Pattern of Age-Related Cognitive Decline in People With HIV Depends on Viral Suppression

James T Kennedy, Sarah A Cooley, Kalen J Petersen, and Beau M Ances

599

Introduction

- HIV infection is sometimes associated with persistent cognitive deficits referred to as HIV-Associated Neurocognitive Disorder (HAND)[1]
- The introduction of combined antiretroviral therapies (cART) has led to both increases in lifespan and decreases in severe HAND[2]
- As the population of people living with HIV (PWH) increases, it is important to understand if PWH follow the same cognitive aging trajectory as people without HIV (PWoH) and if viral control influences this trajectory

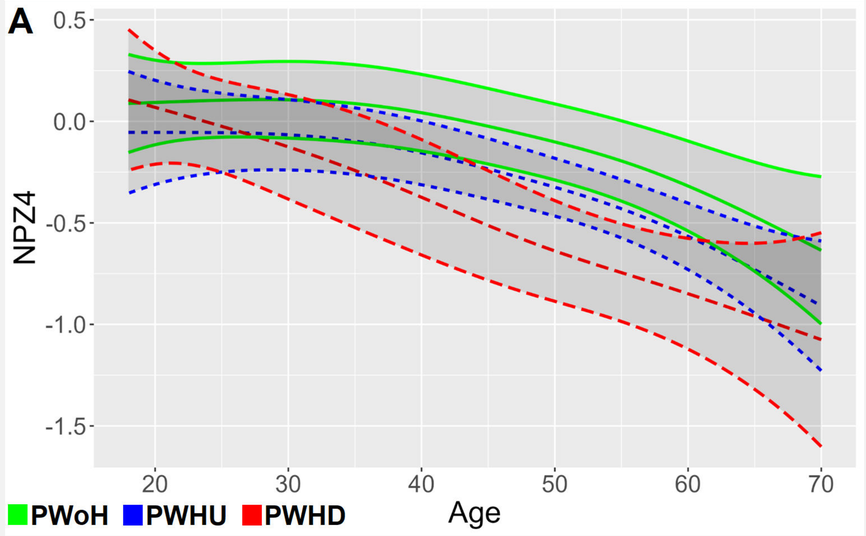
Methods

- PWH, undetectable (viral load ≤50/ml, PWHU) and detectable (PWHD), and PWoH were recruited from the St. Louis region and repeatedly administered a cognitive battery covering multiple domains consisting of
  - Category Fluency (Animals), measures language
  - Hopkins Verbal Learning Test learning subtest (Learn)
  - Trails A (Psychomotor/Processing Speed)
  - Trails B (Executive Function)
- Tests normalized to the 1st time the test was taken and averaged (timed measures inverted) to form a composite (NPZ4)
- Age and group effects were explored in generalized additive mixed models (GAMMs)
  - Controlled for education, sex, ethnicity, and times test taken
  - False discovery rate correction applied to individual measures only

	Baseline			All Sessions		
	PWoH	PWHU	PWHD	PWoH	PWHU	PWHD
N	269	297	94	321	494	122
% Male	51%	71%	78%	51%	72%	83%
% White	39%	28%	18%	41%	30%	23%
Age	36.79 (15.53)	47.4 (13.25)	36.78 (15.75)	39 (15.79)	48.31 (13.04)	39.22 (16.37)
Education	13.88 (2.31)	13.16 (2.51)	12.91 (1.88)	13.89 (2.29)	13.14 (2.53)	12.98 (1.97)
Viral Load	-	22 (7)	45701 (8872)	-	22 (6)	38369 (80267)
NPZ4	0.3 (0.64)	-0.18 (0.73)	-0.21 (0.78)	0.27 (0.65)	-0.14 (0.71)	-0.2 (0.78)
Animals	22.42 (5.33)	19.47 (5.14)	18.49 (5.16)	22.27 (5.42)	19.59 (5.02)	18.48 (5.38)
Learn	24.39 (4.9)	21.36 (5.53)	21.69 (5.65)	24.14 (4.97)	21.64 (5.47)	21.98 (5.49)
Trails A*	27.76 (10.27)	34.73 (16.9)	34.16 (16.52)	27.86 (10.18)	33.72 (15.46)	33.99 (15.6)
Trails B*	75.36 (40.24)	91.91 (46.93)	93.81 (51.4)	76.15 (42.14)	92.31 (47.41)	95.53 (52.07)

Demographic information and cognitive values for participants at baseline and across all sessions. PWoH: People without HIV, PWHU: People with undetectable HIV, PWHD: People with detectable HIV. Mean and standard deviation (Mean (SD)) are provided for continuous measures. Cognitive measures with an asterisk are timed test where higher scores mean worse performance, for all other values higher scores reflect better performance.

Relationship between Age and Cognition by HIV Group



Estimate of relationship between cognition and age and 95% confidence intervals for A) NPZ4 and B) the measures it is derived from. Green: PWoH, Blue: PWHU, Red: PWHD

Key Points

- **PWoH had highest cognitive scores, PWHD lowest**
- **Pattern of global change similar for PWoH/PWHU**
- **PWHD had sharper decline than PWoH/PWHU**
  - **PWHU initially similar to PWoH for executive functioning/processing speed, diverge age 50-60s**

Variable	Parametric Effect Estimates							Age Association			Slope Differences			Adj R^2
	Int	Edu	Sex	Times Taken	PWoH x PWHU	PWoH x PWHD	PWHU x PWHD	PWoH	PWHU	PWHD	PWoH x PWHU	PWoH x PWHD	PWHU x PWHD	
NPZ4	**-1.182**	**0.088**	*-0.092*	**0.073**	**-0.208**	**-0.382**	**-0.174**	**2.984**	**2.984**	**1.000**	1.000	**2.196**	**2.196**	0.369
Animals	**15.609**	**0.370**	0.324	0.197	**-1.941**	**-3.570**	**-1.634**	**1.291**	1.000	**1.000**	1.000	1.797	*1.730*	0.176
Learn	**13.232**	**0.709**	**-1.311**	0.289	**-0.951**	-0.877	0.014	**1.865**	**1.000**	**1.000**	1.000	1.000	1.000	0.279
Trails A	**42.351**	**-0.780**	0.726	**-2.167**	**3.444**	**6.241**	**2.897**	**2.579**	**3.032**	**2.580**	**2.115**	**1.000**	1.897	0.192
Trails B	**163.519**	**-5.490**	6.501	**-3.996**	2.798	**11.381**	**8.311**	**1.000**	**2.546**	**1.000**	**3.149**	**1.000**	*1.000*	0.238

GAMM model output. Estimates provided for parametric effects, + numbers for group comparisons = greater values in 2nd group. Estimated degrees of freedom (EDF) provided for age association and slope differences. EDF measures linearity of an association with 1 = linear and higher numbers = more nonlinear. Green cells = significant at $p < .05$, yellow = trend at p .05 - .1.

Results

- Significant age effects and group differences in cognition were observed in most analyses
  - Generally find cognition best in PWoH, worst in PWHD
- Slope shape differences were observed in NPZ4 (PWoH and PWHU vs PWHD) and Trails A/B (PWoH vs PWHU and PWHD)
  - While initially similar to PWoH, Trails A/B diverge around ages 50-60 in PWHU, performing increasingly worse than PWoH at older ages

Conclusions

- HIV infection is associated with a decrease in cognition
- The global cognitive aging trajectory in virally suppressed people with HIV mirrors that of people without HIV
  - Executive functioning and psychomotor/processing speed decline faster in PWHU at older ages
- People with detectable HIV have worse performance at older ages

Acknowledgements

This research was supported by grants K23MH08175 from NIMH, R01NR014449, R01NR012657, R01NR015738, R01NR012907 from the NINR, the ICTS., and the Riney Fund. We would like to thank our participants who make our work possible.

References

- Antinori, A. et al. (2007). Updated research nosology for HIV-associated neurocognitive disorders. *Neurology, 69* (18), 1789-1799.
- Clifford, D.B. and Ances, B.M. (2013). HIV-associated neurocognitive disorder. *Lancet Infect Dis, 13*(11), 976-986.