Cognitive Aging with HIV

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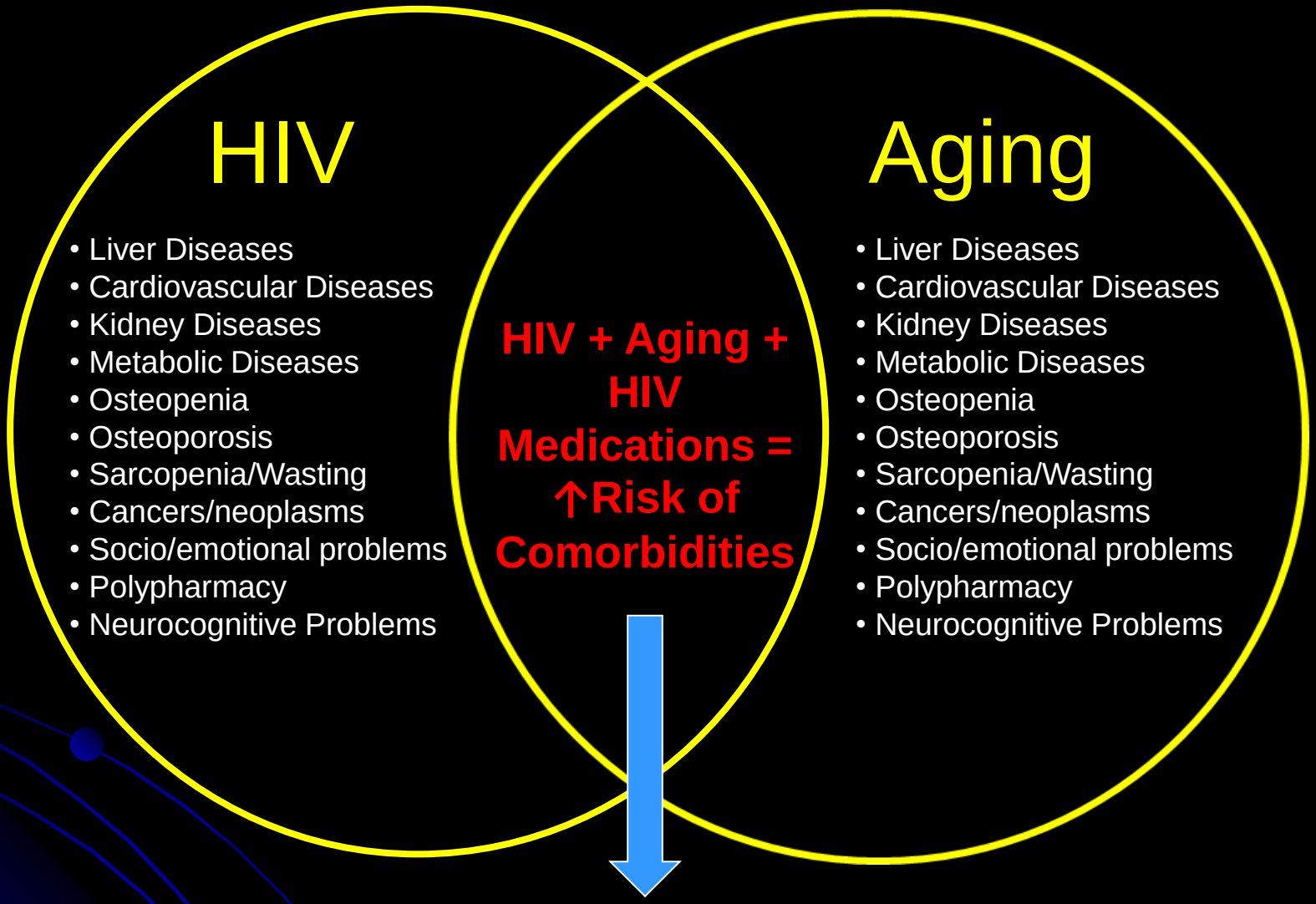
Learning Objectives

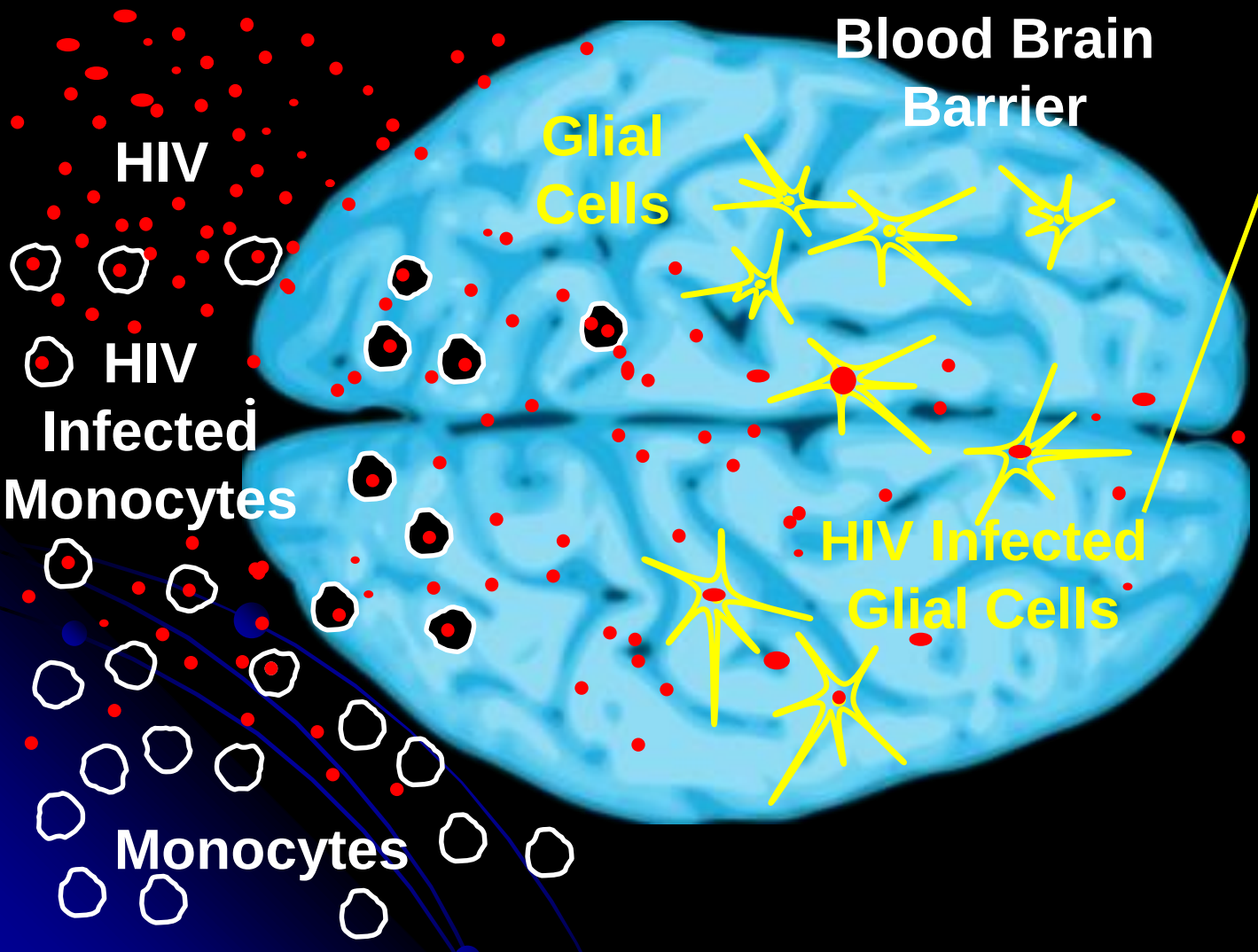
- ✓ To review possible causes of neurocognitive impairment in adults with HIV, especially as they age.
- ✓ To present evidence-based recommendations for treating and addressing neurocognitive problems in patients with HIV.



With the growing numbers of older adults with HIV, this is a concern for nurses and the healthcare system.

Vance, D. E. (2010). Aging with HIV: Clinical considerations on an emerging population. *American Journal of Nursing, 110*(3), 42-47.

How does HIV enter the brain?



↑ Neurotoxic Molecules

↓

↑ Neuro-inflammation/
↓ Neuronal Health

↓

↓ Cognitive Reserve

↓

↑ Cognitive Impairment

* It is both monocytes and particularly macrophages.

Vance, D. E., Humphrey, S. C., & Batey, D. S. (in press). HIV-related cognitive dysfunction: Implications for aging and social work. *Social Work in Mental Health.*

FRASCATI CRITERIA

- **HIV-Associated Neurocognitive Disorder (HAND) Criteria**
  - Frascati Criteria (Post-cART)
- **Asymptomatic Neurocognitive Impairment (ANI)**
  - > 1 SD normative mean on at least 2 cognitive domains (attributable to HIV)
- **Mild Neurocognitive Disorder (MND)**
  - > 1 SD normative mean on at least 2 cognitive domains (attributable to HIV)
  - Mild functional decline (e.g., self/proxy-report of decline in 2 ≥ IADLs, vocational impairment, poor performance in laboratory based IADLs)
- **HIV-Associated Dementia (HAD)**
  - > 2 SD normative mean on at least 2 cognitive domains (attributable to HIV)
  - Mild functional decline (e.g., self/proxy-report of decline in 2 ≥ IADLs, vocational impairment, poor performance in laboratory based IADLs)

How many adults with HIV have HAND? 14% 30% 50% 70%?

How many adults with HIV have HAD? 2% 5% 10% 14%?

~20% Bi-directional Fluctuation over Time (Antinori et al., 2007. *Neurology, 69,* 1789-1799.)

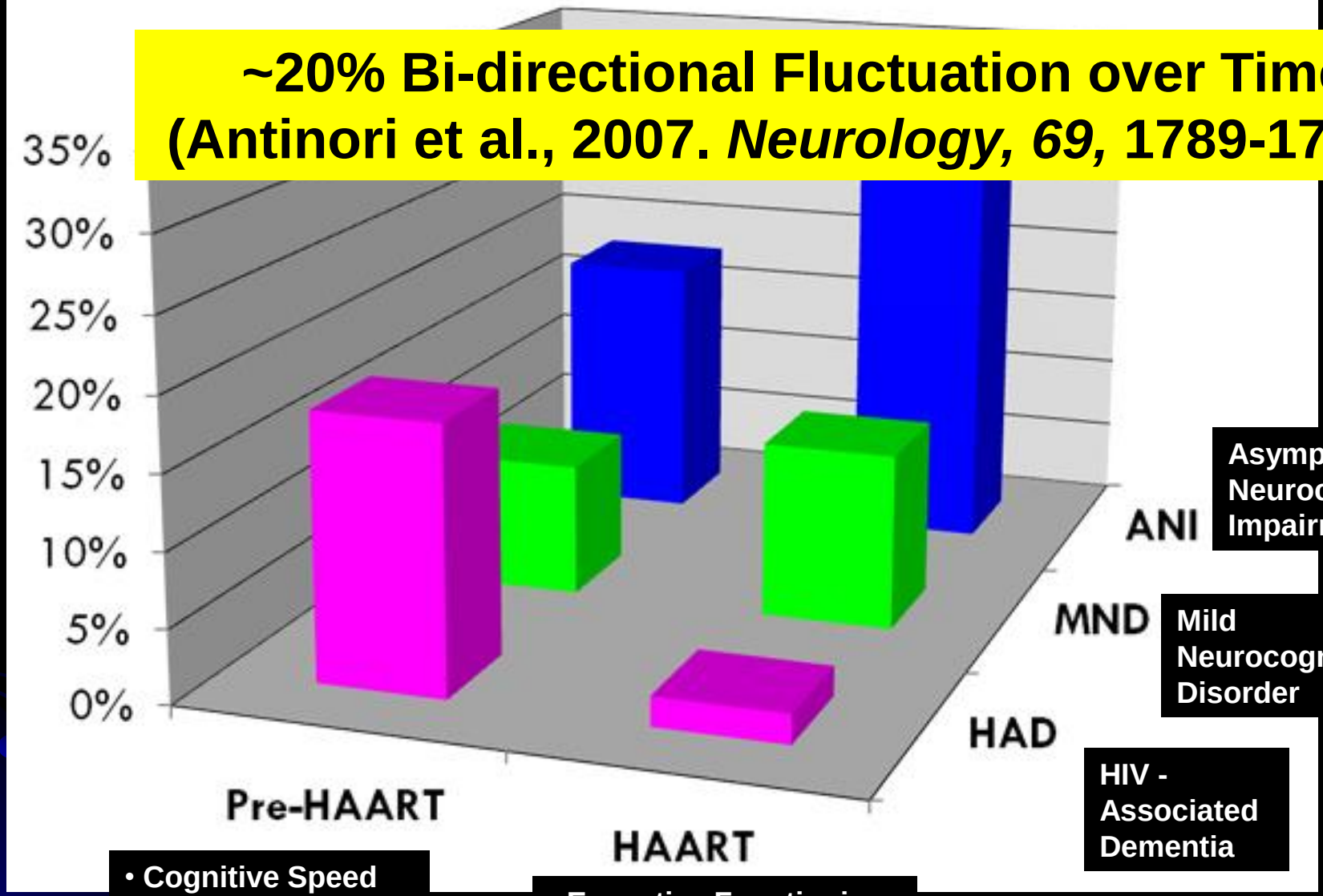


Figure 1. Note. Croteau, D. Pharmacologic interventions for HIV-associated neurocognitive disorders. *Psychology and AIDS Exchange Newsletter.* Retrieved from http://www.apa.org/pi/aids/resources/exchange/2013/01/pharmacologic-interventions.aspx

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- Age: 56
- AIDS Diagnosis: 2007
  - CD4 Count – 6 cells/mm^3
  - 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!”

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- **2010 Neuropsychological Assessment: Mixed Results**

- "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. Specifically, Mr. Nicholas scored in the mildly to moderately impaired range on the Controlled Oral Association By Letter subtest (raw=22), consistent with verbal fluency deficits (**due to deficits in frontal lobe functioning**) associated with HIV-related dementia."

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- **TODAY**

- “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.”

- “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.”

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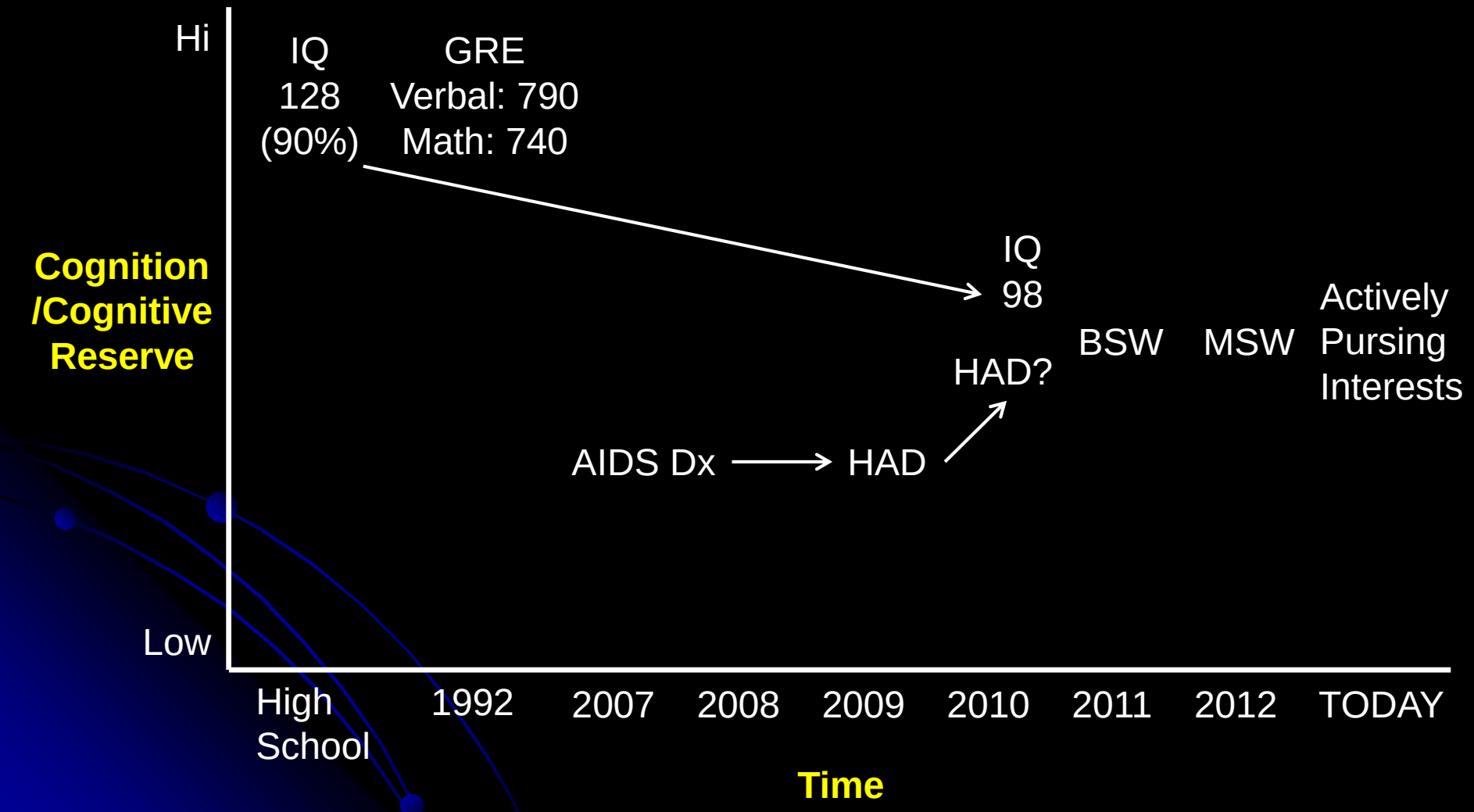

Hi
IQ
128
(90%)
GRE
Verbal: 790
Math: 740
Cognition /Cognitive Reserve
IQ
98
BSW
MSW
Actively Pursing Interests
HAD?
AIDS Dx
HAD
Low
High School
1992
2007
2008
2009
2010
2011
2012
TODAY
Time

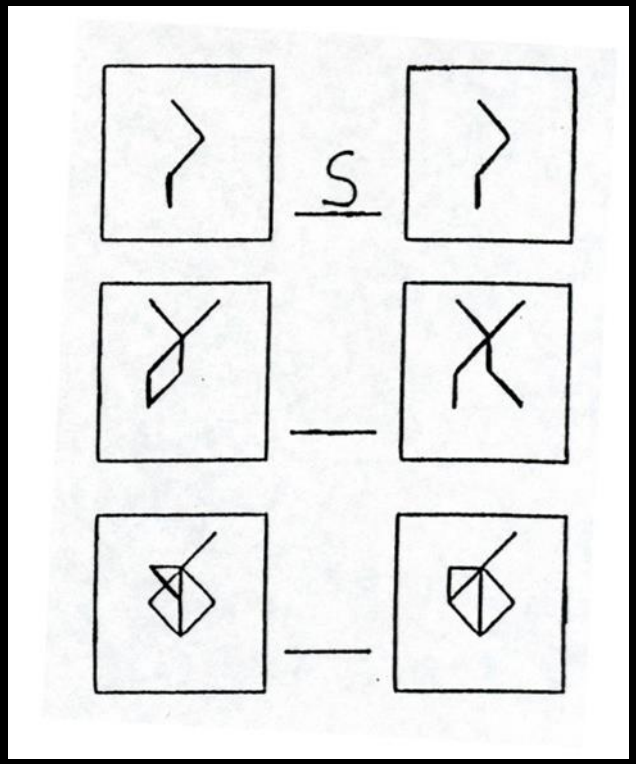


TABLE 2

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

	HIV-POSITIVE		HIV-NEGATIVE		
	YOUNGER (*n* = 55)	OLDER (n = 33)	YOUNGER (*n* = 43)	OLDER (n = 41)	FINDINGS
	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.

Vance, D. E., Fazeli, P. L., & Gakumo, C. A. (2013). The impact of neuropsychological performance on everyday functioning between older and younger adults with and without HIV. *Journal of the Association of Nurses in AIDS Care, 24*(2), 112-125.

Cluster Analysis

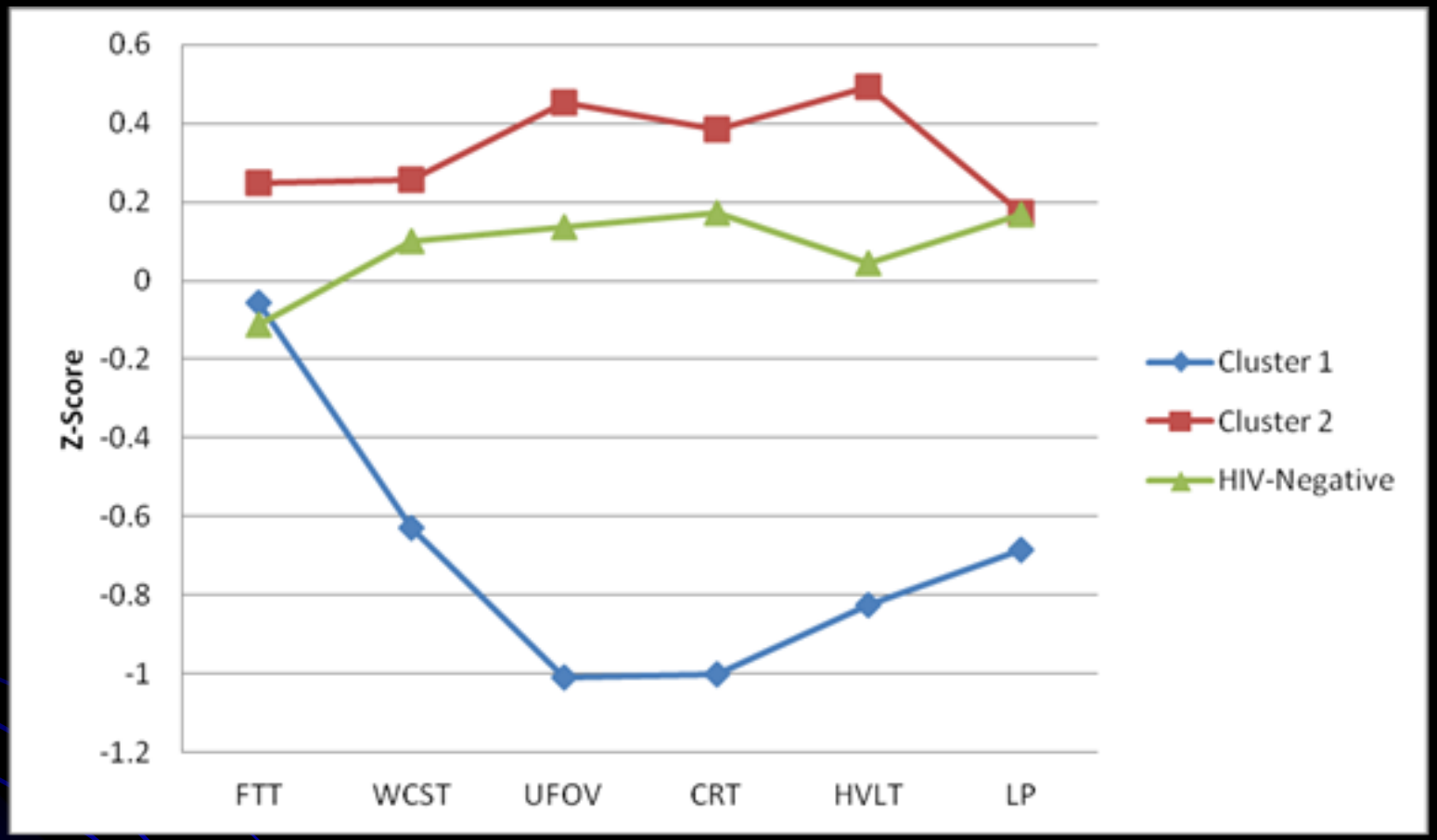


Figure 1. *Z*-scores for Cognitive Test Performance for Clusters 1 and 2, and the HIV-Negative Group. *Note.* FTT = Finger Tapping Test; WCST = Wisconsin Card Sorting Test; UFOV® = Useful Field of View; CRT = Complex Reaction Time; HVLT = Hopkins Verbal Learning Test; LP = Letter and Patter Comparison. For the purpose of clarity, higher *z*-scores reflect higher performance for all variables.

Fazeli, P. L., Crowe, M., Ross, L. A., Wadley, V., Ball, K. K., & Vance, D. E. (2014). Cognitive functioning in adults aging with HIV: A cross-sectional analysis of cognitive subtypes and influential factors. *Journal of Clinical Research in HIV/AIDS and Prevention, 1*(4), 1-12. DOI: 10.14302/issn.2324-7339.jcrhap-13-191

Table 5

Demographic and Mental and Physical Health Differences of the HIV+ Clusters and the HIV-Negative Reference Group (Total $N = 162$)

	Cluster						
	Cluster 1 ($n = 32$)		Cluster 2 ($n = 46$)		HIV- Group ($n = 84$)		
Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*	*p*-value
Age	51.27	10.84	43.36	8.83	47.93	13.06	< .05 [a]
No. Over Age 50 (%)	19 (59%)		12 (26%)		41 (49%)		< .01 [a, c]
No. Men (%)	22 (69%)		37 (80%)		33 (39%)		< .05 [b, c]
No. Heterosexuals (%)	20 (63%)		19 (41%)		78 (93%)		< .05 [b, c]
No. Caucasians* (%)	8 (25%)		21 (46%)		29 (36%)		*ns*
No. Working (%)	2 (6%)		10 (22%)		35 (42%)		< .001 [b, c,†]
Income	1.56	0.84	1.87	1.61	1.98	1.53	*ns*
Education (years)	12.66	2.51	12.85	2.49	12.79	1.68	*ns*
No. Med. Conditions	1.94	1.24	1.34	1.02	1.06	0.99	< .01 [a, b]
No. w/ Hepatitis C (%)	14 (44%)		12 (26%)		6 (7%)		< .001 [b, c,†]
No. w/ Mood Prob. (%)	18 (56%)		26 (57%)		33 (39%)		*ns*
No. w/ Stroke (%)	6 (19%)		1 (2%)		5 (6%)		< .05 [a, b]
No. w/ Hypertension (%)	20 (63%)		18 (39%)		32 (38%)		< .05 [a, b]
No. w/ Diabetes (%)	4 (13%)		5 (11%)		10 (12%)		*ns*
No. Medications	5.25	3.85	4.54	3.04	2.18	2.74	< .001 [b, c]
POMS Total	35.59	32.94	35.39	45.05	28.26	37.89	*ns*
POMS-Positive	16.94	6.43	18.28	6.87	19.27	6.52	*ns*
POMS-Negative	52.53	30.55	53.67	40.53	47.54	34.87	*ns*
Stressful Life Events	263.56	151.71	271.59	132.10	238.51	164.16	*ns*
ASI-Alcohol Use	0.07	0.15	0.35	0.75	0.24	0.45	*ns*
ASI-Drug Use	0.03	0.06	0.03	0.08	0.02	0.04	*ns*

Notes. *M* = Mean; No. = number; *SD* = standard deviation; Working = currently working either part-time or full-time; For income, 1 = $0 - $10,000 and 8 = over $70,000; No. Med. Conditions = total number of neuromedical conditions; Mood prob. = self-reported mood problems (depression or anxiety); POMS Total = Profile of Mood States total mood disturbance score; Stressful life events = Social Readjustment Scale score; ASI = Addiction Severity Index. * = All others were African American except one who was Native American who was HIV-positive.

[a] Cluster 1 differs from Cluster 2 at $p < .05$

[b] Cluster 1 differs from HIV- Group at $p < .05$

[c] Cluster 2 differs from HIV- Group at $p < .05$

† $p < .10$ for Cluster 1 versus Cluster 2

Fazeli, P. L., Crowe, M., Ross, L. A., Wadley, V., Ball, K. K., & Vance, D. E. (2014). Cognitive functioning in adults aging with HIV: A cross-sectional analysis of cognitive subtypes and influential factors. *Journal of Clinical Research in HIV/AIDS and Prevention, 1*(4), 1-12. DOI: 10.14302/issn.2324-7339.jcrhap-13-191

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

(example 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).

BEHAVIORAL COGNITIVE INTERVENTIONS

Methods

Speed of Processing Training

Baseline

Posttest

No-Contact Control

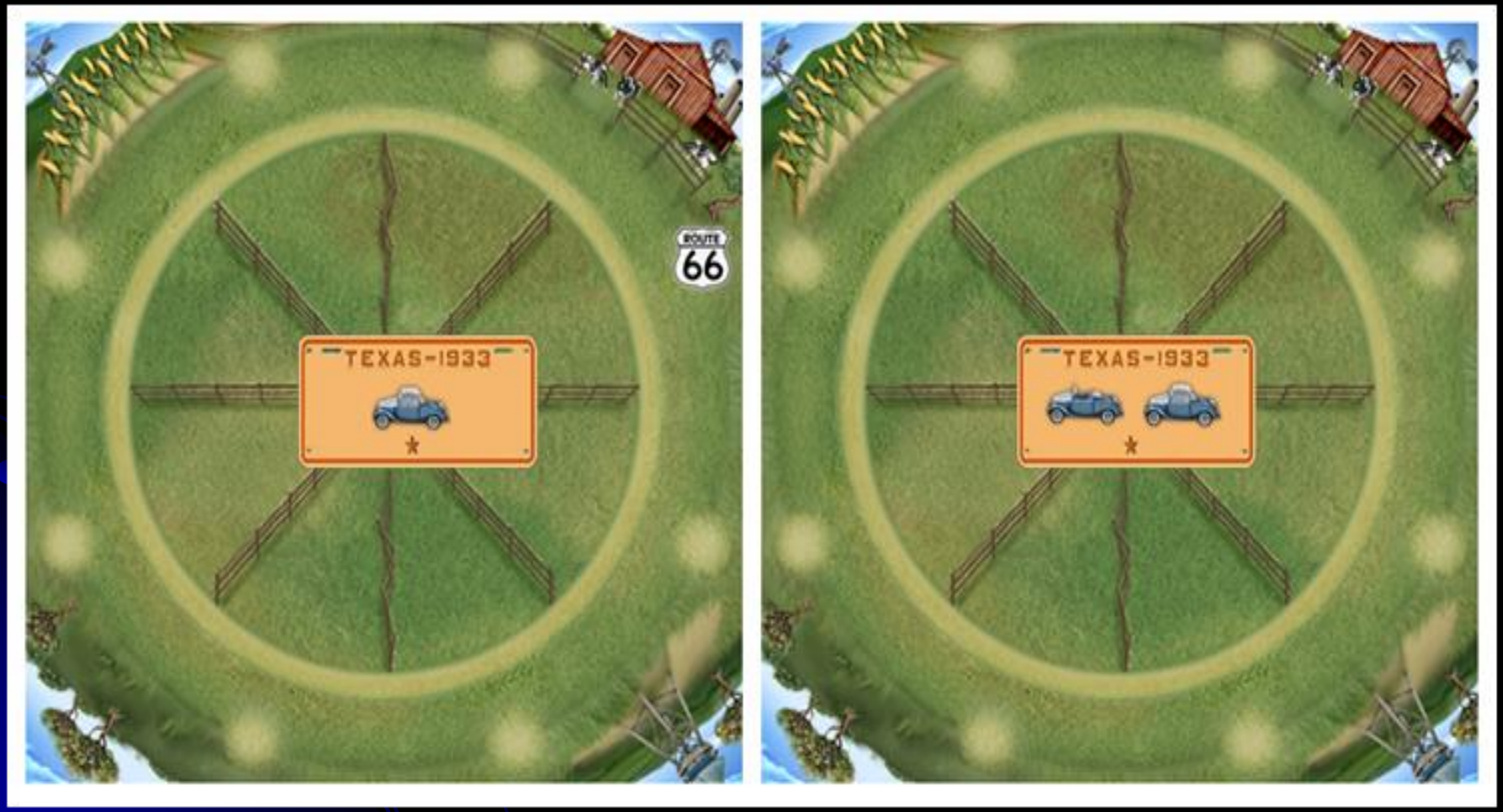
R03

CCTS Study

Neuropsychological & Everyday Functioning Measures (5-6 weeks apart)

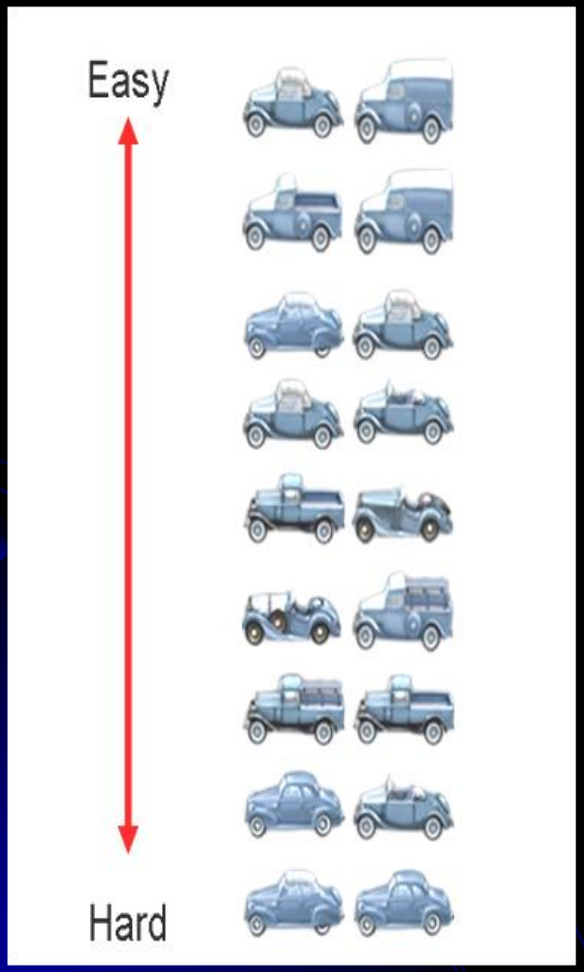
Methods

- Speed of Processing Training

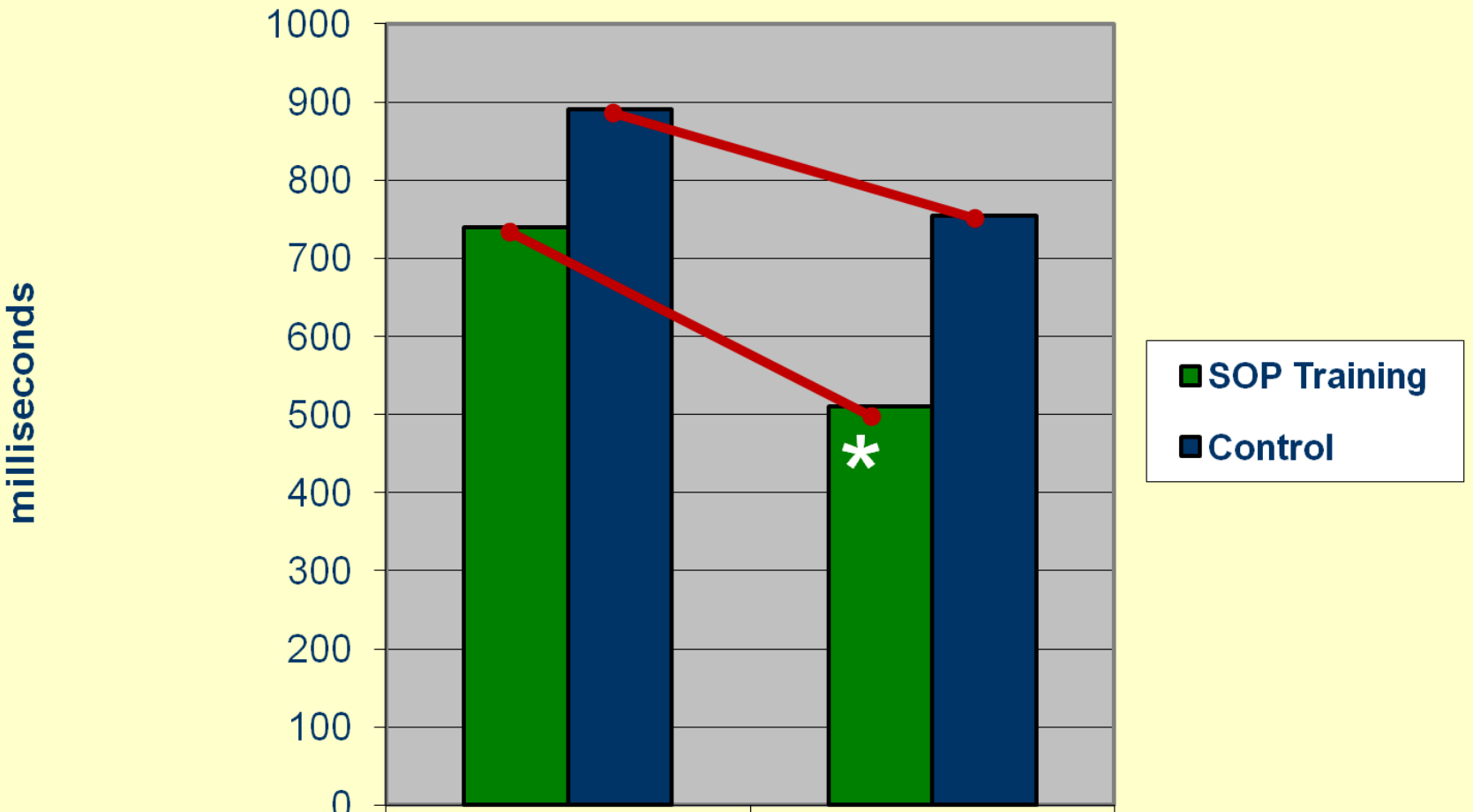


Methods

- Speed of Processing Training (continued)

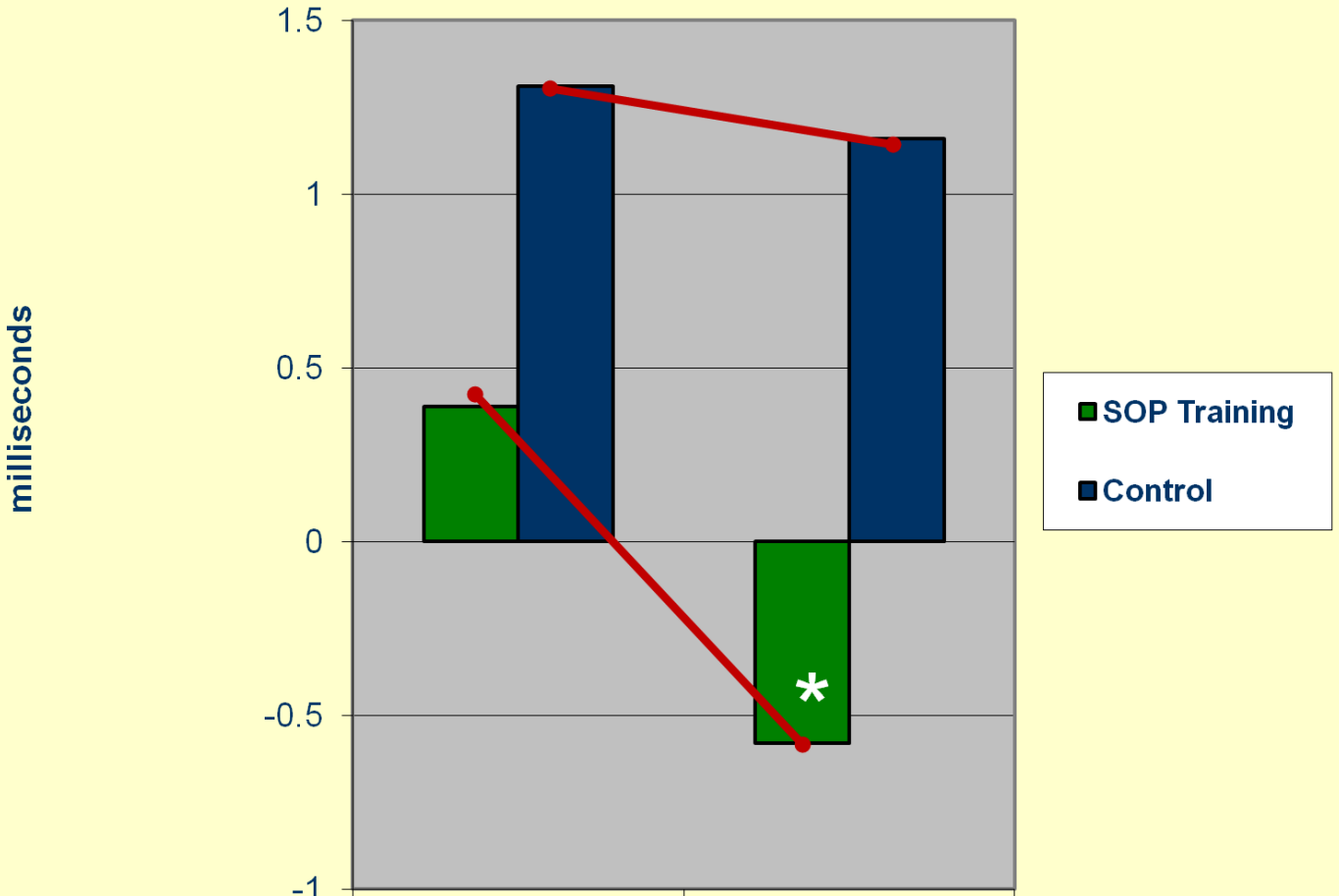


Pre and Post UFOV Scores for Training Groups



	Pre-Training	Post-Training
SOP Training	740	509.75
Control	890.09	753.75

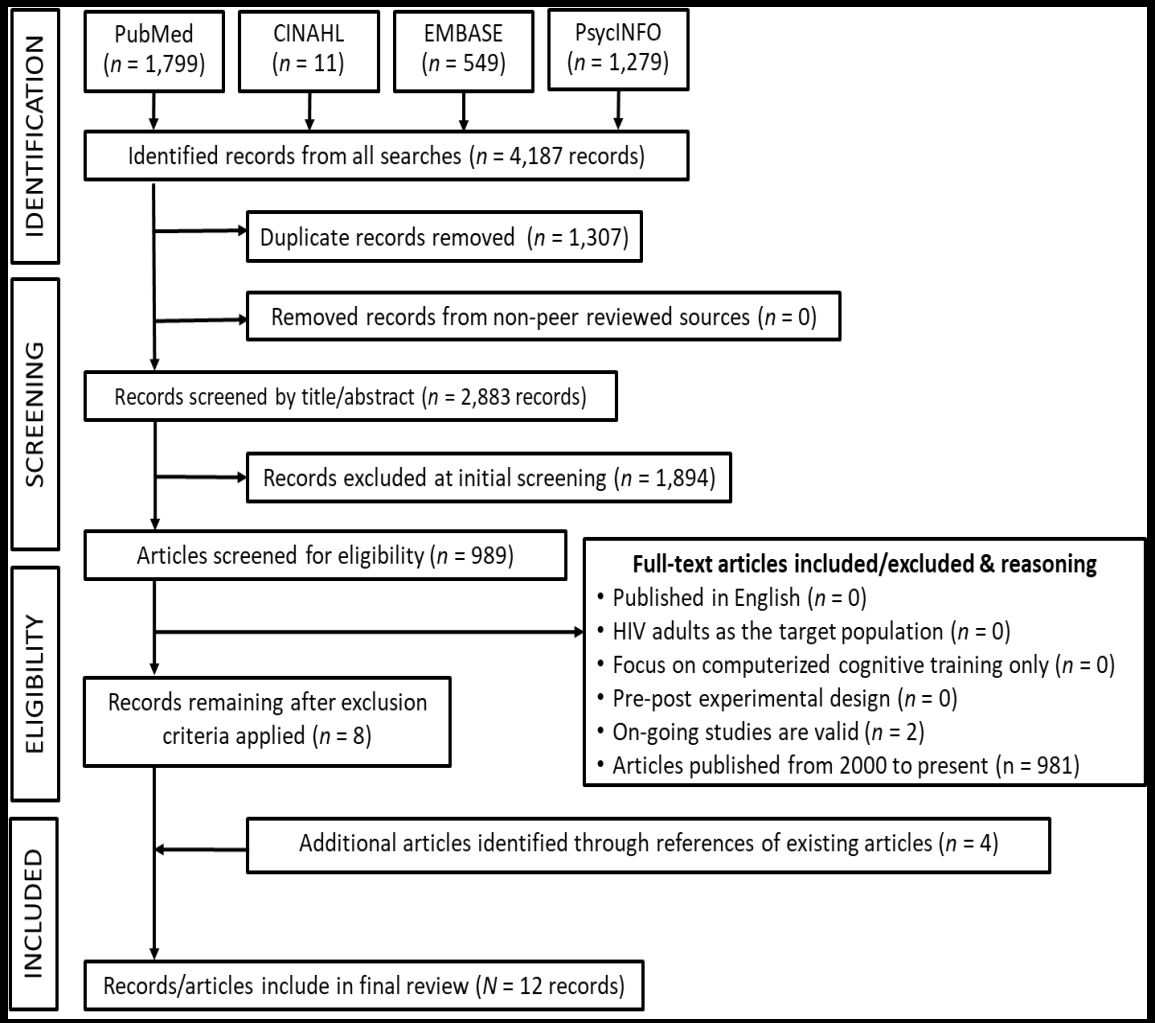
Pre and Post TIADL Scores for Training Groups



	Pre-Training	Post-Training
SOP Training	0.39	-0.58
Control	1.31	1.16

Cognitive Training in HIV Adults

- For the most part, cognitive training programs have shown improvement in domains in which training was targeted.
- Targeted areas of training varied ranging from speed of processing, attention, and memory.
- Improvement in overall cognitive functioning is not well established.



Vance, D. E., Fazeli, P. L., Cheatwood, J., Nicholson, C., Morrison, S., & Moneyham, L. (2019). Computerized cognitive training for the neurocognitive complications of HIV infection: A systematic review. Journal of the Association of Nurses in AIDS Care.

Cognitive Effects of Ketogenic Diet in Older, PLWH With HIV-Associated Neurocognitive Impairment (HANI)

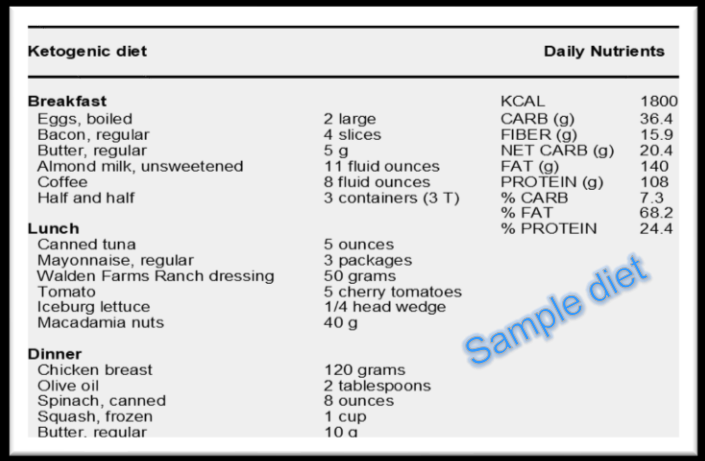
(Morrison, Fazeli, Gower, Willig, Younger, Sneed, & Vance) JANAC (under review)

GOAL: Examine effects of a ketogenic diet on cognition in older PLHW with HANI

- 14 community-dwelling older adults with HIV *(≥ 50 years)*
- **Two Groups** *(random assignment)*
  1. Ketogenic diet group **(KGD)**: (*n* = 7)
  2. Patient choice diet **(PCD)** (*n* = 7)

INTERVENTION:

- **12-week diet intervention**
  - Eucaloric *(i.e., weight maintaining)*
    - Energy requirements: *Harris-Benedict formula (activity factor of 1.35 x10%*)*
    - Carb 43%; protein 20-25%; and fat 30-35%
    - Food selected from menu/weekly courier delivery



Ketogenic diet		Daily Nutrients	
Breakfast		KCAL	1800
Eggs, boiled	2 large	CARB (g)	36.4
Bacon, regular	4 slices	FIBER (g)	15.9
Butter, regular	5 g	NET CARB (g)	20.4
Almond milk, unsweetened	11 fluid ounces	FAT (g)	140
Coffee	8 fluid ounces	PROTEIN (g)	108
Half and half	3 containers (3 T)	% CARB	7.3
		% FAT	68.2
Lunch		% PROTEIN	24.4
Canned tuna	5 ounces		
Mayonnaise, regular	3 packages		
Walden Farms Ranch dressing	50 grams		
Tomato	5 cherry tomatoes		
Iceburg lettuce	1/4 head wedge		
Macadamia nuts	40 g		
Dinner			
Chicken breast	120 grams		
Olive oil	2 tablespoons		
Spinach, canned	8 ounces		
Squash, frozen	1 cup		
Butter, regular	10 g		

Sample diet

- **KGD:** Cognitive gains in the domains of executive function, speed of processing, attention, and visuospatial tracking
- **PCD:** Remained same or worsened
  - Anecdotal: TNF-a decreased in the KDG only
  - Tolerated well, no changes in cardiometabolic indicators

ENGAGMENT

- 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 (ALF) 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)

Fazeli, P. L., Woods, S. P., Heaton, R. K., Umlauf, A., Couaux, B., Rosario, D., …The HNRP Group (2014). An active lifestyle is associated with better neurocognitive functioning in adults living with HIV infection. *Journal of Neurovirology.* DOI:10.1007/s13365-014-0240-z

ENGAGEMENT

Older adults (*N* = 181) were randomly assigned to control and experimental groups.

Experimental group: attended 20 weekly social meetings during which they worked in teams to develop creative solutions to problems

Control group: did not attend any social meetings

- Compared to the control group, the experimental group who engaged in team problem-solving exhibited a positive change in neurocognitive ability from pretest to posttest.

- Areas of improvement observed in the experimental group were processing speed, inductive reasoning, and divergent thinking.

Social Engagement

Neurocognition

Stine-Morrow, E. A., Parisi, J. M., Morrow, D. G., & Park, D. C. (2008). The effects of an engaged lifestyle on cognitive vitality: A field experiment. *Psychology and Aging, 23*(4), 778-786. doi:10.1037/a0014341

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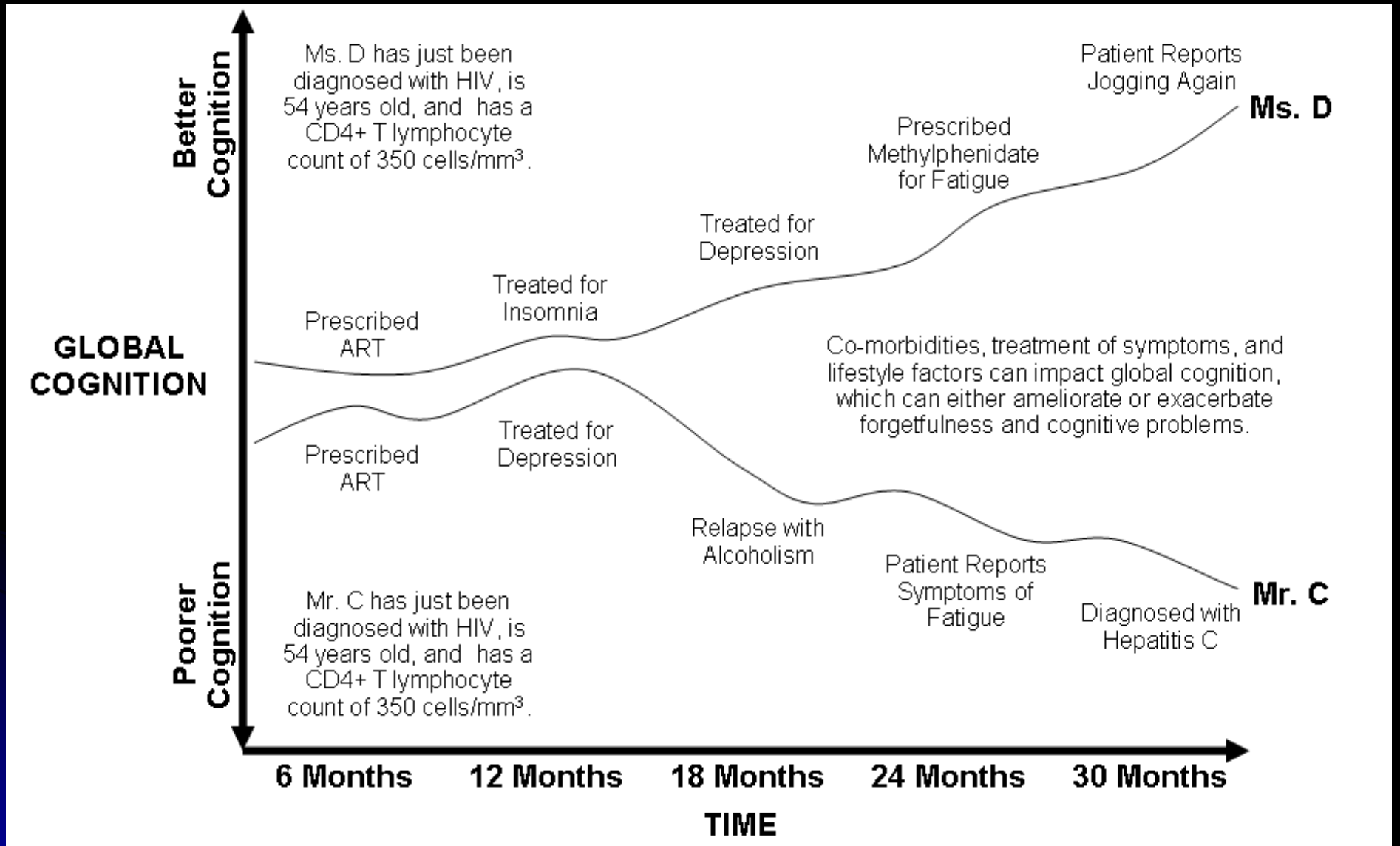
Suggests and Compensation Strategies by Nick

- **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.

Vance, D. E., Nicholas, N., & Humphrey, S. C. (2015). HIV neurocognitive impairment and aging: Perspectives on neurocognitive reserve and behavioral remediation/compensation strategies. Austin Journal of Neuropsychiatry and Clinical Neurosciences, 1(1): 1002.

PARTING THOUGHTS


Better Cognition
Poorer Cognition
GLOBAL COGNITION
Ms. D has just been diagnosed with HIV, is 54 years old, and has a CD4+ T lymphocyte count of 350 cells/mm3.
Prescribed ART
Treated for Insomnia
Treated for Depression
Prescribed Methylphenidate for Fatigue
Patient Reports Jogging Again
Ms. D
Co-morbidities, treatment of symptoms, and lifestyle factors can impact global cognition, which can either ameliorate or exacerbate forgetfulness and cognitive problems.
Mr. C has just been diagnosed with HIV, is 54 years old, and has a CD4+ T lymphocyte count of 350 cells/mm3.
Prescribed ART
Treated for Depression
Relapse with Alcoholism
Patient Reports Symptoms of Fatigue
Diagnosed with Hepatitis C
Mr. C
6 Months
12 Months
18 Months
24 Months
30 Months
TIME

TAKE HOME POINTS

- ✓ Use it or loose 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.
- ✓ Be on the lookout for new therapeutic strategies (e.g., brain fitness programs, tDCS)
- ✓ Compensation strategies are available.