HIV DNA Peripheral Reservoirs Have a Nonlinear Impact on Brain Pathology

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Background

The contribution of peripheral blood mononuclear cells' (PBMCs) HIV DNA levels to HIV-associated dementia (HAD) and non-demented HIV-associated neurocognitive disorders (HAND) in chronically HIV-infected adults with long-term viral suppression on combined antiretroviral treatment (cART) is not fully understood.

Aims

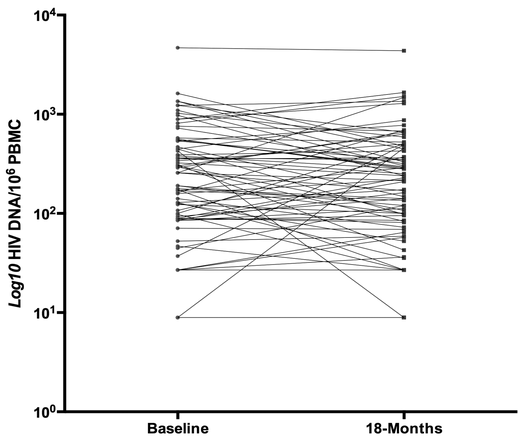
To establish the contribution of HIV DNA within PBMCs to HAD and non-demented HAND in chronically HIV-infected patients with long-term viral suppression.

Methods

Prospective observational cohort.

80 adults with chronic HIV infection underwent at two visits 18 months apart:

- **Assessments of neurocognition;**
- **Pre-morbid cognitive ability;**
- **HIV DNA in PBMCs was measured by real-time PCR.**



Baseline and follow-up study sample demographic, laboratory and clinical characteristics

	Baseline	Follow-up	p
Age	55.08±7.53	56.74±7.61	<.0001
Education	14.06±2.75	14.11 ± 3.20	.85
Gender (count)	79 males / 1 female	-	
Ethnicity (% Anglo-Australian)	98.7%	-	
Australian standardized Predicted WAIS-III VIQ	108.97±7.22	-	
HIV Risk groups (%MSM)	86.2%	-	
HAND %	53.7%	-	
ANI / MND / HAD %	36.2% / 10.0% / 7.5%	-	
History of HAND %	15.0%	-	
Median Nadir CD4-T cell count (cells/mL)	194	-	
Median Current CD4-T cell count (cells/mL)	556	614	<.0001
Plasma HIV RNA <50 cp/mL	97.5%	87.5%	.08
Always undetectable % (vs. not always)	-	85%	
CSF HIV RNA <50 cp/mL (N=34)	97%	-	
Median HIV duration (years)	19.1	-	
AIDS (CDC 1993)	67.5%	No new CDC C	
Median Current cART duration (months)	29	37	
ART treated during 1st year of HIV infection	20.0%	-	
Log(n) HIVDNA in PBMCs	5.21 ± 1.42	5.12 ± 1.40	.45

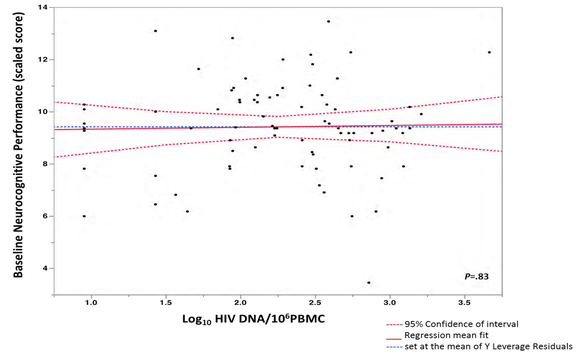
Results

At baseline, 46% had non-demented HAND; 7.5% had HAD. Neurocognitive decline occurred in 14% and was more likely in those with HAD (p<.03).

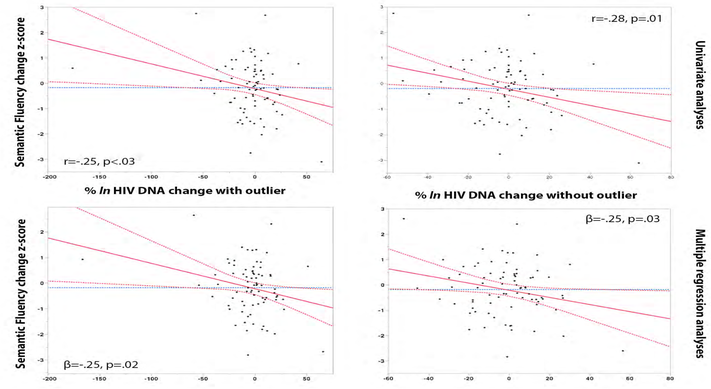
Low pre-morbid cognitive ability was uniquely associated with HAD (p<.05). Log10 HIV DNA copies were stable between study visits (2.26 vs. 2.22 per 106 PBMC).

Baseline HIV DNA levels were higher in those with lower pre-morbid cognitive ability (p<.04), and higher in those with no ART treatment during HIV infection 1st year (p=.03).

Baseline HIV DNA was not associated with overall neurocognition.



% In HIV DNA change was associated with decline in semantic fluency in unadjusted and adjusted analyses (p=.01-.03), and motor-coordination (p=.02-.12) to a lesser extent.



Conclusions

PBMC HIV DNA plays a role in HAD pathogenesis, and this is moderated by pre-morbid cognitive ability in the context of long-term viral suppression.

While the HIV DNA levels in PBMC are not associated with current non-demented HAND, increasing HIV DNA levels were associated with a decline in neurocognitive functions associated with HAND progression.

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