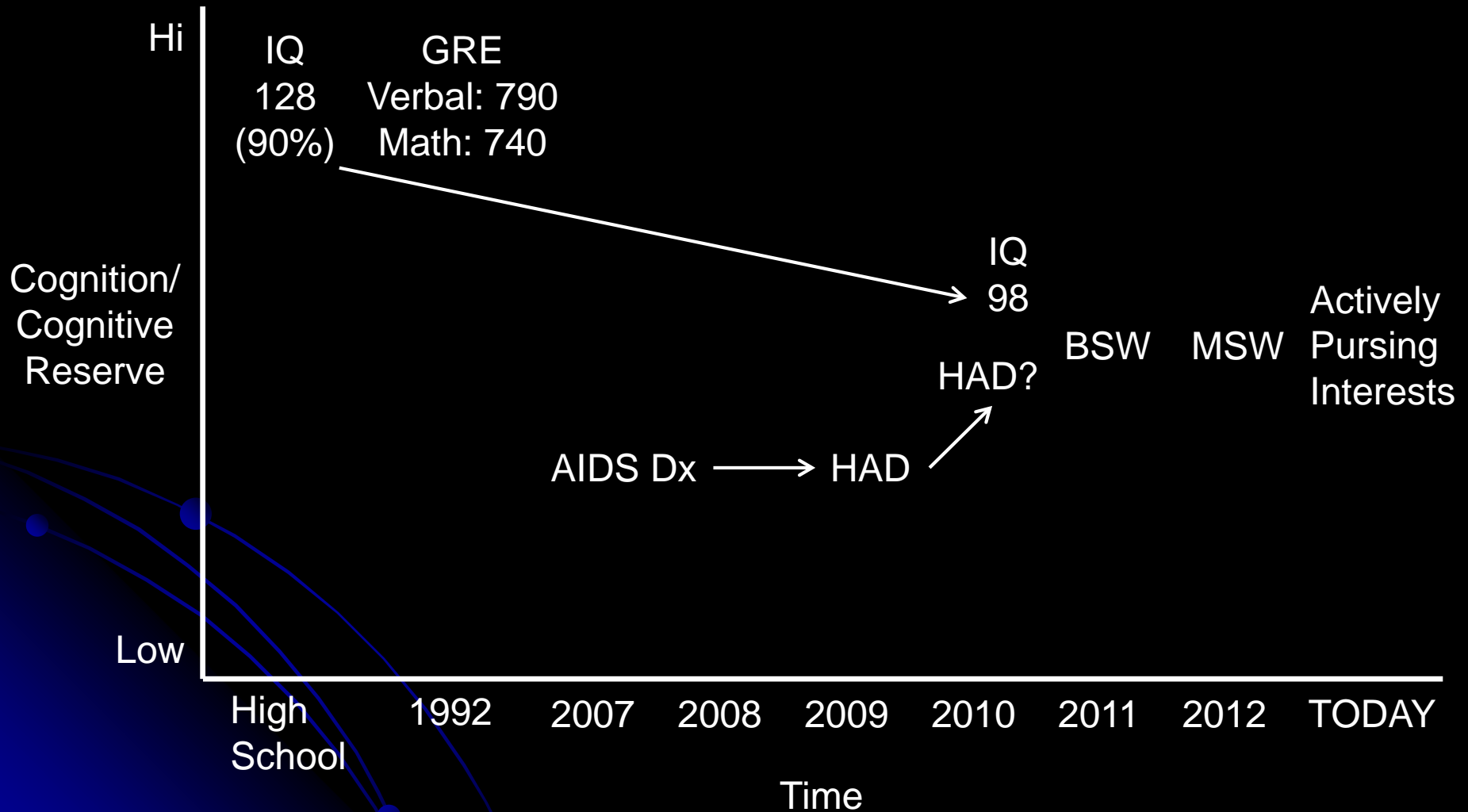
Nick.ms

- TODAY

- 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



Cognitive Aging with HIV

TABLE 2
Adjusted Means of Neurocognitive and Everyday Performance between Groups (N = 172)

	HIV-POSITIVE		HIV-NEGATIVE		FINDINGS
	YOUNGER (n = 55)	OLDER (n = 33)	YOUNGER (n = 43)	OLDER (n = 41)	
	M (SD)	M (SD)	M (SD)	M (SD)	
PSYCHOMOTOR SPEED					
Finger Tapping Test (number of taps)	103.23 (14.92)	96.31 (14.73)	104.35 (14.74)	92.34 (14.50)	A‡
SPEED OF PROCESSING					
Useful Field of View (milliseconds)	693.09 (357.39)	861.12 (354.15)	530.01 (354.25)	736.00 (348.45)	A‡, H†
Complex Reaction Time (seconds)	3.76 (1.07)	4.20 (1.06)	3.26 (1.06)	3.55 (1.04)	A†, H‡
Letter Comparison (number correct)	47.34 (10.95)	41.99 (10.86)	51.17 (10.83)	44.72 (10.65)	A‡
Pattern Comparison (number correct)	33.96 (7.21)	28.77 (7.12)	36.18 (7.13)	32.13 (7.01)	A‡, H†
MEMORY FUNCTIONING					
Hopkins Verbal Learning (number correct)	24.97 (6.00)	22.32 (5.92)	24.67 (5.79)	22.64 (5.83)	A†
EXECUTIVE FUNCTIONING					
Wisconsin Card Sorting (number correct)	62.65 (18.76)	57.92 (18.50)	63.39 (18.49)	64.47 (18.25)	ns
EVERYDAY FUNCTIONING					
Timed Instrumental Activities of Daily Living (z-score composite)	-0.31 (3.05)	2.12 (2.99)	-0.57 (3.00)	-0.66 (2.96)	A†, H‡, HxA‡
Observed Tasks of Daily Living (total score)	68.43 (7.37)	66.64 (7.29)	70.13 (7.29)	69.24 (7.17)	ns

Notes: A = Age main effect detected; H = HIV main effect detected; HxA = HIV x Age interaction detected; M = mean; ns = not significant; SD = standard deviation. † = sig. at < .05; ‡ = sig. at < .01.

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.

Cluster Analysis

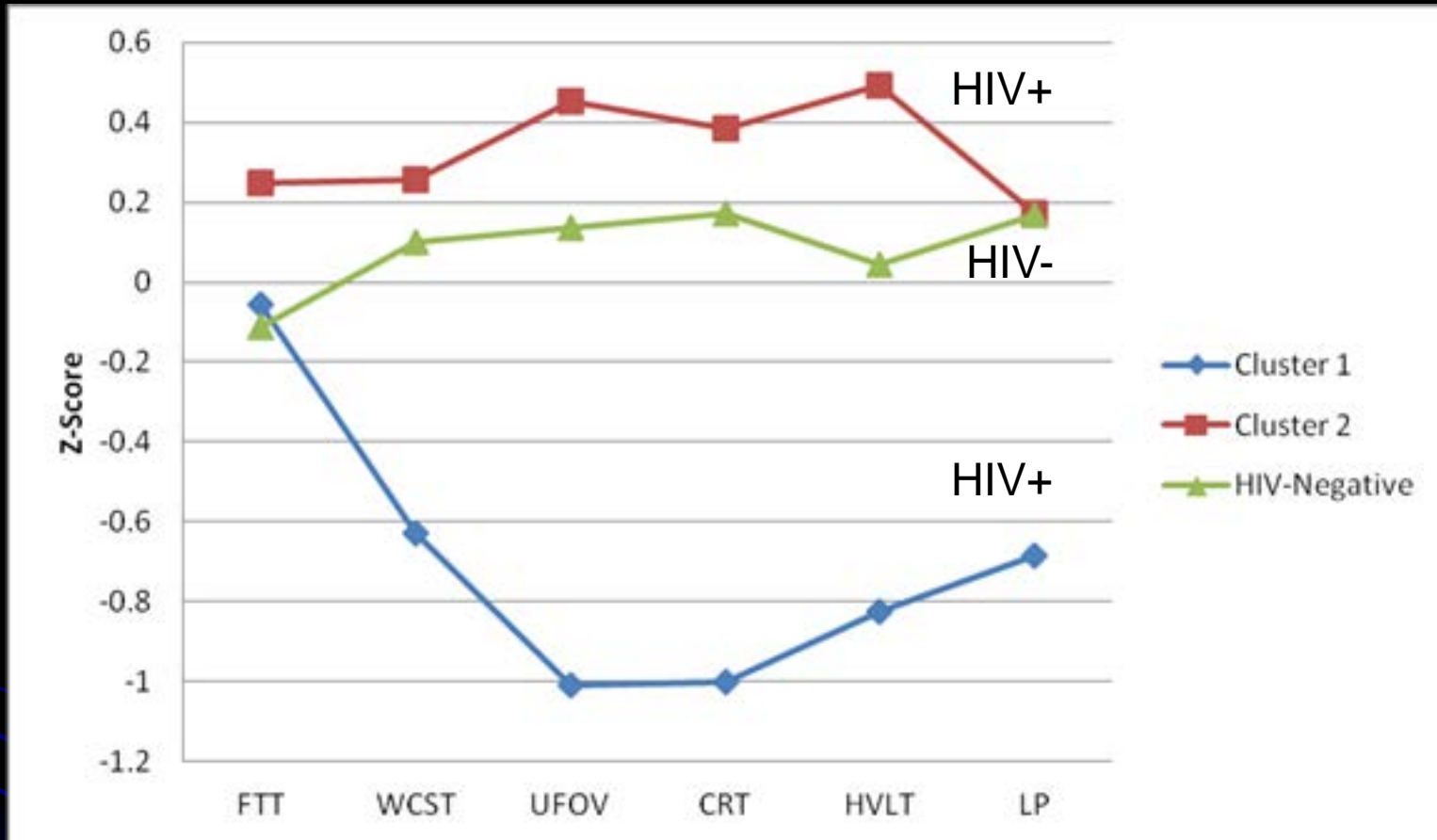


Figure 1. Z-scores for Cognitive Test Performance for Clusters 1 and 2, and the HIV-Negative Group. *Note.* FTT = Finger Tapping Test; WCST = Wisconsin Card Sorting Test; UFOV[®] = Useful Field of View; CRT = Complex Reaction Time; HVL = Hopkins Verbal Learning Test; LP = Letter and Pattern Comparison. 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).
- **Employment** (Woods, Weber et al., 2011).
- **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.

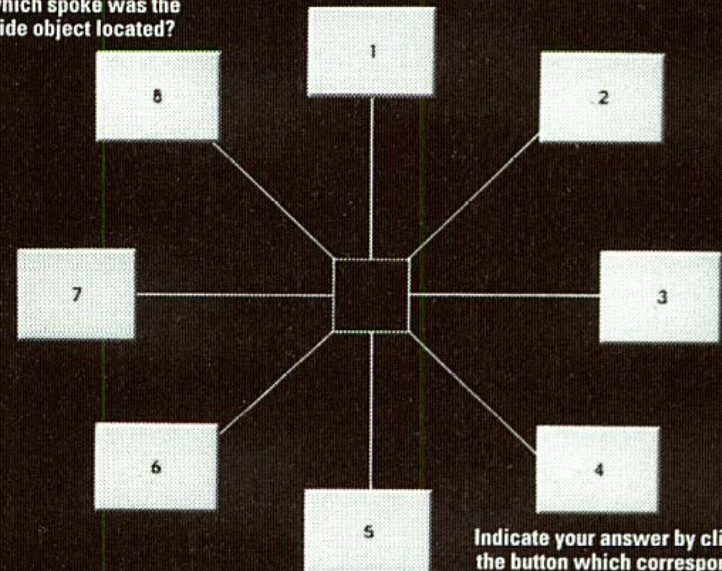
Touch continue for a demonstration



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



On which spoke was the outside object located?

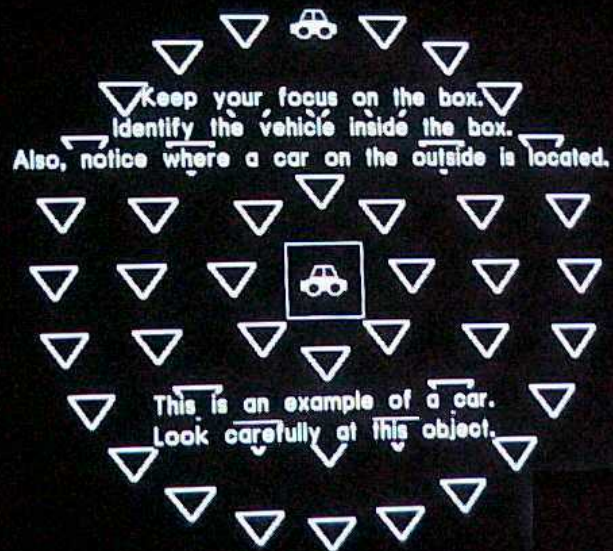


Indicate your answer by clicking the button which corresponds to the location of the target.

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.

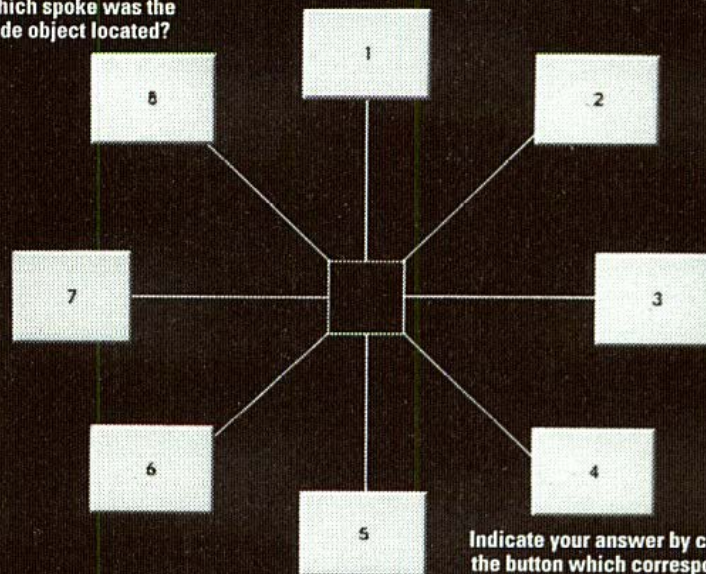
Touch continue for a demonstration



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



On which spoke was the outside object located?

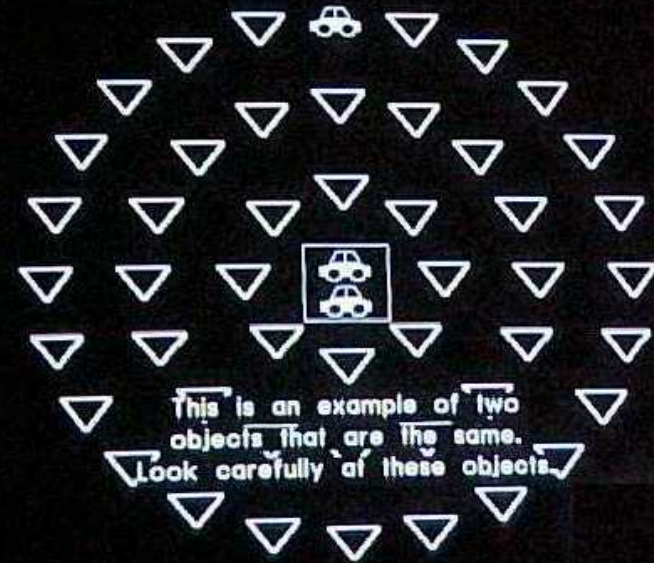


Indicate your answer by clicking the button which corresponds to the location of the target.

Welcome to UFOV Test 4

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

Touch continue for a demonstration

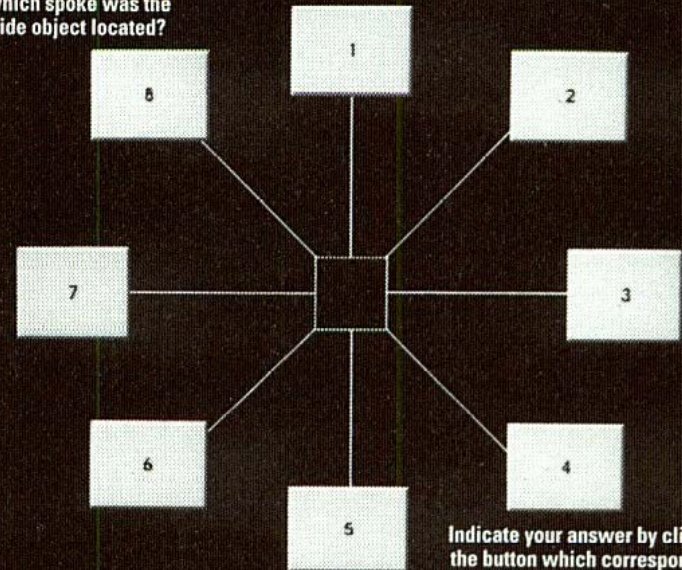


After each presentation you will be asked this question.
Were the objects the same or different?

Same

Different

On which spoke was the outside object located?



Indicate your answer by clicking the button which corresponds to the location of the target.

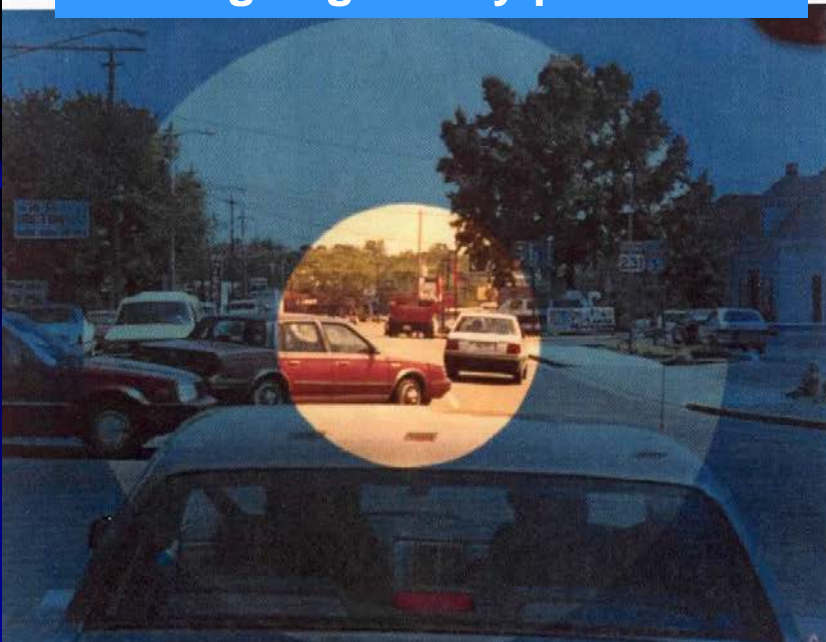
GOOD UFOV – Can see more information at a moment's glance.



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



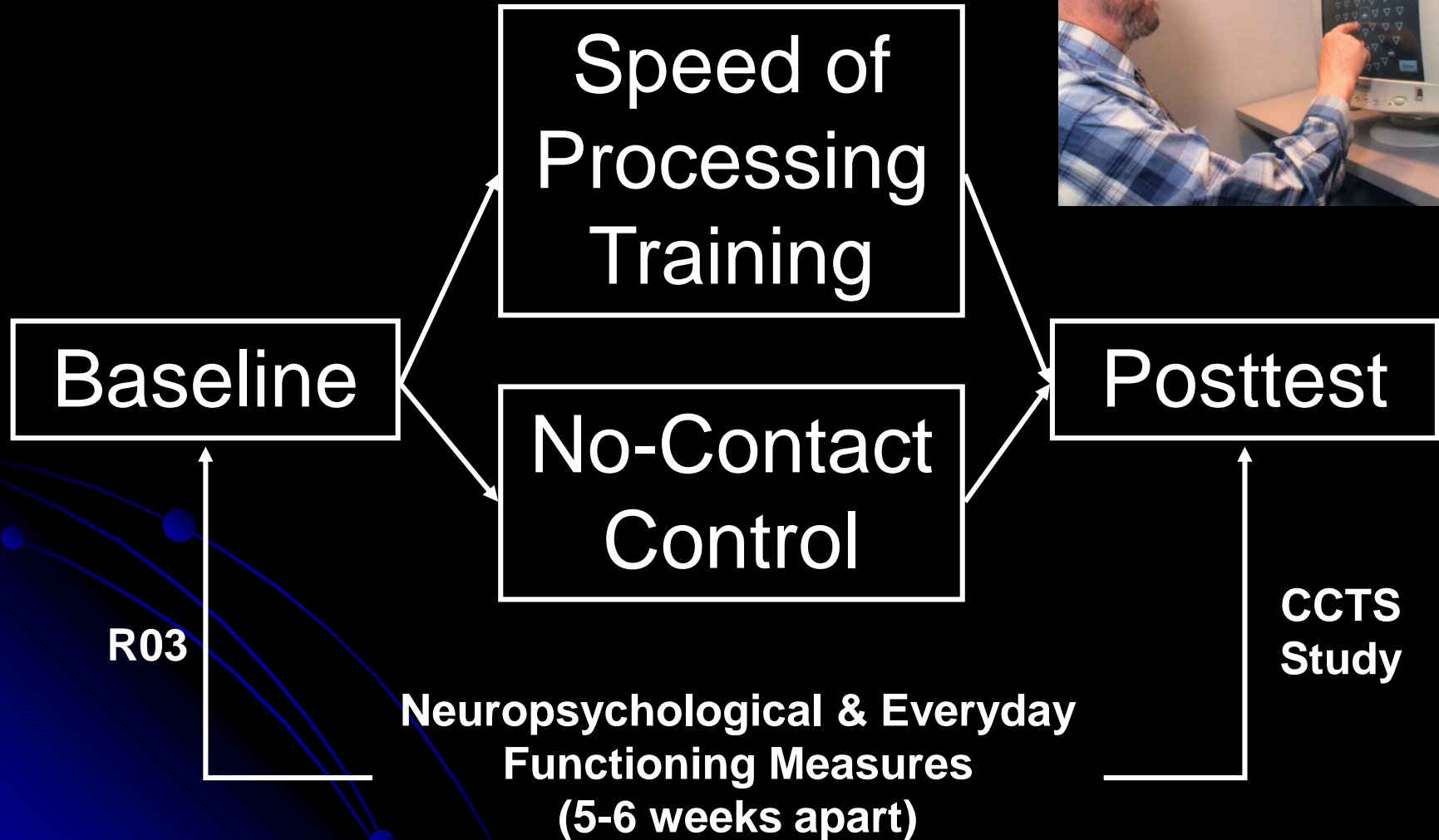
In Our Previous Driving Simulator Study

- 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

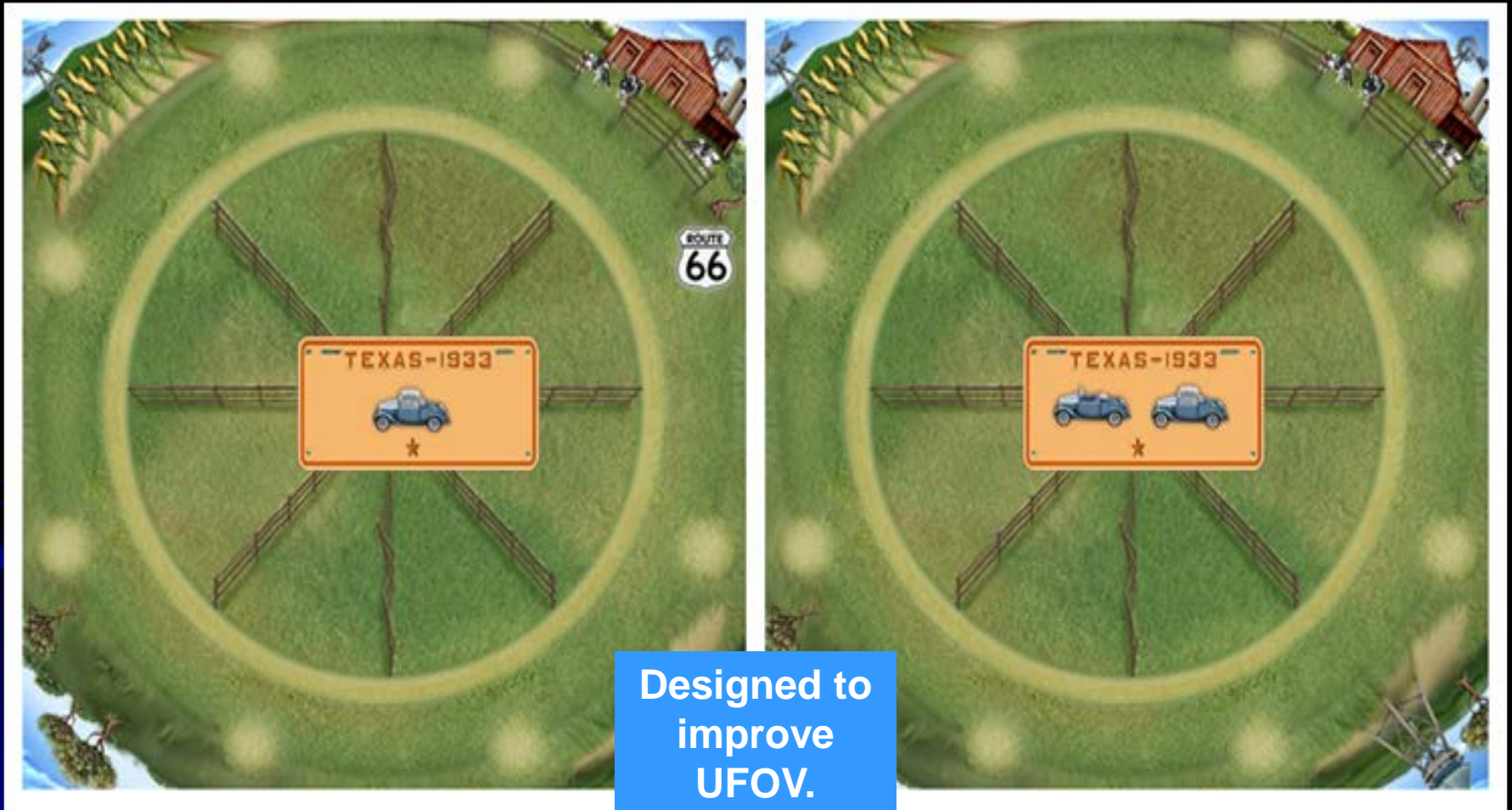
- This **speed of processing training** protocol has been used to improve the rate at which normal, community-dwelling older adults process information (Vance, Dawson, Wadley, Edwards, Roenker, Rizzo, & Ball, 2007).
- It has been shown to improve driving performance and measures of everyday functioning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



Methods

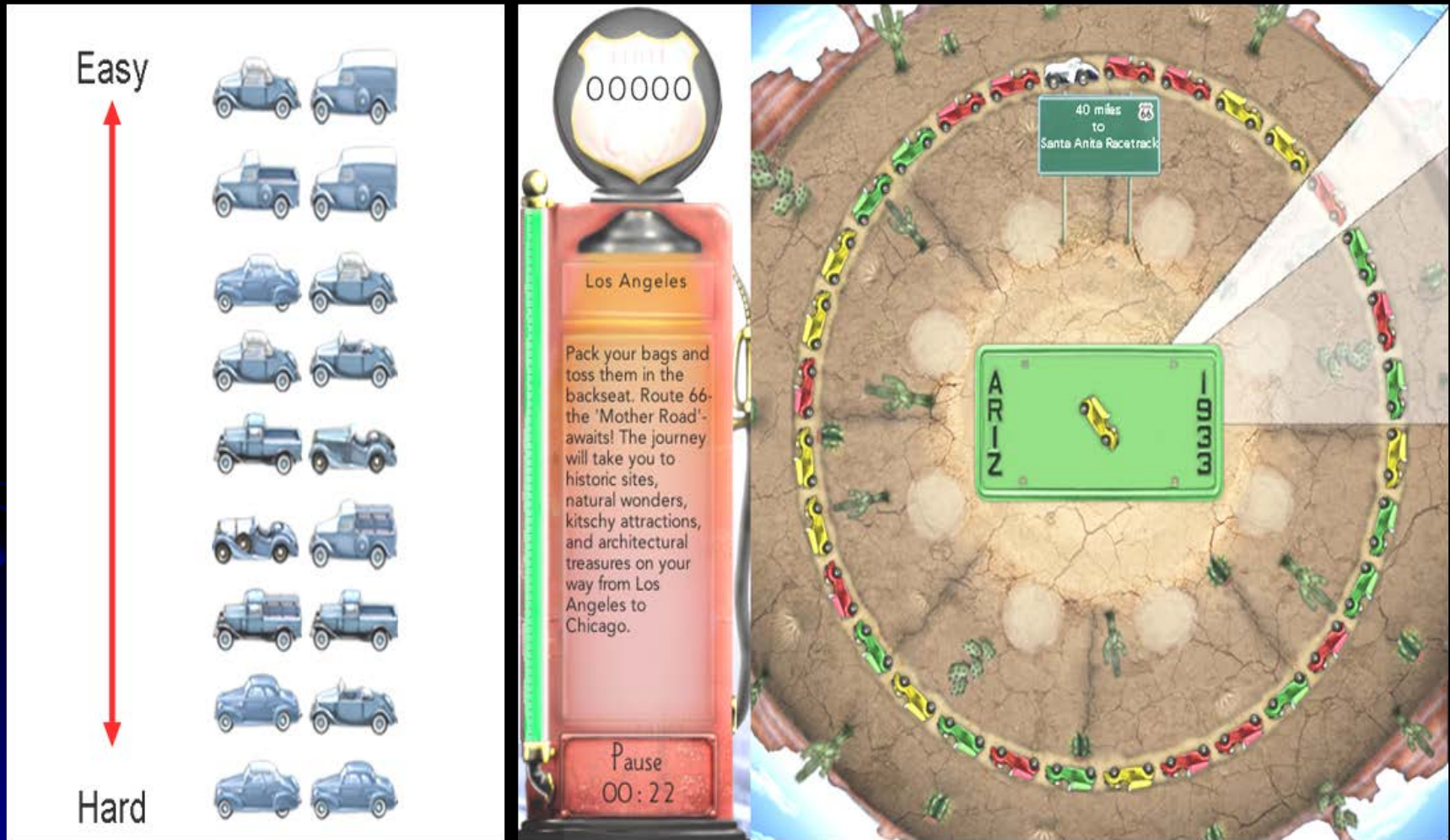
- Speed of Processing Training



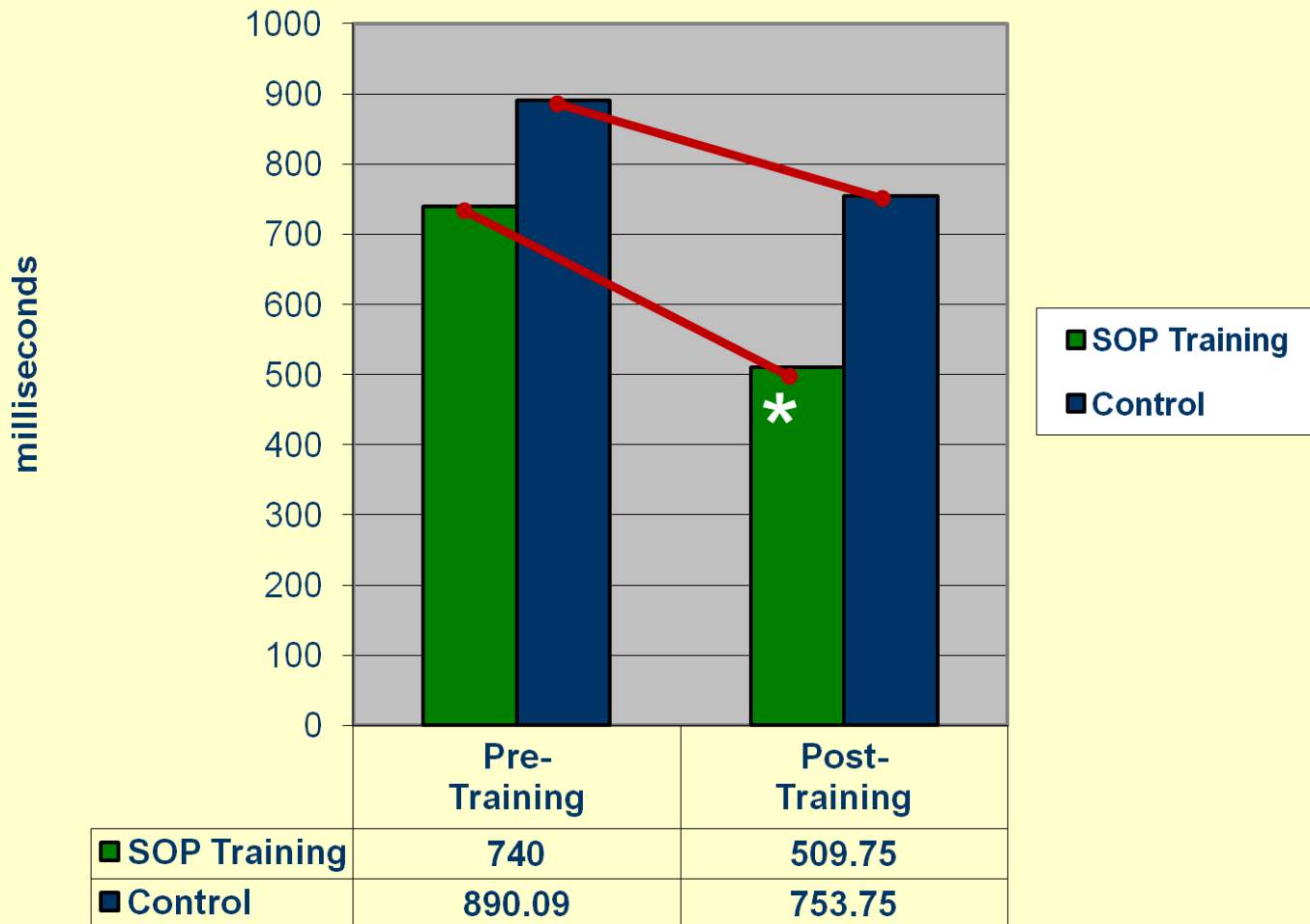
Vance, D. E., Dawson, J., Wadley, V. G., Edwards, J. D., Roenker, D. L., Rizzo, M., & Ball, K. K. (2007). The Accelerate Study: The longitudinal effect of speed of processing training on cognitive performance of older adults. *Rehabilitation Psychology, 51*(1), 89-96. DOI: 10.1037/0090-5550.52.1.89

Methods

- Speed of Processing Training (continued)



Pre and Post UFOV Scores for Training Groups



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 moments glance.

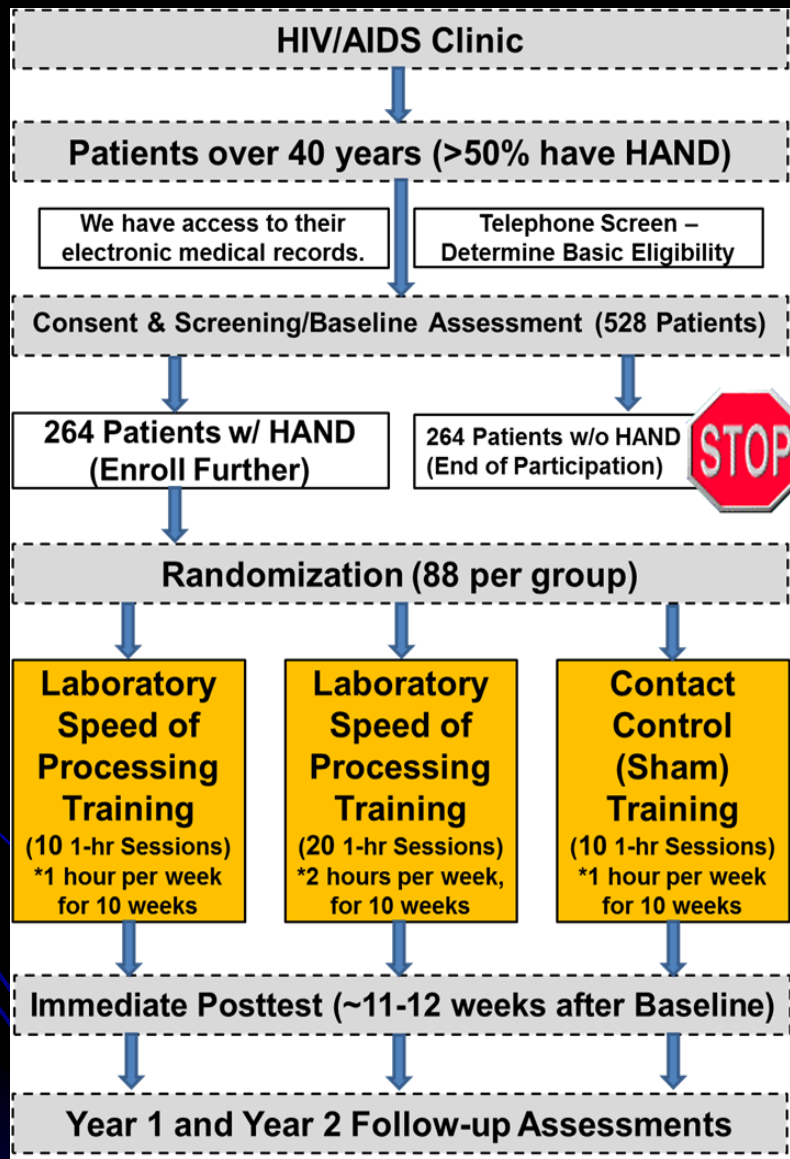
ACTIVE Studies

HIV ISSUES	SOP TRAINING BENEFITS
Decreased Speed of Processing	Improved Speed of Processing
Poorer Driving	Improved Driving
Poorer IADL Performance	Improved IADL Performance
Decreased Locus of Control	Improved Locus of Control
Risk for Depression	Protection against Depression
Poorer Self-rated Health	Improved Self-rated Health
Poorer Health-related Quality of Life	Improved Health-related Quality of Life

THE THINKFAST STUDY

Driving Simulation assessed at Baseline, Posttest, Year 1, and Year 2

Retrospective and Prospective Accident Reports will be gathered from the Division of Motor Vehicles.



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)

Case Study from THINKFAST

A simple qualitative comparison was completed between baseline and post-test.

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

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 → 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.

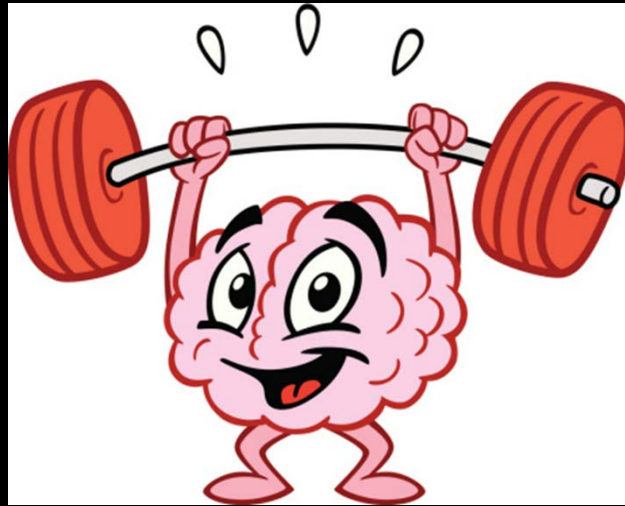
3. CONCLUSION

TAKE HOME POINTS

- ✓ **Use it or lose 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