Neuroimaging Correlates of Frailty and HIV

Jeremy F. Strain PhD[1], Robert X Smith PhD[1], Sarah Cooley[1], Robert H. Paul[3], Beau Ances MD, PhD[1]
Washington University School of Medicine in St. Louis[1], Department of Neurology
Washington University School of Medicine in St. Louis[2], Department of Neuroscience[2],
Missouri Institute of Mental Health, University of Missouri in St. Louis

Introduction

- Antiretroviral therapy can promote a longer lifespan by preventing further viral DNA integration.
- Viral Reservoirs can persist in virally suppressed HIV+ individuals and act as chronic suppliers of viral antigen for decades.
- Chronic HIV patients are often afflicted with a variety of age-related comorbities that can manifest as cognitive sequelae.
- Frailty is a phenotypic assessment that examines differet physical attributes as a generic metric for secondary anatomical etiologies.
- Frailty was defined by the Fried criteria any subject with >2 was designated as Frail and <3 was designated as Non-Frail (NF)

Aims

- In a data driven approach we assessed the relationship between brain integrity, neuropsychological performance (NP), and fraitly in a well-controlled HIV+ population.

NP Methods

- Global Deficit scores (GDS) were derived from a NP battery of tests.
- Domains included executive function, psychomotor speed, and memory.

ASL Methods

- Resting Cerebral Blood Flow (rCBF): Pseudocontinuous arterial spin labeling time, (1.5 seconds labeling time, 1.2 seconds post-labeling delay) was used to measure perfusion of arterial blood into cortical and subcortical brain tissue. Acquired images have a resolution of 3.4x3.4x5.0 mm.
- Voxel-wise analysis was performed between subjects labeled as Frail vs NF

	Frail (>2)	NF (<3)
N	11	78
Gender: Male/Female	4/7	10/68
Age M(SD)	57.7 (4.96)	55.27 (6.58)
Current CD4	586 (299)	631 (267)
Nadir CD4	165 (193)	109 (117)
Viral Load	<20	<20

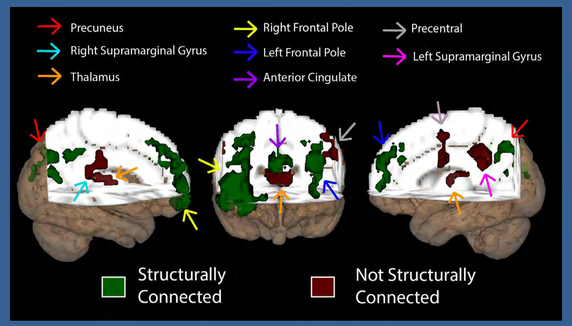


Figure 1: Results for the voxel-wise comparison for CBF between Frail and NF HIV+ individuals. Eight ROI's were identified and those labeled in green were found to be structurally connected (see below).

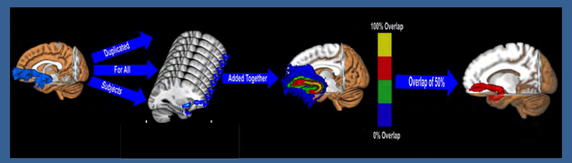


Figure 2: Depiction of our methodology for creating white matter tracts from each CBF region.

DTI Methods

- Correction for motion and eddy current distortions followed by skull stripping using FSL 5.0.4.
- Fractional Anisotropy (FA) maps were generated with DTIFIT.
- Tract Based Spatial Statistics was performed with a skeleton of 2.5 threshold.
- Each significant ASL-region derived from the voxel-wise comparison for Frail vs NF was treated as a seed region for probabilistic tractography in 9 subjects from the Human Connectome Project (Figure 2).
- These white matter tracts were used as regions of interest and overlaid onto our HIV cohort .
- All FA values within each of the tracts were averaged together to create a summarized FA for all connections between the structurally connected ASL regions.

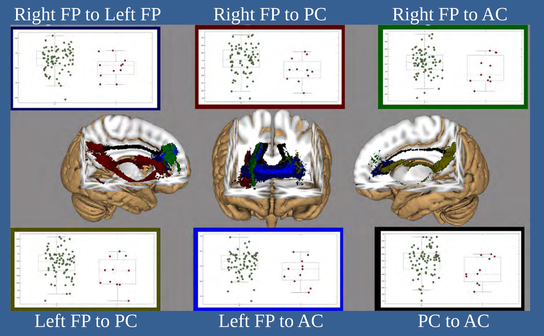
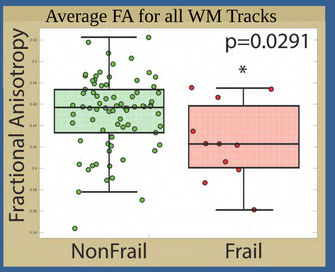
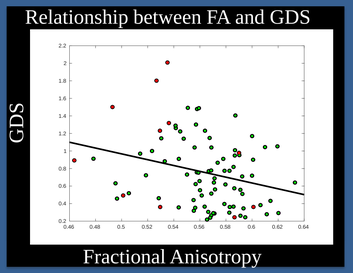


Figure 3: White matter tracts between the 8 CBF regions.

Results

- The voxel-wise results for the CBF analysis are shown in Figure 1 with 8 clusters that were significantly different between Frail and NF.
- Mann-Whitney tests of the median revealed significantly lower FA for white matter connecting the four regions between frail and NF HIV+ individuals (p=0.03).
- Across the entire cohort a negative association was seen for Average FA and performance in the executive domain (p=0.02; r=-0.25) and GDS (p=0.01; r=-0.2731).
- A linear model incorporating FA and CBF significantly predicted GDS outcome (p=0.009) but only CBF significantly improved the model (p=0.034).





Summary

- We conclude that HIV+ frail individuals have reductions in CBF and decreased structural connections between those regions that were directly connected.
- Both lower CBF and reduced FA in these ROI's predicted poorer cognitive performance suggesting a possible etiology to the behavioral changes associated with the frailty index.
- CBF was the stronger predictor within the model suggesting white matter integrity may be a secondary degenerative process.
- This multi-modality approach suggests that the frailty index is capable at identifying secondary pathologies that reflects accentuated functional and structural damage in HIV+ individuals.