ST VINCENT'S CENTRE FOR APPLIED MEDICAL RESEARCH
A DIVISION OF ST VINCENT'S HOSPITAL SYDNEY

Premature Cognitive Aging among a community sample of optimally treated Australian living with HIV

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Htein Linn Aung, MBBS, MPH
PhD Student (St Vincent's Clinical School, UNSW & St Vincent's Applied Medical Research Centre)

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Outline

- **Background**
- **Objectives**
- **Method**
- **Results**
- **Implications**

Background

- PLHIV are aging at an unprecedented rate. About **46%** of PLHIV in Australia were over 50 years of age in 2017 *(Kirby Institute., 2018)*.
- Emerging evidence of **premature, accentuated and/or accelerated** aging effects among PLHIV *(Wing, E.J., 2016 & Pathai, S., Bajillan, H., Landay, A. L., & High, K. P., 2014)*.
- Chronic **inflammation and immune activation** may explain.
- **Evidence of premature cognitive aging has not been clear yet** *(Aung, H.L., 2020).*
- If this is true, there will be a major public health implication.

Objective

- To determine premature cognitive aging among a community sample of optimally treated PLHIV

Premature cognitive aging

"Significant interaction effect of HIV status and age on cross-sectional neurocognitive test performance covering both the normal and abnormal performance range (i.e., HIV and older age synergistically lead to significantly poorer neurocognitive *performance compared to HIV or/and aging effect alone)"* *(Aung, H.L., 2020)*

METHOD

Participant Recruitment

- Secondary data from a study conducted at **Holdsworth House medical practice** in Sydney
- **Sample Size**: 254 PLHIV and 72 HIV-negative gay and bisexual men
- **Recruitment and data collection**
  - Baseline - October 2011 and October 2012
  - Follow-up – Six months after
- **Exclusion criteria**
  - Alcohol or substance intoxication at the time of assessment.
  - No participants had major neurological/psychiatric disorder.

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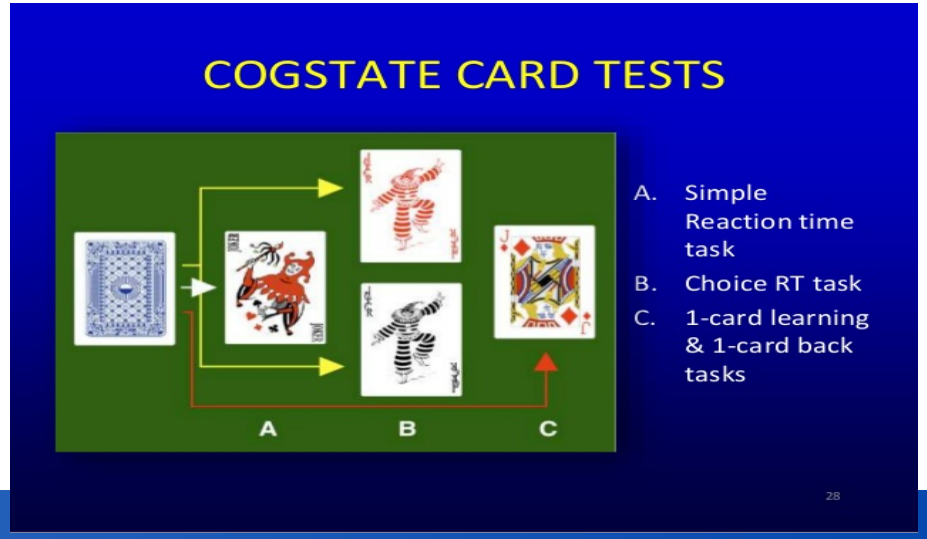
Predictor variables

Category	Detailed variables or tool used to assess
Demographics	Age, education and ethnicity
Mood status	Depression Anxiety Stress Scales (DASS)
HIV neurological history	HAND and CNS opportunistic infections
Non-HIV neurological history	Minor stroke, minor traumatic brain injury, and other minor neurological problems
Comorbidities	CVD, Diabetes, Hepatitis C coinfection, Treated syphilis
Activities of daily living	Modified version of the Lawton and Brody scale
Substance and Alcohol use	Mini International Neuropsychiatric Interview alcohol and substance use sections
HIV-related	ART status, Duration of diagnosis with HIV, duration of cART, CPE, current and nadir CD4, CDC Stage, and HIV viral load

Outcome (Cognitive Screen)

- Neurocognitive screening tool - ***Cogstate Computerized Battery (CCB)***
- Covers information processing speed, attention and working memory, verbal learning and memory
- **Six measures**: Detection speed, Identification speed, One Back accuracy & reaction time, International Shopping List (ISL) task learning total correct and ISL task delayed recall total correct.
- Used age-uncorrected global z score (GZS).
- Corrected for **practice effect** to the month 6 data.



Statistical Analysis

- **Linear mixed-effect model** including all baseline and follow-up visits
- **Random effect** – Subjects
- **Main Fixed Effects** – Baseline Age and HIV status
- **Covariates** - HIV Brain Involvement History, AUD, SUD, DASS Anxiety Score, Mental Illness, CDC Stage C, Depression, Non-HIV Neurology History, Time (month 0 or month 6)
- HIV-negative participants were coded as “No” for CDC Stage C and HIV neurological history and coded “0” for duration of HIV infection.

RESULTS

Participants' Characteristics

- Total participants
  - Baseline: 254 PLHIV and 72 HIV-negative
  - Month 6: 208 PLHIV and 58 HIV-negative

  (No neurocognitive outcome difference between those came for follow-up and those who did not)
- Mean age - 49 years (SD=10.2)
- Majority of HIV-positive participants were stable on cART (**92% taking cART** and **84% virally suppressed**) and were started cART early (**only 15% with CDC Stage** C)

Difference between HIV-positive and HIV-negative participants

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Variable	Younger HIV-Neg (38)	Older HIV-Neg (34)	Younger HIV-Pos (138)	Older HIV-Pos (116)	p
Anxiety disorder based on DASS (Baseline)	7 (18%)	3 (9%)	**45 (32%)**	26 (22%)	0.02
Current Substance Use Disorder (Baseline)	2 (5%)	0 (0%)	**39 (28%)**	12 (10%)	<.0001
Current Alcohol Use Disorder (month 6)	**5 (19%)**	1 (3%)	11 (10%)	2 (2%)	0.01
Current Substance Use Disorder (month 6)	2 (7%)	0 (0%)	**20 (18%)**	6 (6%)	0.004
Low eGFR rate (<60)	0 (0%)	0 (0%)	4 (3%)	**12 (12%)**	0.02
CVD	5 (13%)	15 (44%)	19 (14%)	**53 (46%)**	<.0001
Diabetes	0 (0%)	**4 (12%)**	3 (2%)	9 (8%)	0.02
Treated Syphilis	1 (3%)	8 (24%)	35 (25%)	**35 (30%)**	0.007

Younger- <50 years, Older - ≥50 years

Difference between young and old HIV-positive

Variable	Younger HIV-Pos (138)	Older HIV-Pos (116)	p
CD4 cell count (Baseline) (cp/mL)	**667 (278)**	590 (238)	0.02
CD4 cell count (month 6) (cp/mL)	**689 (269)**	608 (219)	0.02
Nadir CD4 cell count (cp/mL)	**346 (210)**	278(169)	0.005
On ART	122 (88%)	**111 (96%)**	0.04
Duration diagnosed with HIV (Years)	11.2 (7.7)	**17.4 (8.4)**	<.0001
Duration of ART (Years)	7.5 (7.2)	**12.1 (7.1)**	<.0001
HIV brain involvement history	10 (7%)	**22 (19%)**	0.005

Younger- <50 years, Older - ≥50 years

Comparisons of CCB global score across HIV status and age groups

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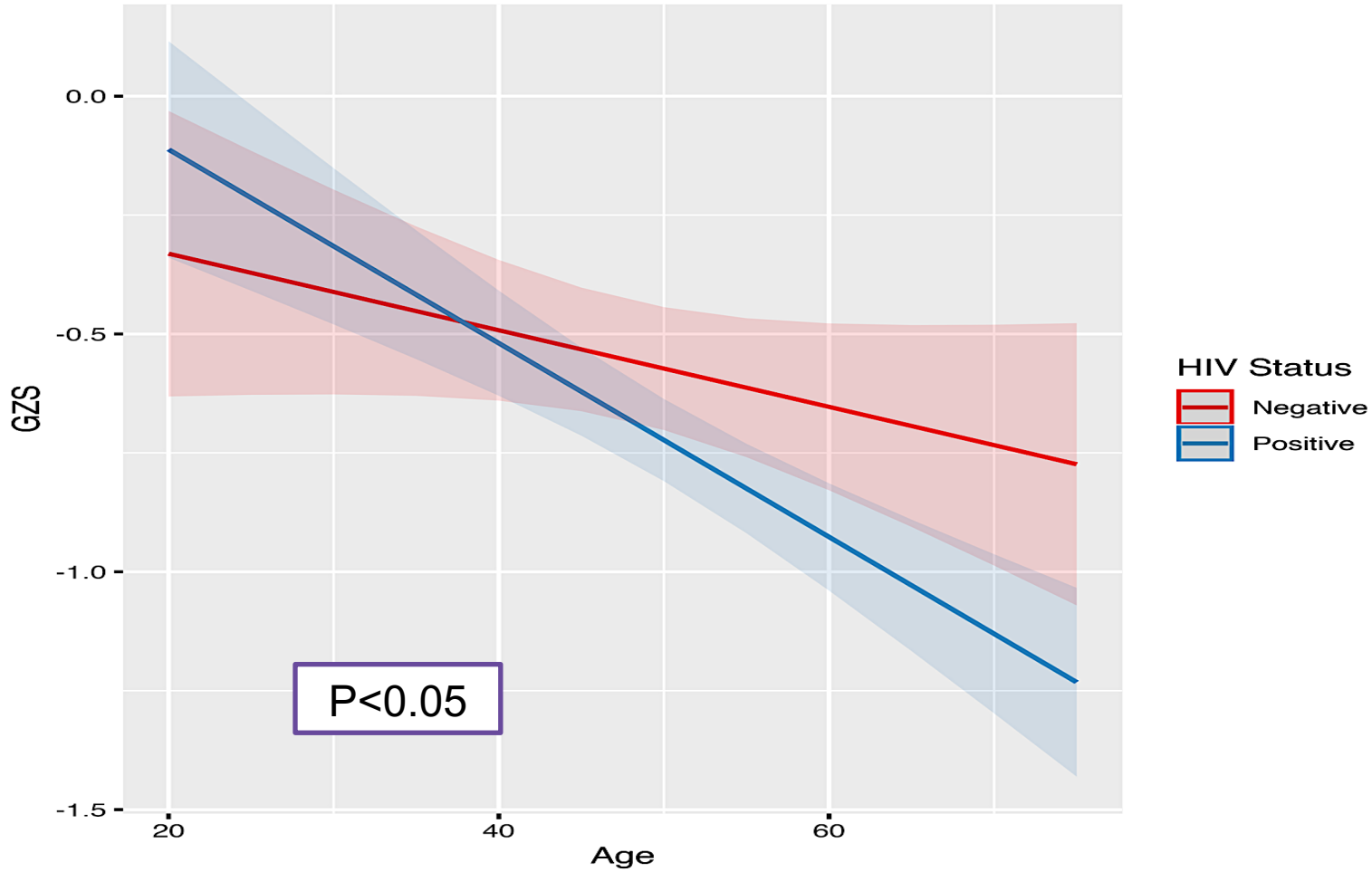
	Younger HIV-	Older HIV-	Younger HIV+	Older HIV+	All	p
	N=38	N=34	N=138	N=116	326	
Baseline Global Z-Score	-0.6 (0.4)	-0.7 (0.4)	-0.7 (0.5)	**-1 (0.7)**	-0.80 (0.59)	<.0001
	N=27	N=31	N=109	N=99	266	
Month 6 Global Z-Score (practice effect corrected)	-0.5 (0.4)	-0.6 (0.3)	-0.8 (0.5)	**-1 (0.7)**	-0.84 (0.59)	<.0001

Linear mixed effects model results

Variable	B	Standard Error (SE)	95% CI	β	95% CI
Baseline HIV Status (Positive)	0.39	0.29	-0.18, 0.95	0.27	-0.13, 0.67
Baseline Age (continuous)	-0.008	0.005	-0.02, 0.002	-0.13	-0.29, 0.03
Time (Month 0 VS Month6)	-0.04	0.02	-0.08, 0.01	-0.03	-0.07, 0.01
HIV Brain Involvement History (Yes)	-0.22*	0.1	-0.43, -0.02	**-0.12**	-0.22, -0.01
Non-HIV Neurology History (Yes)	-0.09	0.07	-0.22, 0.04	-0.07	-0.16, 0.03
AUD (Yes)	-0.07	0.06	-0.18, 0.05	-0.03	-0.08, 0.02
SUD (Yes)	0.13*	0.06	0.07, 0.24	**0.07**	0.004, 0.14
History of mental illness (Yes)	-0.13	0.08	-0.29, 0.03	-0.08	-0.17, 0.02
CDC Stage C (Yes)	-0.22*	0.09	-0.38, -0.05	**-0.12**	-0.22, -0.03
DASS Anxiety Score	-0.01**	0.003	-0.02, -0.004	**-0.11**	-0.19, -0.04
Lifetime history of depression (Yes)	-0.08	0.06	-0.19, 0.04	-0.06	-0.16, 0.03
HIV Status (Positive)*Baseline Age	-0.01*	0.006	-0.02, -0.0006	**-0.43**	-0.85, -0.02

*p<0.05; **p<0.01

Global Z-Score predicted by the linear mixed-effect model



Conclusions

- Need **regular cognitive screening** among older PLHIV which warrants implementation studies.
- Cognitive screening should focus those with **HIV involvement history and AIDS diagnosis**.
- Regular **mental health screening** is also warranted among PLHIV to preserve both mental and cognitive functioning. Future neuropsychology studies among PLHIV should also consider the role of anxiety in addition to depression.

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Contact email – h.aung@amr.org.au