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Machine Learning Quantifies Accelerated White Matter Aging in Persons with HIV

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BACKGROUND

- Persons with HIV (PWH) may undergo pathological white matter changes as they age
- These can be quantified using the brain age gap (BAG), the difference between true age and neuroimaging-predicted 'brain age'
- Hypothesis: white matter aging, i.e. progressive accumulation of microstructural changes, is accelerated in PWH with detectable viral load (VL)
- Co-morbid risk factors for white matter aging remain uncertain

METHODS

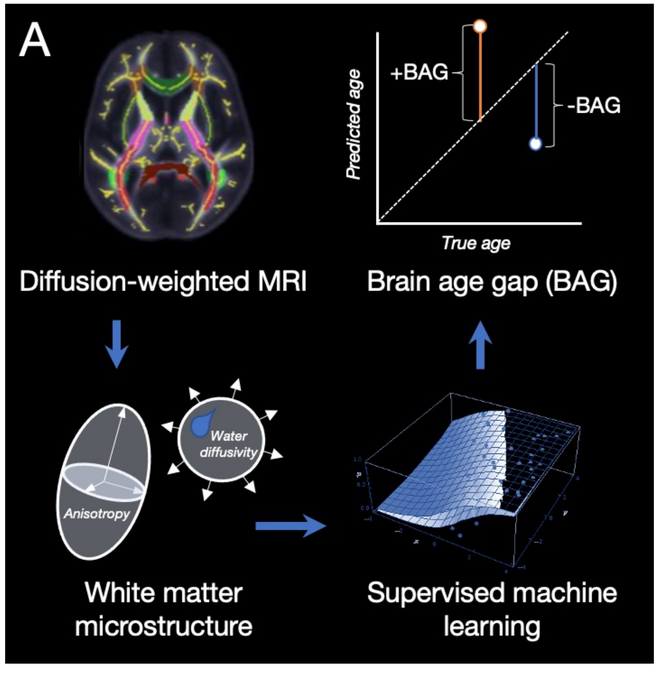
Study Design

- 290 PWH (age=48.2±13.7 yr.; 23% female; 65% Afr.-Amer.; 85% virally suppressed) & 165 HIV- controls (age=37.5±16.3 yr.; 47% F; 56% A.A.) imaged
- Age, race, biological sex were co-variates in all analyses
- Diffusion MRI on 3-Tesla Siemens scanner (TR/TE=9100/104ms, resolution=2x2x2mm, 30 gradient directions)
- Potential risk factors for white matter aging quantified: plasma VL, current CD4+ lymphocytes, nadir CD4+, hepatitis C, body-mass index, 10-year Framingham cardiovascular risk score, global cognitive z-score
- Cognitive function quantified using standard 15-question, 5-domain neuropsychological battery

Machine Learning and Statistics

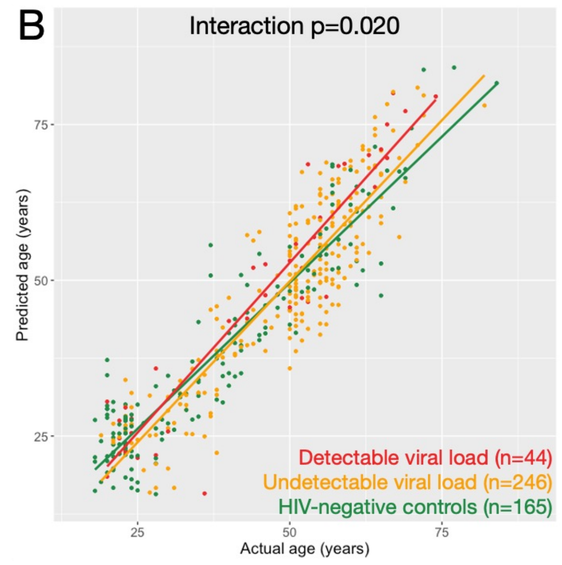
- Gaussian process regression model trained to predict age from diffusion scalars (mean diffusivity & fractional anisotropy)
- Training data: 624 publicly available healthy controls from Cambridge Center for Aging and Neuroscience (CamCAN)
- Trained model used to quantify BAG in PWH and HIV- controls (Fig. A)
- Interaction model applied: BAG ~ age × VL + covariates
- Potential risk factors for white matter aging identified using generalized linear regression with backwards variable selection and stop criterion of p<0.10

Older persons with detectable HIV show **accelerated** accumulation of age-like **white matter** changes on diffusion MRI, quantified with **machine learning**. These changes are associated with greater **cardiovascular** risk and reduced **cognitive** performance.



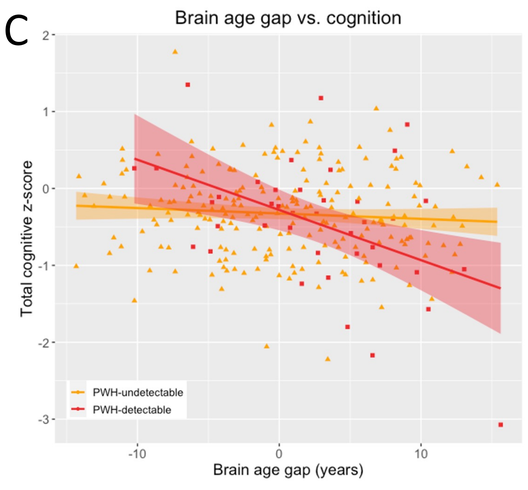
RESULTS

- Trained model predicted age in unseen participants with mean absolute error = 5.3 years after linear de-trending (R^2=0.48; p<0.001)
- Age and VL (>50 copies/mL) had a significant interactive effect on BAG (p=0.020; Fig. B)
- PWH with detectable VL accumulated +1.5 years BAG per decade vs. HIV- controls
- Backwards selection identified features associated with white matter aging: greater 10-year Framingham risk (p=0.002) & lower global cognitive z-score (p=0.043)
- Cognitive association with BAG was specific to those with detectable VL (p<0.001, Fig. C)



CONCLUSIONS

Aging with detectable HIV and elevated cardiovascular risk are significant correlates and potential risk factors for white matter pathology, and may contribute to the etiology of cognitive impairment in PWH.



ADDITIONAL INFORMATION

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