Interaction Between Age, Brain Volume, and HIV Status in Predicting Cognition

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BACKGROUND

- Aging and HIV infection are independently associated with worse cognitive performance[1] and decreased brain volume[2]
- Previous research typically used small, cross-sectional datasets
- It is unknown if the longitudinal relationships between brain volumes, cognition, and aging differs in people with HIV (PWH) compared to people without HIV (PWoH).
- Within PWH it remains poorly characterized if detectable viral suppression affects these relationships in PWH.

METHODS

- A detailed series of cognitive tests and T1 MRI scans were performed in PWoH and PWH from the St. Louis area.
- PWH were further divided into undetectable (≤50 viral load/ml; PWHU) and detectable (PWHD).
- Four common cognitive tests was converted to an uncorrected Z-score and averaged (reversing timed tests) to form a cognitive composite. Cognitive tests included:
  - Category Fluency, Hopkins Verbal Learning Test – Learning scale, Trails A, and Trails B
- MRI scans were processed with FreeSurfer 5.3 to generate regional brain volumes and corrected for intracranial volume
- Nonlinear age (A), regional brain volume (V), cognition (C), and HIV group (H) relationships (C~AxH, V~AxH, C~VxH, and C~AxVxH) were explored using generalized additive mixed models
  - ID was treated as a random variable and sex, education, scanner, and time since baseline as parametric
  - A false discovery rate correction for significance at $p < 0.05$ was applied to all results

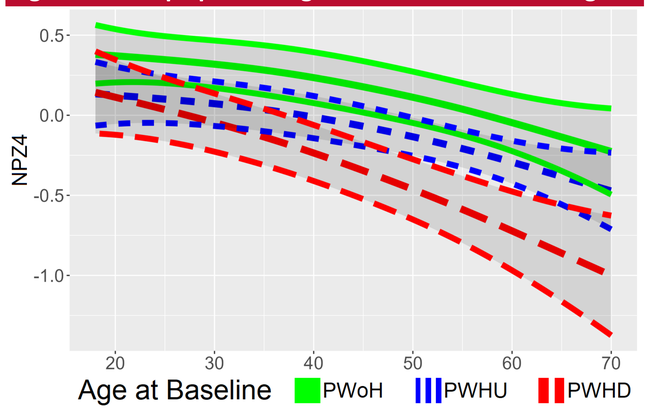
Table 1: Demographics

	Baseline			All Sessions		
	PWoH	PWHU	PWHD	PWoH	PWHU	PWHD
N	259	240	84	308	421	112
% Male	53	79	82	53	74	83
% AA	57	69	79	56	71	76
Age (years)	36.1 (15.2)	46 (13.4)	36.1 (15.4)	38.5 (15.7)	47 (13.2)	38.5 (16.2)
Education (years)	14 (2.4)	13.2 (2.5)	12.9 (1.7)	14 (2.3)	13.2 (2.6)	13 (1.9)
log(Viral Load)	-	1.34 (0.1)	3.71 (1.2)	-	1.33 (0.1)	3.5 (1.2)
N Sessions	-	-	-	1.17 (0.4)	1.64 (0.9)	1.3 (0.6)

Demographic information for all groups at baseline, across all sessions, and demographic differences at baseline. Mean (standard deviation) given for continuous measures, percentage for group measures. N Sessions: mean (SD) number of sessions of data per group available. AA: African American, PWoH: people without HIV, PWHU: people with undetectable HIV, PWHD: people with detectable HIV.

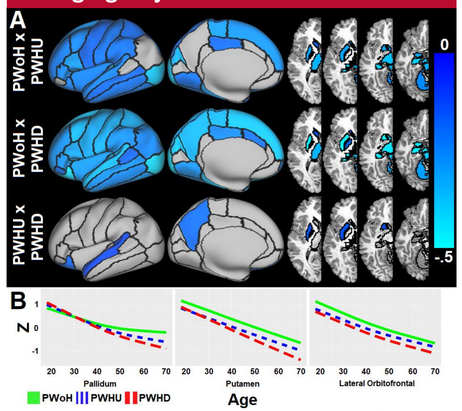
Cognition and brain volume aging trajectories in PWH are similar but lower than PWoH. PWH with detectable virus have faster cognitive decline.

Figure 1: Group-specific cognition estimates across ages



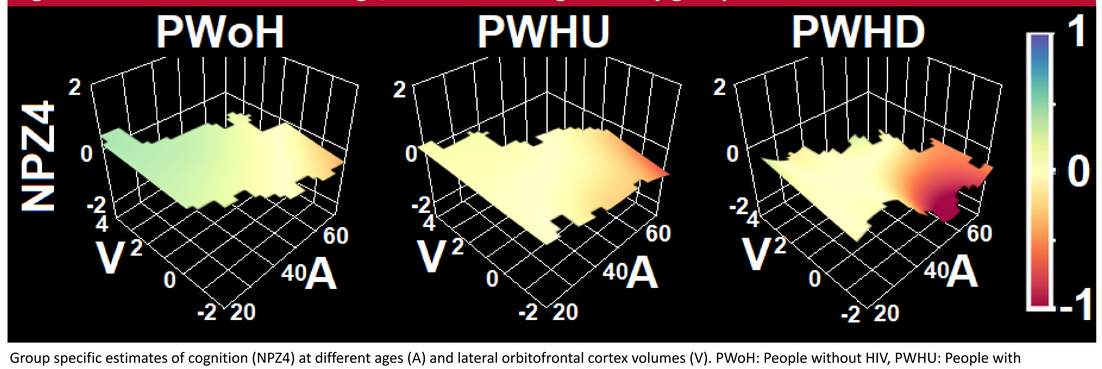
Group specific cognition (NPZ4) estimates between the ages of 18 and 70. PWoH: People without HIV, PWHU: People with undetectable HIV (≤50 viral load/ml), PWHD: People with detectable HIV (>50 viral load/ml).

Figure 2: Group differences in volume and aging trajectories



A: Group differences in brain volume between people without HIV (PWoH), people with undetectable HIV (PWHU), and people with detectable HIV (PWHD). Brain volumes converted to Z-scores, Blue indicates greater volume in first group listed, lighter colors indicate greater effects. B: Group specific slopes, significantly different slopes for pallidum (PWoH vs PWHU/PWHD) and putamen (PWoH vs PWHD)

Figure 3: Interaction between age, volume and cognition by group



Group specific estimates of cognition (NPZ4) at different ages (A) and lateral orbitofrontal cortex volumes (V). PWoH: People without HIV, PWHU: People with undetectable HIV (≤50 viral load/ml), PWHD: People with detectable HIV (>50 viral load/ml). Better cognitive performances in blue-green, worse in orange-red. Age/volume/cognition relationship significantly differs in PWHD only, demonstrating worse cognitive performance at low volumes and older ages relative to PWoH and PWHU.

RESULTS

- Participants consisted of 259 PWoH, 260 PWHU, and 84 PWHD who had 841 total sessions (Table 1)
  - Sample was 71% male and 68% African American with a mean baseline age of 40.2 years old and 13.5 years of education
- Cognitive composite significantly differed amongst all groups (PWoH>PWHU>PWHD) (Figure 1)
- Brain volumes were in general larger in PWoH relative to PWH in most regions (Figure 2A)
  - PWHU had greater brain volumes than PWHD in several regions including lateral orbital frontal cortex, superior temporal, precuneus, and putamen
- Cognition, age, and volume were significantly associated for each of the groups (Figure 3)
- Slopes were identical for PWoH and PWHU across analyses but significantly differed compared to PWHD for
  - Age and cognition (Figure 1)
  - Age and volume in the lentiform (Figure 2B)
  - Interaction of age, volume, and cognition (Figure 3)
- Slope interaction analyses found that low volumes at older ages were more deleterious to cognitive function in PWHD compared to PWHU or PWoH

CONCLUSIONS

- HIV legacy effects are observed for cognition and brain volume, with similar aging trajectories for PWHU and PWoH
- Detectable viral load was associated with steeper aging slopes for cognition and brain volumes
- Detectable viral load has a more severe effect on cognition at older ages when brain volumes are low
  - Larger volumes protective at older ages in PWHD?

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