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CSF CXCL10 is associated with the presence of low-level CNS HIV during ART

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HIV NEUROBEHAVIORAL RESEARCH PROGRAM
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Background & Significance

- The central nervous system (CNS) is a reservoir of HIV during antiretroviral therapy (ART).[1,2] Our group and others have demonstrated that HIV RNA by single copy assay (SCA) is frequently detected in cerebrospinal fluid (CSF) during ART.[3,4]
- However, the measurement of low-level HIV RNA requires specialized protocols and is not always quantifiable during ART. Therefore, surrogate markers of HIV CNS persistence are needed that are widely available and readily quantifiable.
- In this study, we evaluated two immune markers (CXCL10 and sCD30) that in prior studies have shown promise as markers of HIV persistence.[5,6] We hypothesized that both would be associated with low-level HIV by SCA. We also evaluated the association between these markers and CSF markers of neuronal damage.

Methods

- We performed a cross-sectional analysis of persons with HIV (PWH) on stable combination ART with both plasma and CSF HIV RNA <50 copies/ml by conventional PCR.
- In addition to HIV RNA by SCA in both compartments (plasma and CSF), we measured CSF CXCL10 by single molecule ELISA and sCD30 by standard ELISA.
- We also measured neurofilament light chain (NFL) and neuron specific enolase (NSE), CSF markers that reflect neuronal damage. Comparisons were made with either Wilcoxon rank sum for continuous variables or Fisher's exact test for categorical variables. Logistic regression was performed with CSFHIV+ as outcome (CSF positive by SCA).

Results

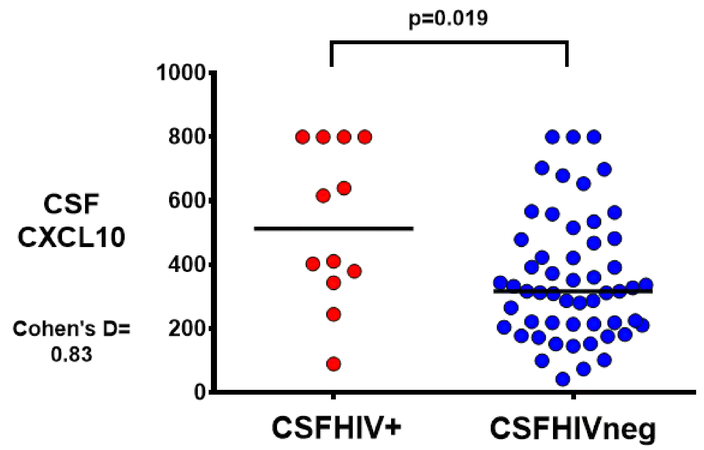
- Paired plasma/CSF samples from 66 HIV+ individuals on suppressive ART were analyzed (see table).
- All participants were on three drug ART with most common regimens being efavirenz/tenofovir/emtricitabine and atazanavir/ritonavir/tenofovir/emtricitabine.
- There were no statistically significant differences between CSFHIV+ and CSFHIVnegative groups in terms of age, sex, or race/ethnicity. There were also no statistically significant differences in terms of duration on current ART regimen.

Results:

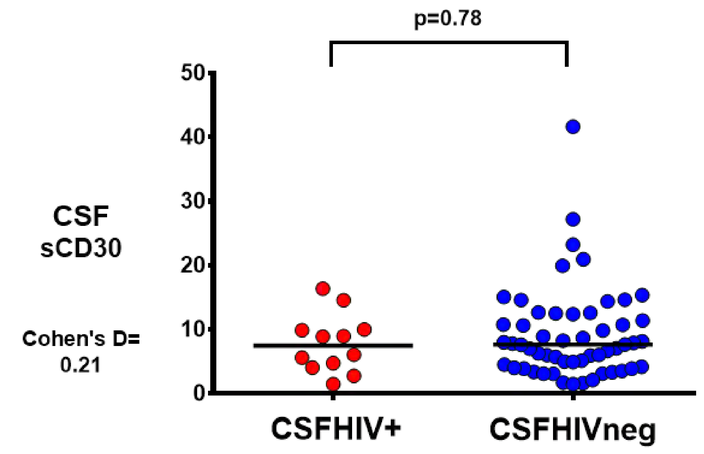
Variable	All participants (n=66)	CSFHIV+ (n=12)	CSFHIVneg (n=54)	P value for difference
Age	45 (41-50)	42 (39-49)	46 (42-50)	0.15
Male Sex	60 (90.9%)	10 (83.3%)	50 (92.6%)	0.3
Race				0.82
White	35 (53%)	8 (66.7%)	27 (50%)	
Black	17 (25.8%)	3 (25.0%)	14 (25.9%)	
Other	14 (21.2%)	1 (8.3%)	13 (24.1%)	
Current CD4+	483 (356-718)	476 (359-752)	500 (351-717)	0.98
Nadir CD4+	98 (21-231)	88 (34-259	104 (14-226)	0.61
Months on current ART regimen	19 (9-36)	15 (5-23)	19 (10-37)	0.19
Proportion with plasma HIV+ RNA by SCA	33 (50%)	10 (83%)	23 (43%)	0.023*
CSF results				
WBC	2 (1-4)	4 (2-7)	2 (1-3)	0.035*
Protein	40 (33-51)	39 (34-55)	41 (32-51)	0.99
CXCL10	341 (218-541)	514 (353-800)	317 (213-480)	0.019*
sCD30	7.6 (4.2-11.6)	7.5 (4.2-10.0)	7.6 (4.1-12.4)	0.78
NFL	572 (407-706)	586 (433-669)	572 (402-732)	0.96
NSE	11039 (8805-14178)	12094 (9780-13623)	10918 (8716-14701)	0.8

Variables are reported as either median (interquartile range) or number (%)
*Denotes p value <0.05)

- CSF CXCL10 concentrations were significantly higher in the CSFHIV+ group (p=0.019), see top figure.
- CSF sCD30 concentrations were not statistically different between CSFHIV+ and CSFHIVnegative groups (p=0.78), see bottom figure.
- In the logistic regression model that incorporated both CSF CXCL10 and Plasma HIV positivity, CXCL10 remained statistically associated with CSFHIV positivity,
  Odds ratio for CXCL10 (per 100-unit change)= 1.4 (95% Confidence Interval= 1.02-1.93, p=0.038)
  Odds ratio for PlasmaHIV+ (positive versus negative) = 5.9 (95% Confidence interval= 1.13- 30.98, p=0.035)



CXCL10 concentration measured as pg/ml
horizontal line= median



sCD30 concentration measured as ng/ml
horizontal line= median

Conclusions

- CSF CXCL10 concentrations are higher in people with detectable low-level CNS HIV on ART.
- Higher CXCL10 concentration remains associated with the presence of low-level CNS HIV even when accounting for the presence of low-level plasma HIV.
- CXCL10 may be a promising and more easily measured marker than HIV RNA or SCA to quantify CNS HIV persistence in future studies of HIV eradication interventions.

References

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