# The ABCs of Aging Brain Health in HIV

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# Training Goals and Objectives

- Examine the intersection between aging and HIV and how it increases the risk for poorer brain health and cognitive functioning.

- Review the literature on cognitive aging with HIV.

- Explore methods and interventions to promote brain health and prevent cognitive decline as people age with HIV.

# Disclosures

- I have no potential conflicts of interest to disclose.
- I currently receive grant funding from the National Institutes of Health.
- Some of the slides are derivative of the work I did with the Association of Nurses in AIDS Care (ANAC) on Aging with HIV series. We were given permission to use these slides and share their information.

# Abbreviations

**ART:** Anti-Retroviral Therapy

**HIV:** Human Immunodeficiency Virus

**HAD:** HIV-Associated Dementia

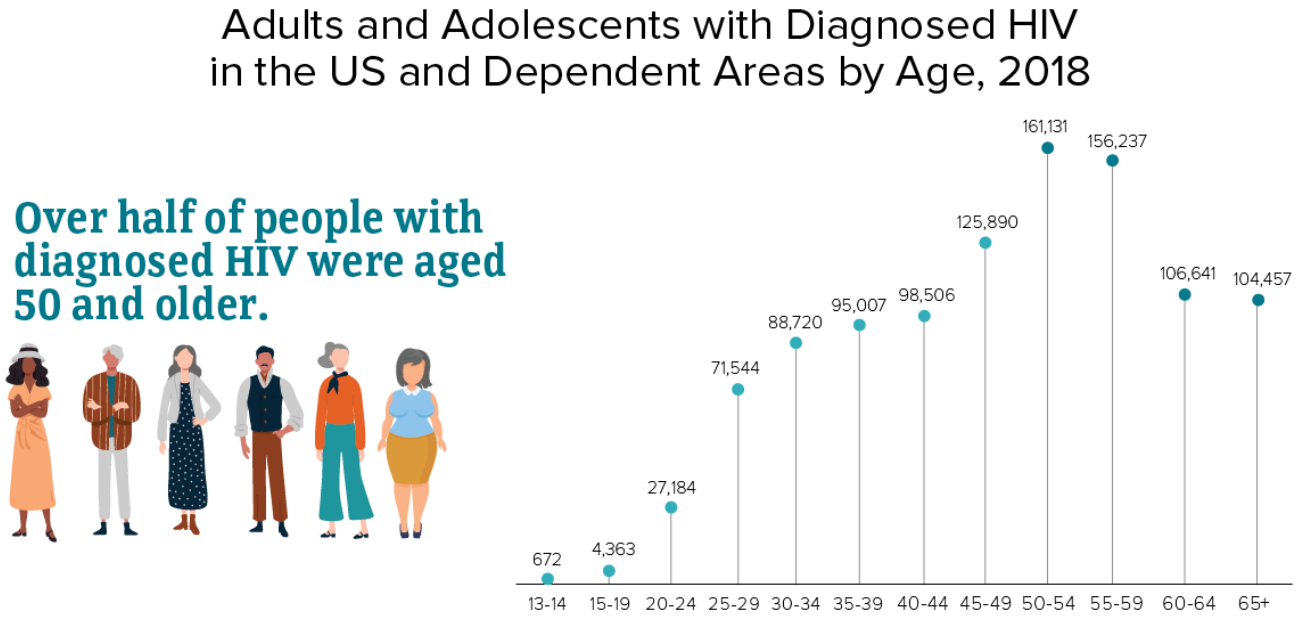
**HAND:** HIV-Associated Neurocognitive Disorder

**MND:** Mild Neurocognitive Disorder

**PLWH:** People Living with HIV

# Aging with HIV: Context

1. By 2030, 70% of People Living with HIV will be 50 and older in the U.S. (Winger, 2016)
2. Multi-morbidity in People Living with HIV
3. Such multi-morbidity can also impact brain health and cognition.




Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2018 (updated). *HIV Surveillance Report* 2020;31.

# Aging with HIV: Context

Brain health and optimal cognitive functioning is essential for successful aging with HIV.

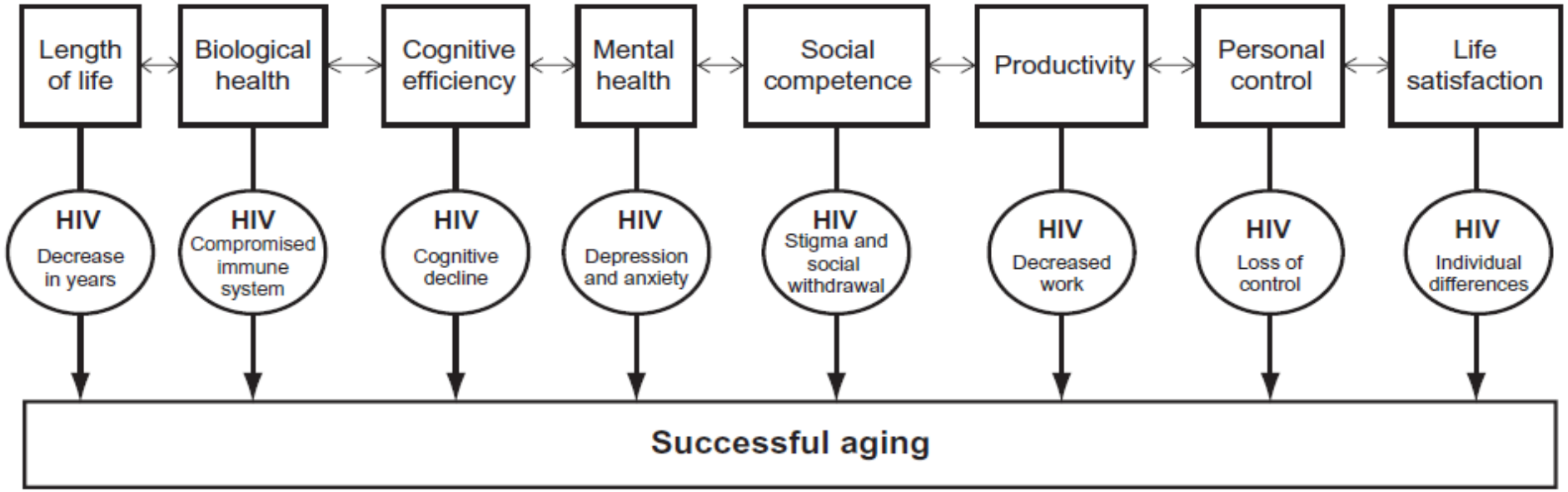
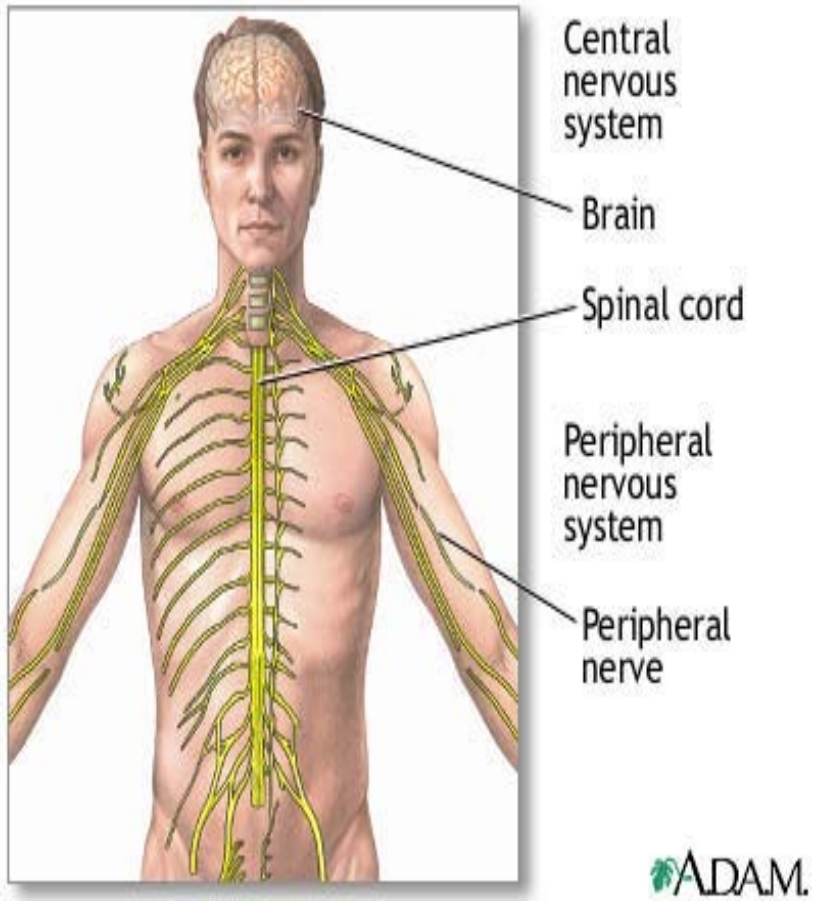



**Figure 1** Factors of and obstacles to successful aging with HIV.

# HIV Impacts the Nervous System

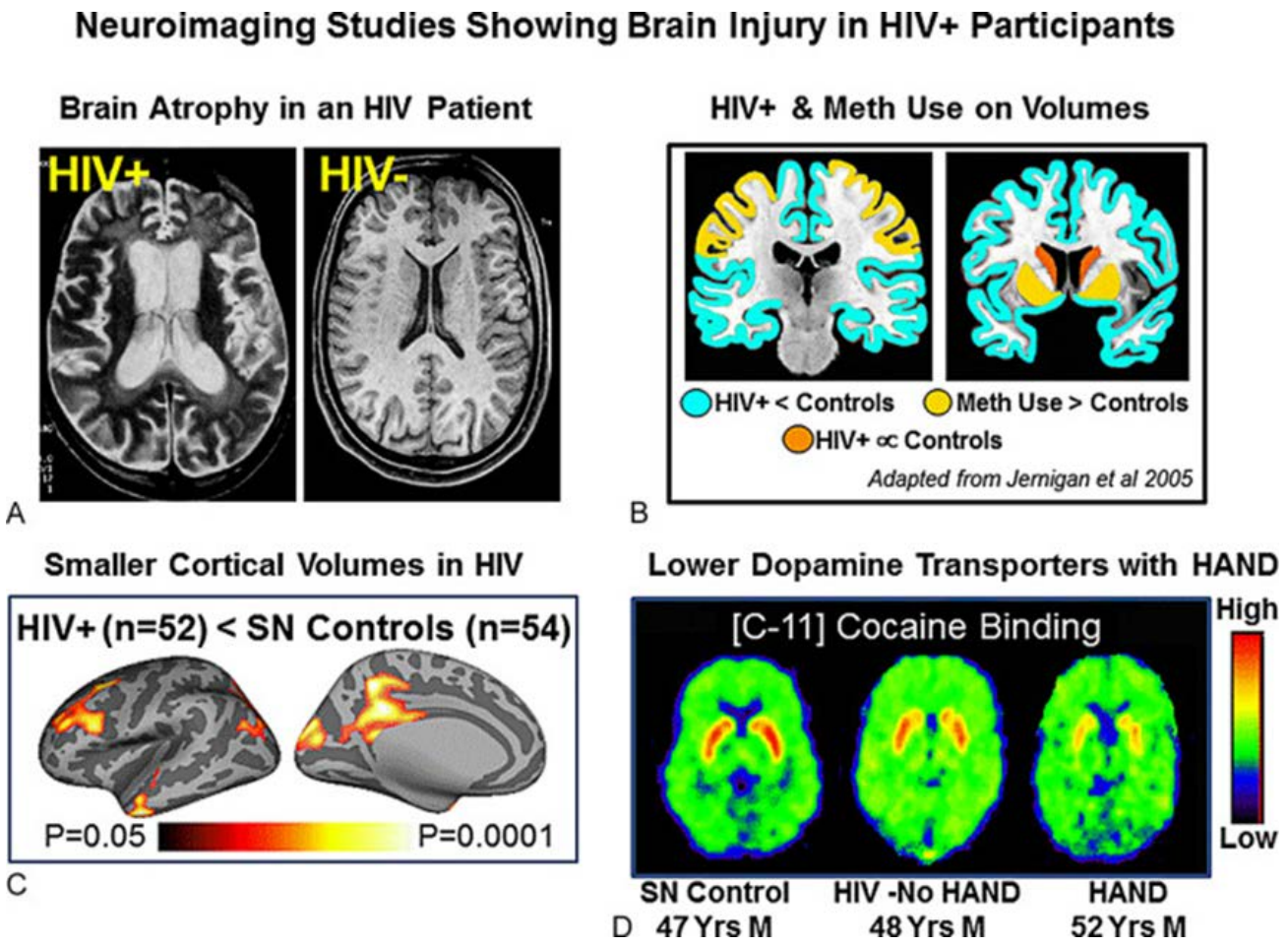
Primary HIV-Neurological Problems

- **HIV-associated dementia and cognitive motor disorders**
- Myelopathy (inflammation of the spinal cord)
- Peripheral neuropathy (damage to the nerves of the peripheral nervous system)
- Myopathy (muscular weakness)



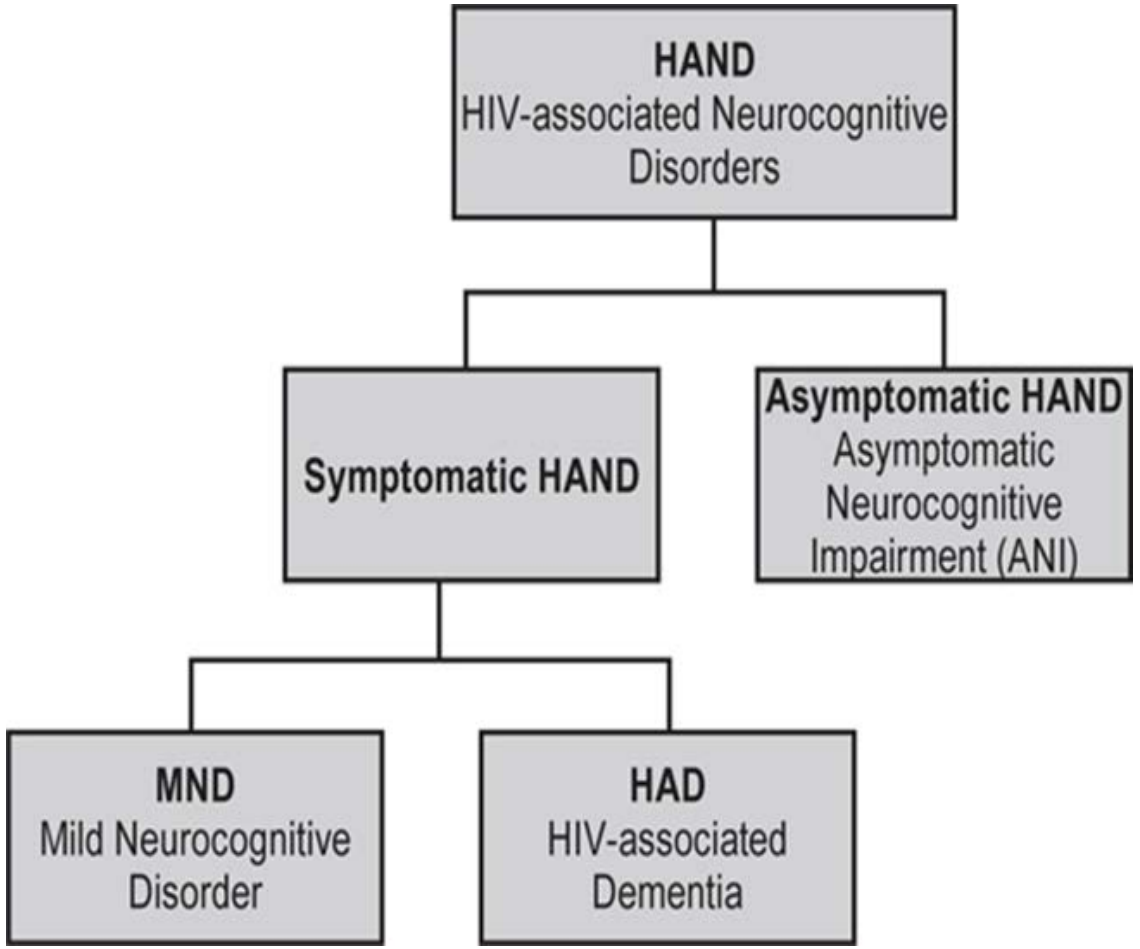
# HIV and the Brain

- The human immunodeficiency virus (HIV) crosses the blood-brain barrier and leads to neuropathological changes.
- The virus has a preference for the frontal-striato-thalamocortical loops.
- In the post-cART era classical HIV-associated brain pathology is less prevalent, but ongoing neural injury may be caused by low-level viral replication in the CNS and chronic inflammation.



# Intersection of Cognitive Aging and HIV

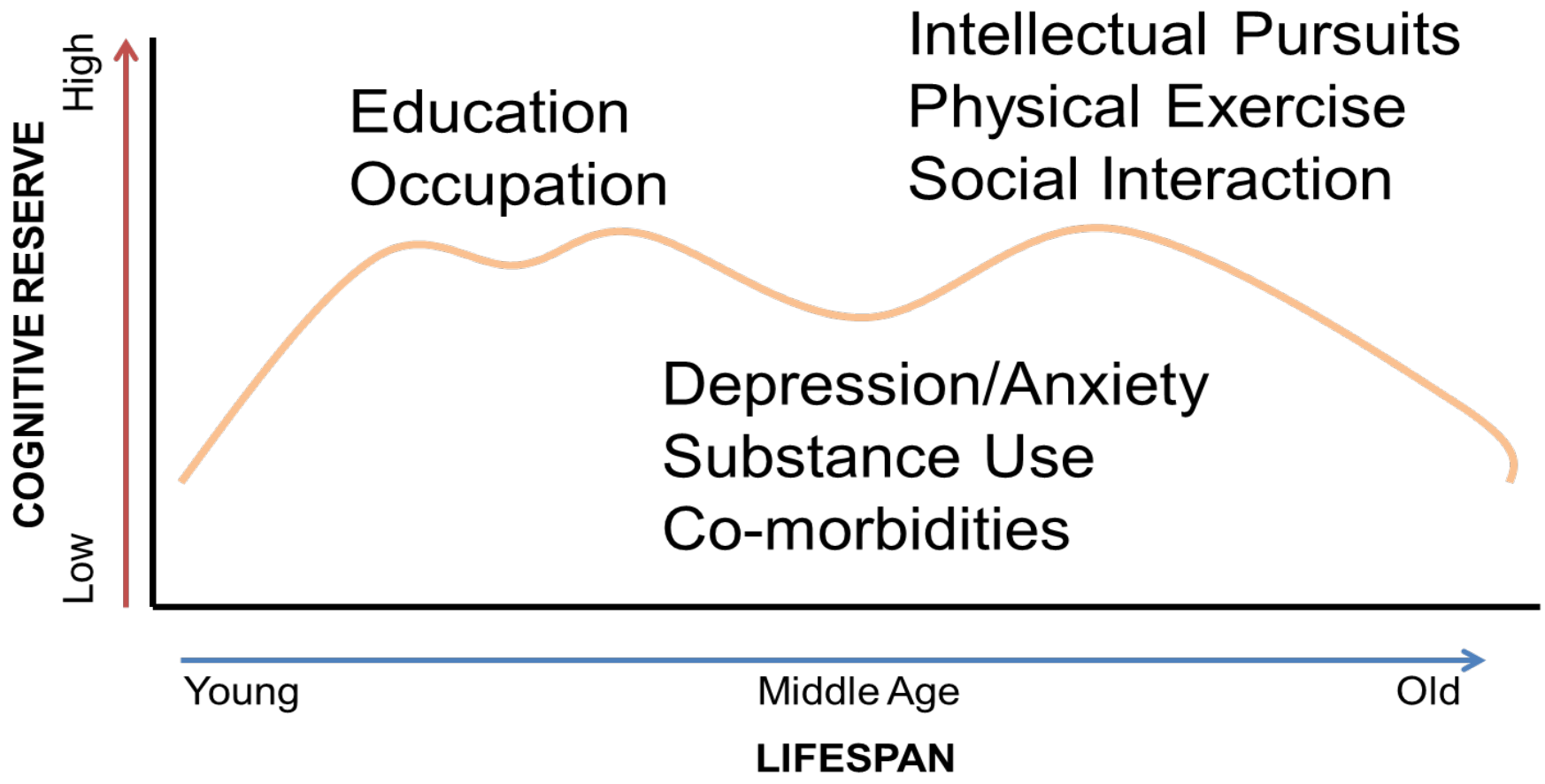
- Some cognitive decline and cognitive complaints are a part of normal aging.
- PLWH are at an increased risk for cognitive and functional impairment as they age.
- Approximately 30-50% of PWH have some form of HIV-Associated Neurocognitive Disorder (HAND)



# Risk Factors of Cognitive Decline

- Not all PLWH experience cognitive decline.
- It is important to be mindful of the role of cognitive reserve.
- Cognitive reserve is the ability of the brain to absorb insults and yet keep working.
- There are many factors involved in promoting or diminishing cognitive reserve, which can impact cognitive aging.

# Cognitive Reserve Over the Lifespan



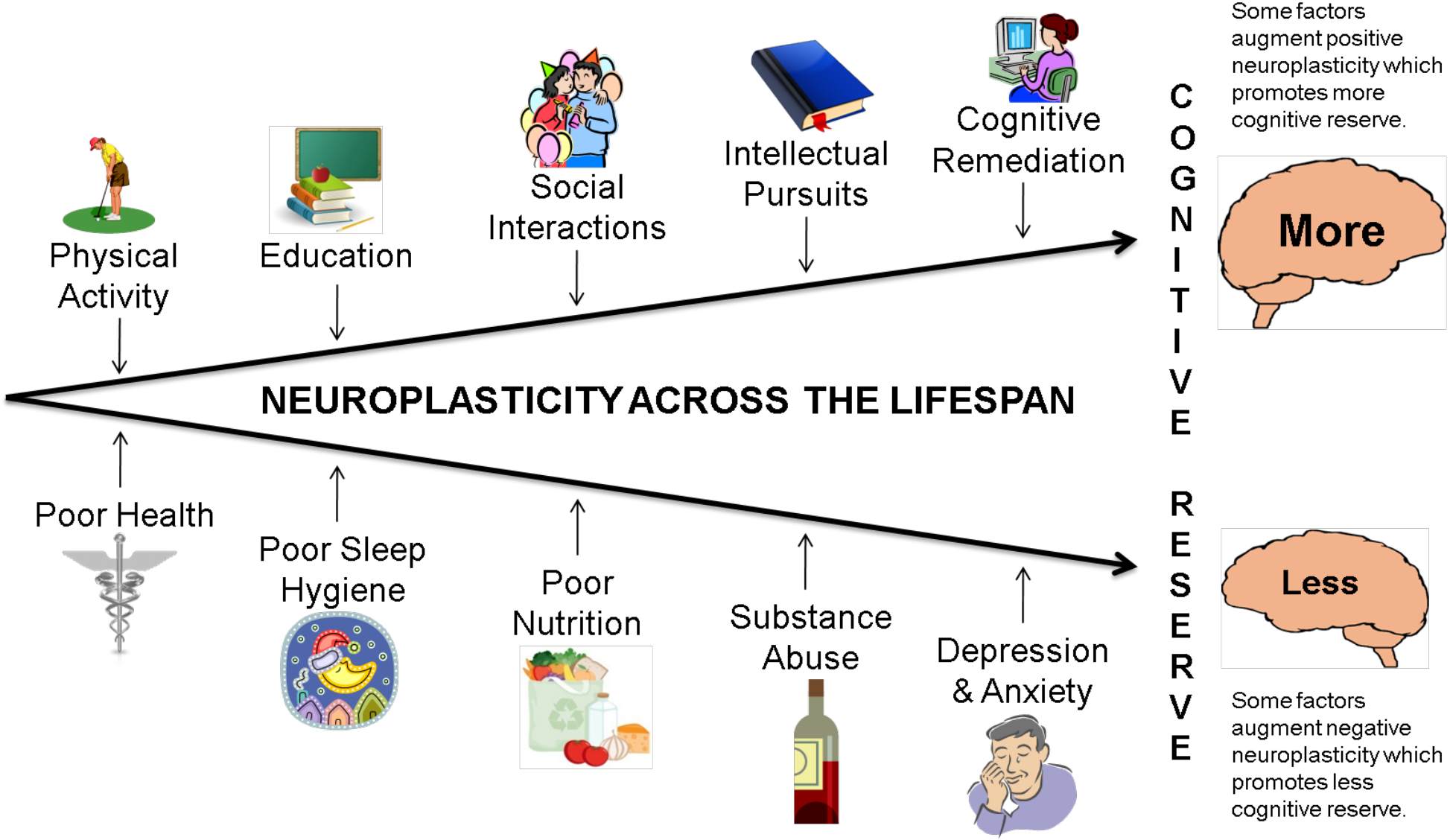

**Cognitive reserve over the lifespan: Neurocognitive implications for aging with HIV.** Vance, D. E., Lee, L., Muñoz-Moreno, J., Morrison, S., Overton, T., Willig, A., & Fazeli, P. L. (2019). Journal of the Association of Nurses in AIDS Care, 30(5): e109-e121.

# Other Risk Factors in the HIV Literature

| | | | |
|---|---|---|---|
| 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 |

**The intersection of cognitive ability and HIV: State of the nursing science.** Waldrop, D., Irwin, C. Nicholson, W. C., Lee, C. A., Webel, A., Fazeli, P. L., & Vance, D. E. (2021). Journal of the Association of Nurses in AIDS Care, 32(3), 306-321. DOI: 10.1097/JNC.0000000000000232

# Prevention and Treatment Strategies



# Cognitive Prescriptions

- 4 Focus Groups → 30 Older (50+) Adults with HIV
- Participants were presented ideas from the Cognitive Rx.
- "It would be easier for you if you sat down with someone and were able to target the things that were a little bit more important for you, whether that was you going to bike for physical exercise or eating certain things. You would want it tailored to what would be easiest for you."

## Rx Cognitive Prescription

| FACTORS | DO'S | DON'TS |
|---|---|---|
| Physical Exercise  | 1. Go for a 30 minute walk every Tuesday and Thursday.<br>2. Stretch daily (e.g., arms, leg, neck, and back). | 1. When you watch TV, don't sit on the couch during commercials; stretch instead. |
| Intellectual Exercise  | 1. Read 1 book (> 200 pages) a month.<br>2. Surf the World Wide Web everyday.<br>3. Start painting again; paint 1 picture a month. | 1. Don't watch the same old TV shows over and over; watch something new occasionally (e.g., PBS, Discovery Channel, History Network). |
| Good Nutrition  | 1. Each more foods rich in antioxidants (e.g., blueberries, oranges, carrots); these are good for brain health.<br>2. Eat wild salmon and olive oil at least once a week; these are very good for brain health. | 1. Avoid that second piece of cake (and that does not mean make the first piece bigger).<br>2. Avoid salt; this contributes to your hypertension. Hypertension is bad for brain health. |
| Sleep Hygiene  | 1. Go to bed at a reasonable hour (between 10-11 pm).<br>2. Engaging in physical exercise will help you sleep better at night. | 1. Avoid caffeine after dinner; it stays in your body for a long time and interferes with sleeping well.<br>2. Avoiding drinking more than 2 glasses of wine in the evening; this interfere with sleeping well. |
| Social Interaction  | 1. Go out to dinner with friends at least twice a week.<br>2. Call your children every week. | 1. Avoid being reclusive; socializing helps with not feeling lonely and depressed. |
| Good Mood  | 1. Take your antidepressant as prescribed.<br>2. Watch funny shows to lighten your mood (e.g., I Love Lucy, M*A*S*H).<br>3. Use your positive words (e.g., I can do it; Anything is possible). | 1. If you feel depressed, talk with a friend or go for a walk.<br>2. Don't dwell on what you can't do; focus on what you can do. |

# Computerized Cognitive Training

**Cognitive Training/Brain Training computerized programs target to improve a variety of cognitive domains.**

Meta-Analysis of 52 Computerized Cognitive Training Studies (Lampit et al., 2014)

**Treatment/effects sizes varied widely by domain and by amount of training/dosage.**

- Verbal memory (g = .08)
- Working memory (g = .22)
- Nonverbal memory (g = .24)
- Visuospatial skills (g = .30)
- Speed of processing (g = .31)
- Attention (g = non-significant)
- Executive functioning (g = non-significant)

# Ketogenic Diet in Older Adults with HAND

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

- 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

- **KGD:** Cognitive gains were detected 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

| 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 | | |

# Engagement – Physical Exercise, Social, and Mental Activity

139 Adults with HIV ($M_{age}$ = 48.7 years; 48% 50+)

Cross-sectional → Active Lifestyle & Neuropsychological Testing

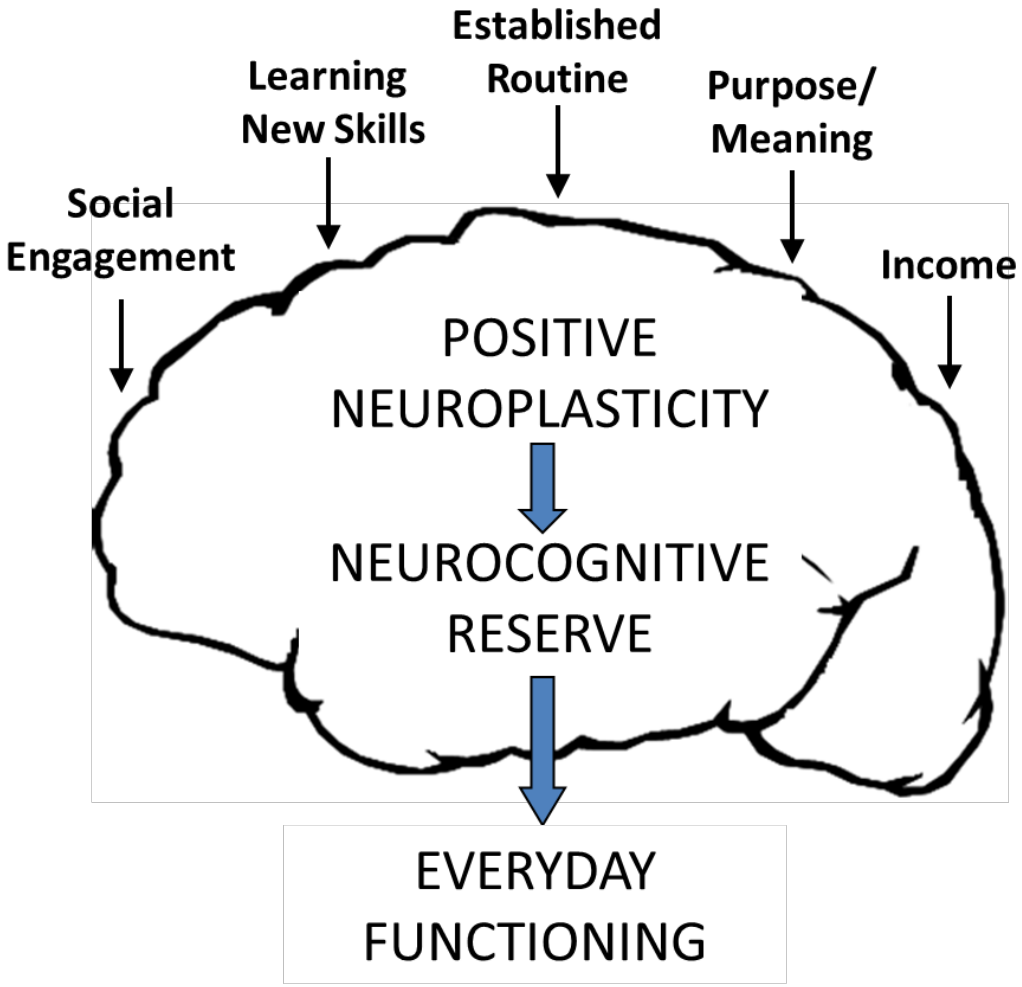
- **Physical Exercise** – Any strenuous exercise in the past 72 hours? No (0)/Yes (1)
- **Social Engagement** – Lawton and Brody ADL Questionnaire
- "Frequently engage in or initiate social activity" No (0)/Yes (1)
- **Mental Activity** – Working full- or part-time? No (0)/Yes (1)
- **Active Lifestyle 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 | ALF 1 – 51% HAND | ALF 2 – 33% HAND | ALF 3 – 20% HAND |
|---|---|---|---|
| (34% ANI, 18% MND, 11% HAD) | (35% ANI, 14% MND, 2% HAD) | (27% ANI, 3% MND, 3% HAD) | (15% ANI, 5% MND, 0% HAD) |

**An active lifestyle is associated with better neurocognitive functioning in adults living with HIV infection**. 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

# Employment

According to one study, only 20% of adults with HIV were continuously employed over a 30-month period
(Rabkin et al., 2004)




**The role of employment on neurocognitive reserve in adults with HIV: A review of the literature.** Vance, D. E., Cody, S. L., Yoo-Jeong, M., Jones, G. D., & Nicholson, W. C. (2015). Journal of the Association of Nurses in AIDS Care, 26(4), 316-329. DOI: 10.1016/j.jana.2015.04.003

# Engagement in Older Adults

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**

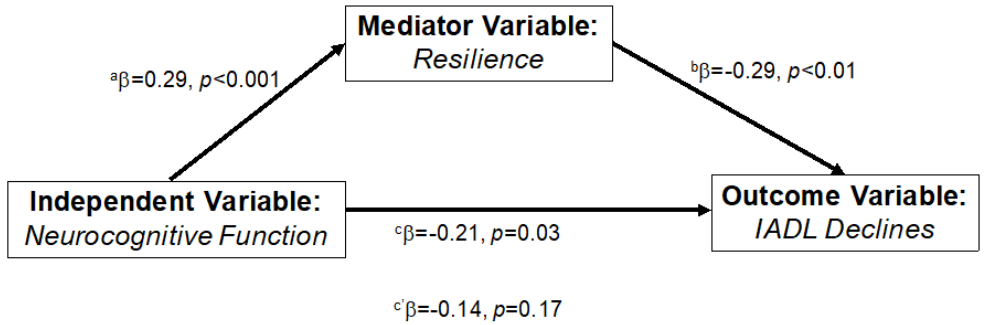
**The effects of an engaged lifestyle on cognitive vitality: A field experiment.** Stine-Morrow, E. A., Parisi, J. M., Morrow, D. G., & Park, D. C. (2008). Psychology and Aging, 23(4), 778-786. doi:10.1037/a0014341

# Resilience

- **Aim:** To explore the role of resilience in cognitive and everyday functioning in a largely African American and low socioeconomic status sample of adults and older adults with HIV

- **Cross-sectional Study:** 100 HIV+ middle-aged and older adults.

**Figure 1. Mediation Model**




a= association between independent variable and mediator
b= association between mediator and outcome variable
c= association between independent variable and outcome variable
c'= association between independent variable and outcome variable when mediator is in the model

Higher resilience was associated with better global neurocognitive functioning (rho = 0.31) and better functioning in most domains.

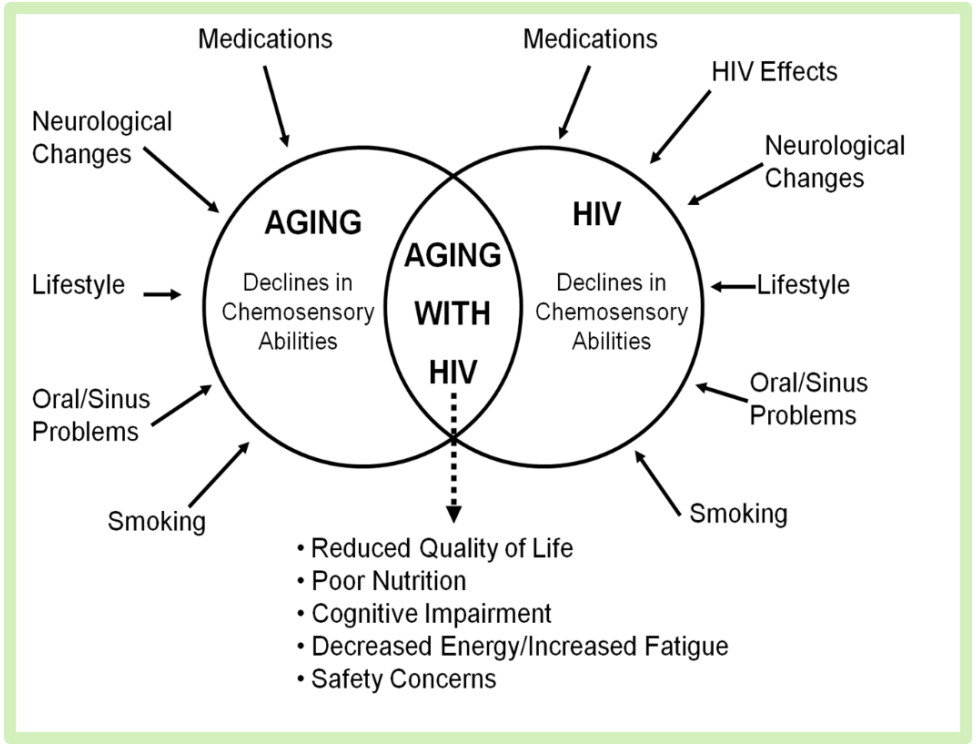
**Resilience attenuates the association between neurocognitive functioning and IADL declines in people living with HIV in the Deep South.** Fazeli, P. L., Moore, R. C., & Vance, D. E. (2019). International Journal of Geriatric Psychiatry, 34, 72-78. (DOI: 10.1002/gps.4988

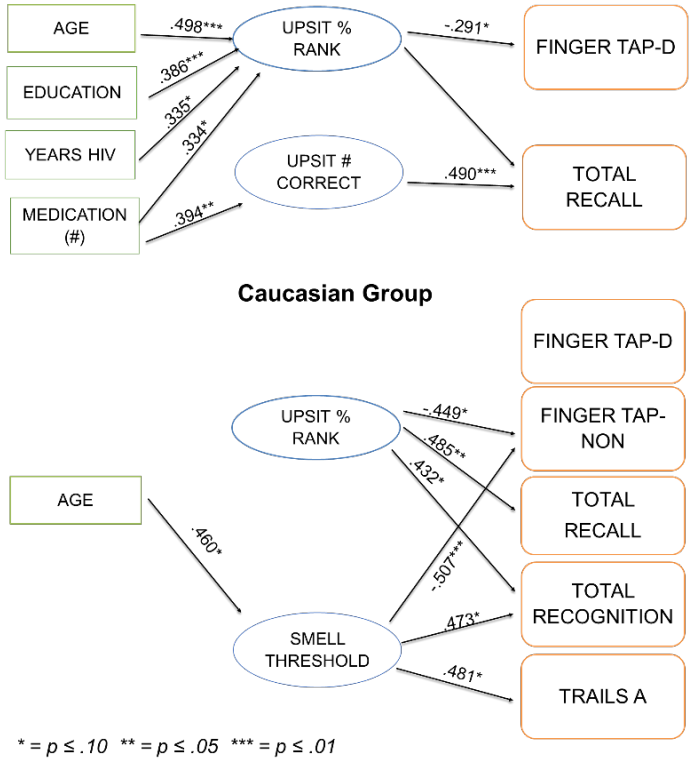
# Olfaction and HIV: Olfactory Training?

Poor olfaction may be a bellwether.

**34 African American Men & 17 Caucasian Men**

- Ages 40 and older with HIV for at least one year (Mage = 54 years)




**The association between olfactory function and cognition in aging African American and Caucasian men with HIV: A pilot study.** Vance, D. E., Cody, S. L., Nicholson, C., Cheatwood, J., Morrison, S., & Fazeli, P. L. (2019). Journal of the Association of Nurses in AIDS Care, 30(5), e144-e155. DOI: 10.1097/JNC.0000000000000086.

**Olfactory dysfunction in aging African American and Caucasian men with HIV: A pilot study.** Vance, D. E., Cody, S. L., Nicholson, C., Cheatwood, J., Morrison, S., & Fazeli, P. L. (2022). Journal of the Association of Nurses in AIDS Care.

# Compensation Strategies

## 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."
  - ***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.

Nick

## 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.

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

# 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.

**IT IS IMPORTANT TO ADHERE TO TREATMENTS TO PROTECT COGNITIVE RESERVE.**

# Picture of Successful Aging

## 'I Don't Fear Aging with HIV'

Diagnosed with HIV in 1992, 53-year-old Paul Durham has had 17 years' experience with both the infection and the health care providers who help him manage it. In a recent interview with *AJN*, Durham spoke highly of the clinicians at Trinity Medical Center in Birmingham, Alabama, saying, "You get to know your nurses a little better than your doctor. I feel lucky to have developed relationships with them; they know me up and down and have pulled me through some tough times."

For the last two years, a daily regimen of the antiretroviral drugs lopinavir and ritonavir (combined as Kaletra) and emtricitabine and tenofovir (combined as Truvada), as well as vitamins, has sustained him. Aside from some fatigue and backache, he reports experiencing no symptoms of HIV or adverse effects from the drugs; he said his physician calls him "a picture of health."

"I don't fear aging with HIV, unless I think too hard about it," Durham said. "I live one day at a time. I feel healthy. I keep up my meds, my routine; I'm in a good, loving relationship; I have hobbies. I'm always busy."

During the first four years after his diagnosis he took azidothymidine (also called zidovudine or AZT), an antiretroviral that made him extremely sick. He's since taken so many drugs that he can't recall their names. He was often too ill to work, and after his employer allowed him to retire, he became withdrawn for a while. But as he continued living with HIV and as the drugs used to treat it improved, he recalled, "I decided to start taking care of my body with diet and exercise, improving my mind and my spiritual side. I'm a pretty positive person now and attitude is everything." He also said that attitudes of health care workers have changed dramatically, especially within the last five years. "People are more aware that you can't catch HIV that easily. My dentist is really friendly," he said. "People just treat me like a normal human being now."

Photo courtesy of Paul Durham.

Durham's friends who are HIV positive are also doing well on various drug regimens. His advice to others aging with HIV? "There's so much hope—if you can turn your attitude around and quit feeling sorry for yourself. Take your meds, go to your doctor, have good friends. Get active in something, and try to find a support group."

Durham is even quick to point out that aging has its benefits. "You start to appreciate things more and become more aware of your mistakes. It's helped me." What's next? He's planning a trip to New Zealand. He said, "I don't hold back anymore. I decided I can't."

*—Alison Bulman, senior editorial coordinator*

# BIG THANKS!!

# Questions????