HIV and Addictions Research Program

Multimodal Brain Abnormalities Associated with Cognitive Impairment in HIV Infection

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Background

- Neurocognitive impairment (NCI) remains a prevalent neurological complication of HIV.
- Noninvasive magnetic resonance imaging (MRI) has yielded important insights into the neuropathology of HIV:
  - Broad reductions in white matter integrity
  - Atrophy in deep gray matter regions and frontal cortex
  - Diminished functional connectivity in major networks
- However, unimodal studies may provide an incomplete characterization of brain alterations that underlie NCI.

Specific Aims

- Identify structural-functional co-alterations in the brain that distinguish people with and without HIV.
- Investigate the relation of multimodal neural co-alterations to cognitive function.

Methods

- Sample: 117 adults aged 18-55 with verified HIV status
  - Exclusions: major neurological disorder, head trauma, severe mental illness, substance dependence, history of illicit drug abuse, <8 years of education
- Neuropsychological testing: 7 domains (2-3 tests each)
  - Demographically corrected T-scores
  - Global cognitive function (mean of all domains)
- MRI protocol: 3T GE Discovery MR750 scanner
  - T1-weighted (T1w) – gray matter morphology
  - Diffusion-weighted imaging (DWI) – white matter integrity
  - Resting-state functional MRI (fMRI) – functional connectivity

TABLE 1. Participant characteristics by HIV status

	HIV+ *N* = 59	HIV- *N* = 58	
Age in years, M (SD)	41.2 (8.5)	37.8 (9.5)	t(115) = 2.04*
Cis-female gender[1], %	24%	34%	$\chi(1)^2 = 1.16$
African-American race, %	76%	66%	$\chi(1)^2 = 1.16$
Education in years, M (SD)	14.1 (2.1)	14.7 (2.1)	t(115) = 1.64
Global T-score, M (SD)	45.3 (6.5)	49.2 (6.5)	t(115) = 3.20**

[1] For all participants, biological sex matched gender identity; *$p < .05$, ** $p < .01$

- HIV characteristics: All HIV+ participants were on ART.
  - Current viral suppression (<50 copies/mL): 78%
  - Years since HIV diagnosis: M = 10.1 (SD =7.8)
  - Current CD4+ count: Median = 598 (IQR = 424)
  - Nadir CD4+ count : Median = 250 (IQR = 297)

Linked structural and functional deficits in brain networks revealed by multimodal MRI **predicts** HIV-associated **cognitive impairment.**

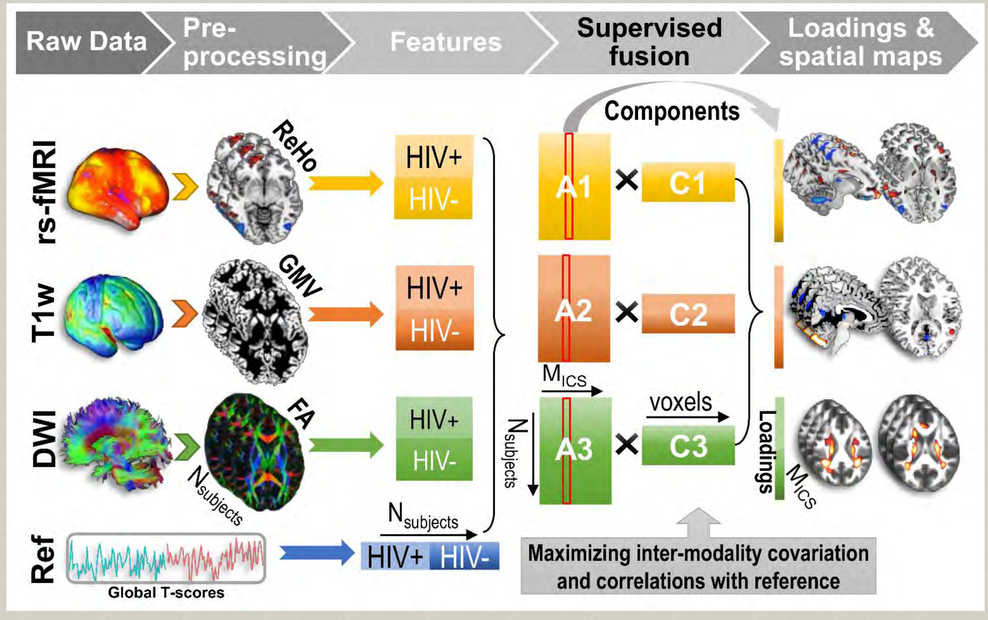

FIGURE 1. Multimodal canonical correlation analysis with reference + joint independent component analysis (MCCAR-jICA). Preprocessed MRI features were fed into the pipeline (ReHo = regional homogeneity; GMV = gray matter volume; FA = fractional anisotropy). Global T-score was used as the reference. Analyses controlled for age, race, and protocol.

Results

- One 3-way component distinguished the HIV+ and HIV- groups.
- This component correlated with global cognitive function, as well as memory, attention, and processing speed.

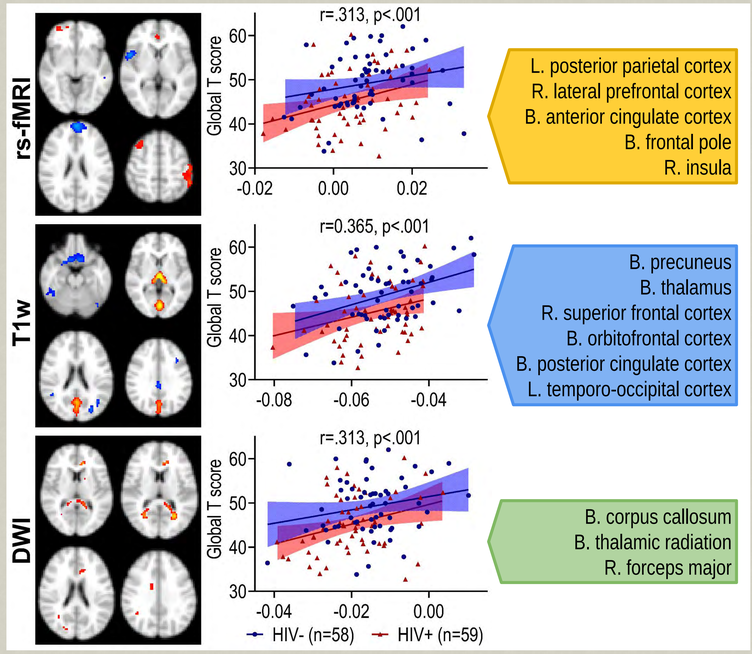

FIGURE 2. Group-discriminating multimodal component. Images are representative spatial maps. Scatter plots show correlation of component loadings with global cognitive function.

Conclusions

- Persons with HIV evidenced differences in a correlated network of regions that involved:
  - Hypertrophy in the thalamus and precuneus, and atrophy in prefrontal and temporo-occipital cortices.
  - Reduced white matter integrity in large segments of the corpus callosum and thalamic projections.
  - Abnormal connectivity in posterior parietal, anterior cingulate, and prefrontal cortices.
- These results suggest that disruptions in linked neural networks may underlie critical cognitive functions.
- Multimodal biomarkers of neuroHIV may aid in diagnosis and tracking of HIV-associated neurocognitive disorders.

Miscellaneous

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