HIV is Independently Associated With Brain MRI White Matter Hyperintensities

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BACKGROUND

Brain white matter hyperintensities (WMH) are nonspecific in etiology but occur commonly in the setting of HIV infection. Their relevance to disease remains uncertain as previous studies have used various methods of estimation in heterogenous groups of people with HIV (PWH). **We aimed to evaluate the frequency, severity and clinical correlations of WMH in the setting of well controlled HIV infection**, using the validated Fazekas visual rating scale.

METHODS

Research protocol images from brain 3D fluid attenuated inversion recovery (FLAIR) on a 3T MRI were reviewed to determine **the Fazekas score (total score of 0-6, 0-3 for periventricular hyperintensity and 0-3 for deep WMH, see Table 2)** in PWH with well controlled infection (antiretroviral therapy for at least one year and plasma viral load <200 copies/ml) and in controls. Simple linear regression was used for covariate selection, and forward stepwise regression was performed to evaluate the effect of HIV on Fazekas scores. Reliability analysis was done to evaluate inter-rater and intra-rater reliability. Correlation analysis was done within the PWH group to identify MRI, CSF and clinical variables that correlate with WMH in this group.

Table 1. Clinical and demographic comparison between cohorts

	PWH (n=203)	Control (n=58)	P-value
Gender (Female, %)	**50 (25)**	**27 (47)**	**0.002**
Ethnicity (Black, %)	112 (55)	36 (62)	0.37
Age (years, mean±SD)	50±9	49±10	0.51
Hypertension (%)	**66 (33)**	**7 (12)**	**0.002**
Diabetes Mellitus (%)	20 (10)	4 (7)	0.99
Hyperlipidemia (%)	**60 (30)**	**4 (7)**	**<0.001**
History of smoking (%)	89 (44)	27 (47)	0.61
BMI (mean±SD)	29±6	28±6	0.36
History of cocaine abuse (%)	**56 (28)**	**9 (16)**	**0.04**

Even after accounting for differences in cerebrovascular risk factors, brain white matter hyperintensities are more evident in people with well-controlled HIV infection compared to controls

RESULTS - 1. Differences between groups

- The PWH group had a significantly different distribution of total Fazekas score (see Figure 2, p=0.005), and the mean total Fazekas score **was significantly higher among the PWH group [2.1 (95%CI 2.0-2.2) vs. 1.6 (95%CI 1.3-2.0) with p=0.0086].**
- Age significantly affected the total Fazekas score and was therefore adjusted for in all calculations.
- After adjusting for age, only history of cocaine abuse had a significant effect on the total Fazekas score in both PWH and control group.
- Since frequency of cocaine abuse was significantly different between the groups, a subgroup analysis based on then history of cocaine abuse was made, and among patients with no history of cocaine abuse, mean total Fazeaks score was significantly higher in the PWH group **[2.0 (95%CI 1.8-2.1) vs. 1.5 (95%CI 1.3-1.7) with p=0.0007].**

Table 2. Fazekas scale definitions

	0	1	2	3
Periventricular WMH	No lesions	Pencil thin lining	Smooth halo	Irregular with extension to deep
Deep WMH	No lesions	Punctate foci	Beginning confluence of foci	Large confluent areas

Table 3. Disease characteristics of the PWH cohort (n=203)

Duration of HIV infection (years, mean±SD)	17±10
Duration of ART (years, mean±SD)	12±8
Duration untreated (years, mean±SD)	6±8
Nadir CD4<200 (%)	91 (45)
CD4 count (cells/mm³, mean±SD)	683±302

Table 3. Reliability analysis (n=49)

	Intra-rater reliability	Inter-rater reliability
Periventricular WMH	**0.89**	**0.73**
Deep WMH	**1**	**0.81**
Total score	**0.92**	**0.83**

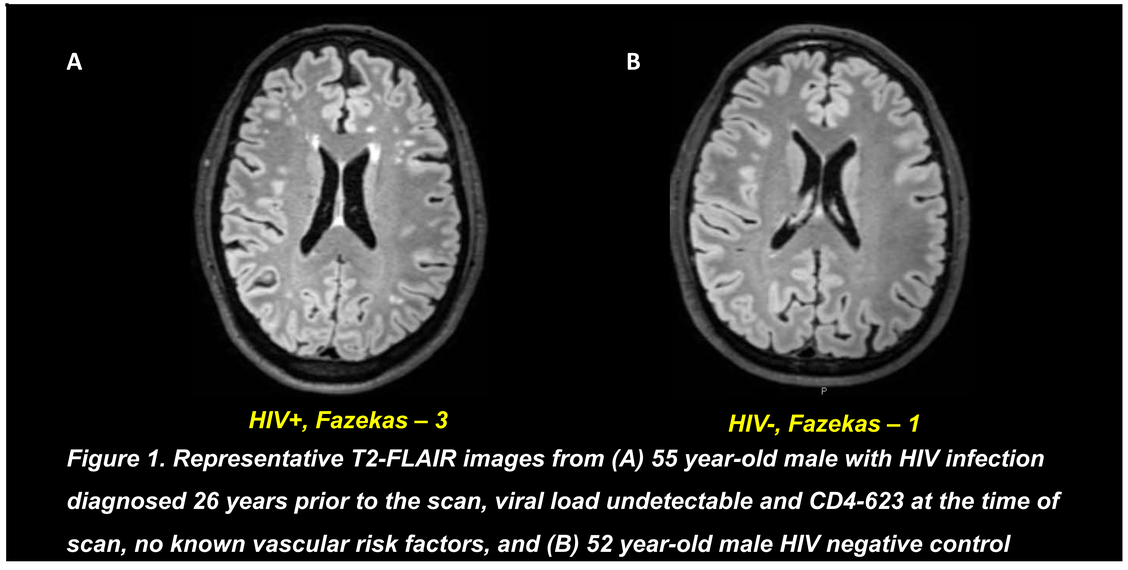
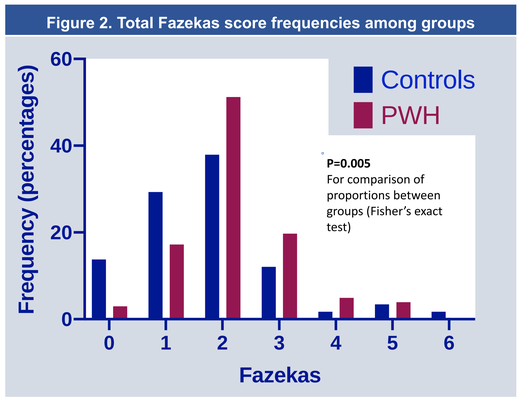


Figure 1. Representative T2-FLAIR images from (A) 55 year-old male with HIV infection diagnosed 26 years prior to the scan, viral load undetectable and CD4-623 at the time of scan, no known vascular risk factors, and (B) 52 year-old male HIV negative control

RESULTS – 2. Correlation within PWH group

- Patients with **history of CD4 count < 200 cells/mm³ (n=91) had a higher score** compared to the rest of the PWH group [2.3 (95%CI 2.1-2.5) vs. 2.0 (95%CI 1.8-2.1), p=0.011].
- Patients with **foci of leptomeningeal enhancement** on the post gadolinium scan had a **higher score** compared to the rest of the PWH group [2.5 (95%CI 2.2-2.8) vs. 2.1 (95%CI 1.9-2.2), p=0.013].
- Patients with **measurable TNF in the CSF had a higher Fazekas score** [2.5 (95%CI 2.2-2.7) vs. 2.0 (95%CI 1.7-2.2), p=0.004].

Figure 2. Total Fazekas score frequencies among groups



CONCLUSIONS

HIV infection contributes to the extent of brain WMH, even in the setting of well controlled infection. Prior immunosuppression evidenced by lower nadir CD4 partially explains this association. The cohort is undergoing serial MRI scans and neuropsychological testing to evaluate the long-term clinical effects of WMH.

Disclaimers and Funding

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- This study was supported by the intramural research program of NINDS, and by the Infectious Disease Clinical Research Program (IDCRP), a Department of Defense (DoD) program executed by the Uniformed Services University of the Health Sciences (USUHS) through a cooperative agreement with The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. (HJF). This project has been supported in part with federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health (NIH), under Inter-Agency Agreement Y1-AI-5072 and from the Defense Health Program, U.S. Department of Defense, under award HU0001190002.