HIV and Addictions Research Program

Cocaine use independently predicts white matter lesion burden in HIV disease

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Introduction

- Neurocognitive impairment remains a prevalent complication of HIV disease, even in patients with sustained viral suppression.
- White matter hyperintensities (WMH), a marker of diffuse small vessel disease, reflect decreased blood flow to deep areas of the brain and contribute to cognitive deficits.
- WMH have been observed at higher rates in persons with HIV (PWH), likely due to persistent immune activation and increased risk of medical comorbidities.
- Aging and cardiovascular disease (CVD) risk factors are the main predictors of WMH.
- Cocaine, a potent central nervous system stimulant, has been linked to increased risk of stroke and white matter injury.
- Cocaine use is disproportionately common in PWH and may contribute to increased WMH burden.

Study Aims

- This study quantified WMH burden in PWH using T2 fluid-attenuated inversion recovery (FLAIR) imaging to:
  1) Investigate the contribution of cocaine use to WMH, after accounting for age and common CVD risk factors.
  2) Examine the correlation of WMH to cognitive function.

Sampling

- 110 adults (range: 18-59 years) with chronic HIV were recruited from infectious diseases clinics in the Durham, NC area
  - Inclusions: antiretroviral therapy, suppressed HIV viral load
  - Exclusions: perinatal infection, major neurological disorder, head trauma, severe mental illness, systemic autoimmune disease, immunomodulatory medication
- Participants were stratified based on cocaine use history:
  - COC+: history of regular use, any use in past 90 days
  - COC-: no history of regular use, 0 days of use past 90 days

Table 1. Participant characteristics by cocaine use status

	COC+ (n=32)	COC- (n=78)	*p*-value
Age in years, M (SD)	50.0 (8.58)	43.5 (9.01)	<.001
Female gender, %	18.7	20.5	.834
African-American race, %	87.5	70.5	<.001
Education in years, M (SD)	12.7 (1.96)	14.3 (2.60)	.002
Years since HIV diagnosis, M (SD)	15.0 (7.13)	14.4 (7.83)	.742
Nadir CD4⁺ T-cell count, Mdn (IQR)	76 (181)	238 (273)	.002
Current CD4⁺ T-cell count, Mdn (IQR)	460 (504)	814 (380)	<.001
Years of regular cocaine use, M (SD)	18.3 (10.7)	0.00	NA
Days of cocaine use in past 90, M (SD)	23.8 (21.0)	0.00	NA
CVD risk score, M (SD)	1.78 (1.24)	1.47 (1.11)	.207

Persons with HIV who use cocaine have higher white matter lesion burden, even after accounting for cardiovascular risk factors.

MRI Protocol

- MRI protocol: 3T GE Discovery MR750 scanner
  - T2 FLAIR: 0.4mm² x 5mm voxels, TR = 10000ms, TE = 120ms
  - T1 anatomical: 1.0mm³, TR = 8.16ms, TE = 3.18ms
  - Lesion burden = total WMH volume / total intracranial volume

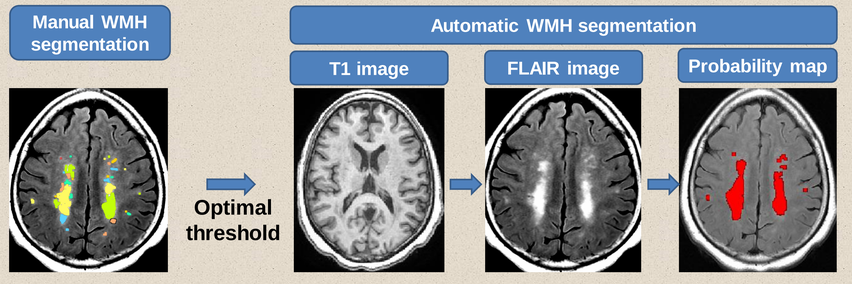

Figure 1. *Processing pipeline for quantifying WM lesion burden.* A neuroradiologist manually segmented a subset of cases to establish the optimal threshold. Using the Lesion Segmentation Toolbox, T1 images were co-registered to FLAIR images and segmented into cerebrospinal fluid, white matter, and gray matter maps. These maps were combined with co-registered FLAIR intensities to calculate lesion probability maps utilizing the lesion growth algorithm.

Assessment Battery

- Cognitive function: neuropsychological testing
  - Battery of tests that assessed 7 cognitive domains
  - Raw scores converted to demographically adjusted T-scores
  - Global T-score = average of 7 domain T-scores
- Cardiovascular disease risk: CVD risk score
  - Sum of common risk factors: diabetes, current smoking, hyperlipidemia, hypertension, obesity, and prior cardiovascular disease (range: 0-6)
- Substance use history: Addiction Severity Index, Timeline Follow-back, urine drug testing, Structured Clinical Interview for DSM5

Results

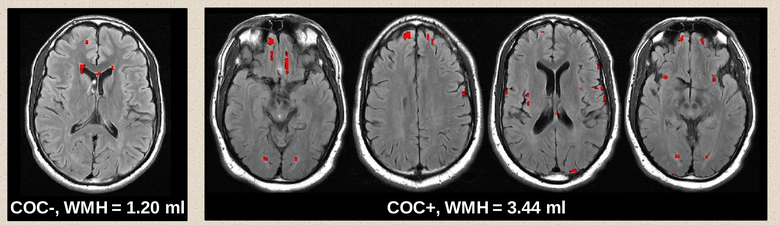

Figure 2. Images show WM lesions in representative participants.

Table 2. Hierarchical regression models predicting WMH

	Step 1: Demographics	Step 2: Clinical Factors	Step 3: Substance Use
Age in years	0.369**	.303*	.169
Male sex	.131	.037	.092
Caucasian race	.128	.034	-.041
CVD risk score	-	.289**	.295**
Nadir CD4	-	-.029	-.047
Current CD4	-	-.025	.055
Years HIV+	-	-.090	-.047
Alcohol use	-		-.083
Marijuana use	-		-.124
Cocaine use	-		.280*

Standardized beta weights reported. *p < .05, **p < .01. Overall model: F = 3.44**, R^2 = .258

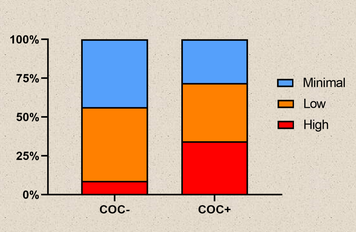

Figure 3. WMH classification by COC group ($\chi^2(2) = 10.84$, p = .004).

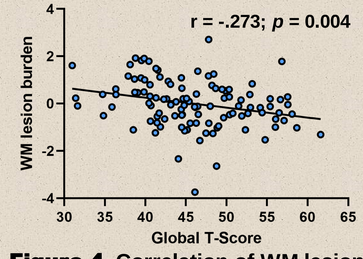

Figure 4. Correlation of WM lesion burden and cognitive function.

Discussion

- Cocaine use in PWH was associated with greater WM lesion burden, even after accounting for age and CVD risk factors.
- WM lesion burden correlated with poorer cognitive function.
- Cocaine use is theorized to potentiate WM damage through increases in dopamine levels and subsequent vasoconstriction.
- Results underscore the importance of reducing cocaine use in PWH to minimize additional WM lesions that may exacerbate neurocognitive impairment.

Miscellaneous

- Funding: R01-DA043241
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