INTRA-INDIVIDUAL STABILITY OF CSF BIOMARKERS OVER 12 YEARS IN PEOPLE WITH HIV (PWH)

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Poster 409

Background

- Even with viral suppression due to successful antiretroviral therapy (ART), inflammation can persist in people with HIV (PWH), particularly as they age[1].
- This persistence can aggravate comorbid physiological, neurological, and cognitive disorders associated with advanced chronological age[2,3].
- Relatively little is known about how soluble biomarkers that reflect these biological processes change over more than a decade.
- To address this gap, we measured soluble biomarkers in both blood and cerebrospinal fluid (CSF) in the same participants over an approximately 12-year time span.

Methods

Participant Characteristics:

Participants were recruited, consented and enrolled into the CNS HIV Antiretroviral Therapy Effects Research (CHARTER) study between 2003 and 2007 (Visit 1), and reassessed at a median 12-year follow-up visit as part of the CHARTER Aging Study between 2015 & 2020 (Visit 2).

Those included in this data analysis completed a battery of demographic screening, behavioral, neuropsychiatric and medical assessments at Visits 1 and 2. Blood specimens were collected at both timepoints from a total of 148 PWH, and CSF specimens were collected from a total of 102 PWH. Twelve biomarkers were quantified by immunoassay. Biomarker concentrations were transformed to reduce skewness. Linear regression (LR) compared biomarker concentrations at Visits 1 and 2, and demographic and disease characteristics were accounted for by multivariable LR (MLR).

Statistical Analysis:

Bivariate correlations were calculated between Visit 1 and Visit 2 values for biomarkers in blood and CSF. LR analysis was performed to determine whether cognitive changes as assessed by a regression-based Summary Change Score (rSCS) over 12 years were associated with demographic, disease, or treatment characteristics.

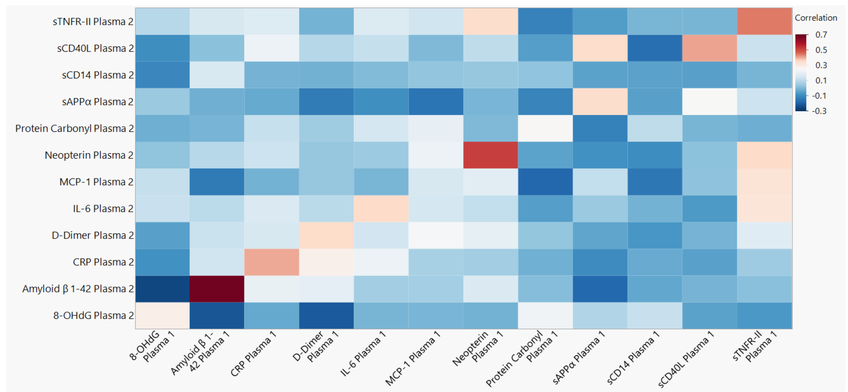
Results

	Visit 1	Visit 2
Age (years)[1]	43.7	56.1
Duration of HIV (years)[1]	10.2	22.6
Duration of ART (years)[1]	5.4	15.6
Sex (Women)[2]	20.9	19.2
Race (Black)[2]	38.6	39.1
Education (years)[1]	13.1	13.1
Body Mass Index[3]	25.2	26.3
Nadir CD4+ Count (/μL)[3]	167.0	106.5
AIDS Diagnosis[2]	63.4%	74.7%
On ART[2]	76.5%	99.4%
CD4+ T-Cell Count (/μL)[3]	472	586
Plasma HIV RNA ≤ 200*	-	89.5%
CSF HIV RNA ≤ 50*	-	92.3%

	Visit 1	Visit 2
Global Deficit Score[3]	0.37	0.43
rSCS[2]	-	-0.30
Global Cognitive Decline[2]	-	-24.3%
Beck Depression Inventory[3]	12	7
Current Major Depressive Disorder[2]	11.9%	8.2%
Diabetes[2]	5.8%	19.8%
Chronic Lung Disease[2]	11.8%	23.3%
Hypertension[2]	21.6%	53.4%
Hyperlipidemia[2]	13.7%	41.1%
HCV Seropositive[2]	23.5%	40.4%
Lifetime Alcohol Use Disorder	28.5%	34.6%
Lifetime Cocaine Use Disorder	7.3%	9.0%
Lifetime Cannabis Use Disorder	20.5%	25.6%
Lifetime Opioid Use Disorder	1.3%	2.6%

Table 1: Demographic and Clinical Characteristics of the study sample.
[1]=Mean, [2]=Percent, [3]=Median, *=of those on ART

a.



b.

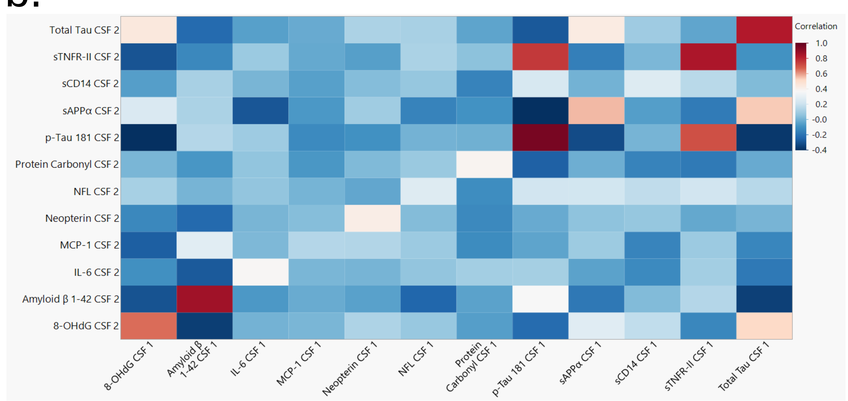


Figure 1: Correlation heatmap illustrating relationship between soluble biomarkers in Plasma (a) and CSF (b) at Visit 1 & 2.

Results

a. b.

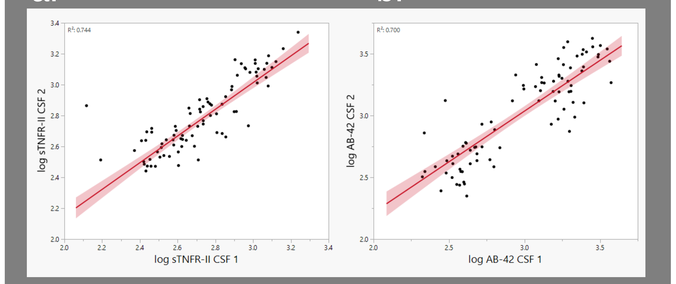


Figure 2: Most significant correlations in soluble biomarkers between Visits 1 & 2 from CSF: sTNFR-II (a) and Aβ-42 (b)

Conclusions

Over 12 years, several biomarkers in CSF remained remarkably stable in PWH who were taking ART.

Biomarker relationships in CSF did not substantially change after adjustment for age, sex, race/ethnicity, CD4+ T-cells, and HIV RNA

Several explanations are possible: These biomarkers may be at low concentrations that do not fluctuate over time. Alternatively, they may be elevated but invariable over time, which could occur, for example, if their concentrations were genetically determined. In contrast, other biomarkers varied much more over 12 years.

Biological processes underpinning neurological complications in PWH may be due to a combination of invariable **and** variable mechanisms that could respond differently to interventions.

References:

1. Sieg et al, Curr., HIV/AIDS Rep., 2021. PMID: 33709322
2. Deeks et al., Immunity 2013. PMID: 24138880
3. Marcus et al., JAMA Network Open 2020. PMID: 32539152

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