Associations between a polygenic risk score for Alzheimer's disease and brain integrity in HIV

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BACKGROUND

- As people with HIV (PWH) continue to live to older ages, it is becoming increasing difficult to differentiate between HIV-related cognitive impairment and age-related neurocognitive disorders (e.g. Alzheimer's disease (AD)).
- Poly genic risk scores (PRS) provide a numeric value that estimates an individual's disease risk based on genetic variations.
- This study utilized PRS scores for individuals that were calculated using the latest genome wide association study for AD (AD-PRS) and included the APOE genotype

METHODS

- 115 older (age>50; male n=94, female n=21) PWH with undetectable viral load (<20 copies/mL)
- All participants completed a blood draw, magnetic imaging, and a comprehensive neuropsychological battery comprised of 15 test covering 5 cognitive domains (learning, recall, executive functioning, psychomotor speed and language).
- Participants were genotyped with an Illumina array platform (GSA), stringent quality control and imputation was performed following standard pipelines
- AD-PRS was computed using the binary logarithm transformation of the reported OR from the sentinel SNPs from the latest AD GWAS, including the *APOE* region, using PRSice.
- Regression analysis was used to assess the relationships between PRS values (covariates age, sex, race) and cognitive tests, domain Z-scores, inflammatory markers (sCD14, sCD163), brain volumes, cerebral blood flow (CBF), and HIV variables (CD4 t-cell count, CD8 t-cell count, CD4:CD8 ratio, duration of infection).

An **elevated polygenic risk score** for Alzheimer's disease was associated with worse cognitive performance, but **not HIV clinical** markers in people with HIV.

Table 1. Participant demographic and clinical characteristics

	PWH (n=115)
Age (years; M ± std)	57.83 ± 6.57
Education (years; M ± std)	14.7 ± 2.69
Sex (% female)	18.3% (n=21)
Race (% AA)	57.4% (n=66)
Duration of HIV infection (months; mean [std])	224 (129, 304)
Recent CD4 T-cell count, median (IQR)	610 (407, 826)
APOE Genotype (% of group)	
2/3	10.4%
2/4	1.7%
3/3	52.2%
3/4	30.4%
4/4	1.7%

RESULTS

- Higher AD-PRS values were associated with worse cognitive test scores for letter number sequencing (p=0.015), animal fluency (p=0.039), verb fluency (p=0.001; Figure 1) and language domain (p=0.024).
- There was a negative correlation between AD-PRS and inflammatory markers sCD163 (p=0.043) and sCD14 (p=0.03), and AD-PRS

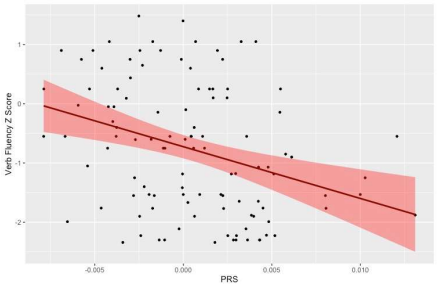


Figure 1. AD-PRS values (shown unadjusted) associated with Verb Fluency Z-Score

RESULTS

- There was a significant positive association between the AD-PRS and CBF in the caudate (p=0.047).
- There was a significant positive correlation found between the AD-PRS and putamen volume (p=0.017) while there was a significant negative correlation between AD-PRS and total gray volume (p=0.032; Figure 2).
- No association was found between AD-PRS and HIV variables.

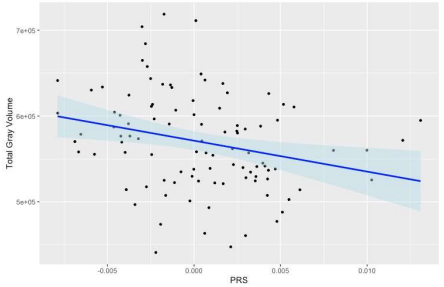


Figure 2. AD-PRS values associated with total gray matter volumes in PWH

CONCLUSIONS

- The elevated genetic risk for AD, measured by AD-PRS associated with some worse cognitive performance for PWH, mirroring patterns in the general population, implying that certain cognitive deficits among older PWH may result from aging rather than HIV-related factors.
- AD-PRS shows no association with HIV clinical markers, supporting previous work suggesting that HIV and AD may affect brain integrity via different processes.

ADDITIONAL KEY INFORMATION

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