No Decline in CSF or Plasma Neurofilament Light Chain Levels post Early ART Initiation

598

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INTRODUCTION

- Early detection of HIV in the CNS has been reported a few days post HIV transmission, initiating neuroinflammation and brain injury even during the early asymptomatic stages of infection that impacts later life brain health.[1]
- It is unknown whether neuronal injury is ongoing during early untreated HIV, and/or declines post-ART.
- In this longitudinal CNS study of participants enrolled during early HIV infection, we modeled longitudinal trajectories of cerebrospinal fluid (CSF) and plasma neurofilament light chain (NfL), a sensitive biomarker of active neuronal damage, and examined associations with lab and neuropsychological (NP) parameters in early infection.

METHODS

- Longitudinal NfL concentrations were measured in CSF and plasma samples collected from men who have sex with men (MSM) in the Primary Infection Stage CNS Events Study (PISCES) in San Francisco, USA (2005-2014).
- The participants were enrolled during primary HIV infection (PHI) stage, that is, within 12 months post HIV transmission.
- Since the samples were collected mostly prior to test and treat guidelines, the participants started ART at variable times during the follow-up period [median days of infection at start of ART was 341 (185-685) days].

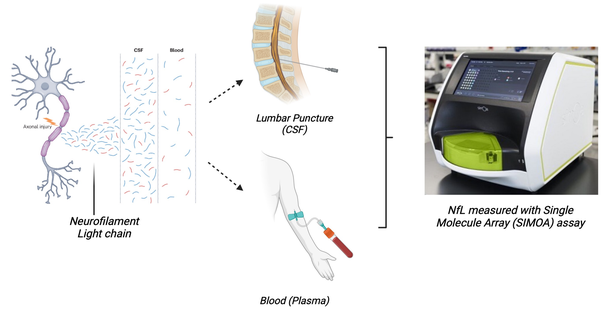


Figure 1: Single Molecule Array was used to measure NfL concentrations

- This longitudinal analysis was based on a total of 166 CSF (n=33) and 336 plasma samples (n=55) sampled over time.
- Linear-mixed models were used to determine longitudinal CSF and plasma NfL trajectories before and after ART initiation while bivariate longitudinal correlation assessed the correlation between CSF and plasma NfL levels with metrics from the motor domain performance and NP outcomes, defined by total z-score from a summed 11 test NP battery (NPZ-11).
- We also measured baseline CSF NfL levels in a matched control group of people without HIV (n=26) to map the baseline 95% confidence intervals of NfL in people without HIV.

RESULTS

In participants longitudinally studied starting at median four months after acquiring HIV, CSF NfL did not decline over time either pre- or post- ART, suggesting that ART does not alter NfL concentration during early stages of HIV.

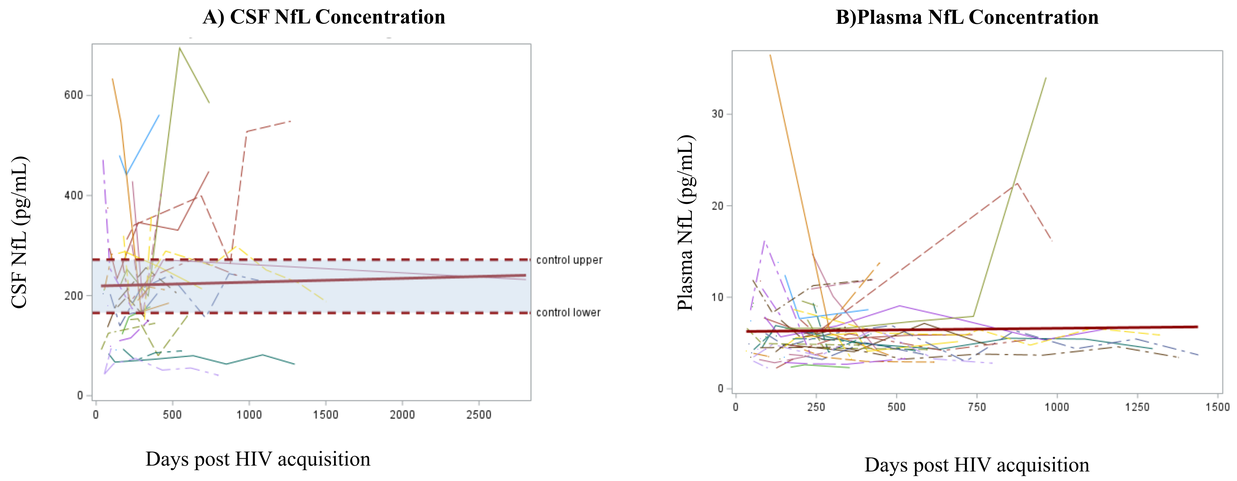


Figure 2: Natural History of A) CSF & B) Plasma NfL Concentrations During Untreated Primary HIV Infection. Although not statistically significant, CSF NfL levels showed a slight increasing trend before ART initiation (ß=0.053, p=0.12) Plasma NfL changes were also not significant (ß=0.00036, p=0.75). *Figure A shows the 95% confidence intervals for the control group of people without HIV.

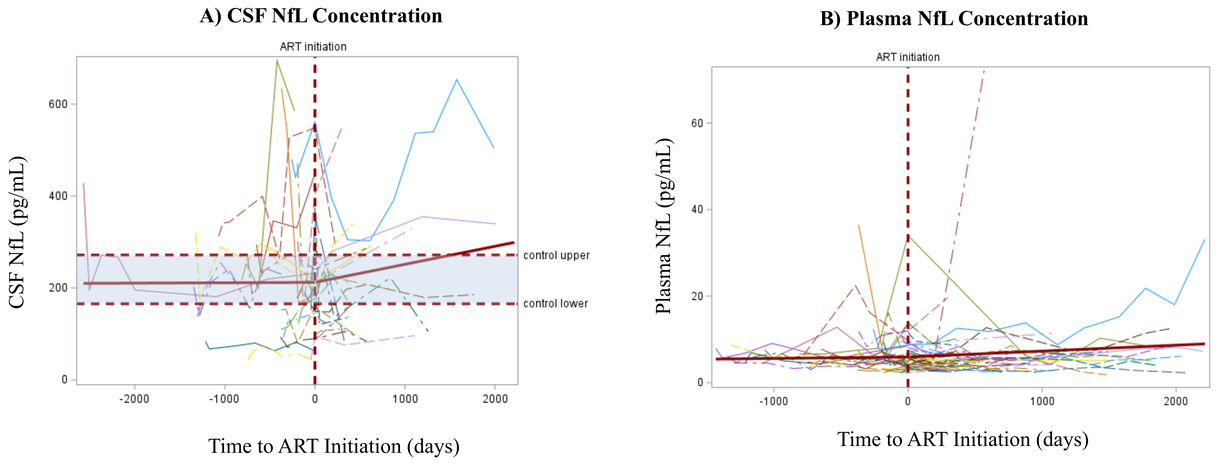


Figure 3:A) CSF & B) Plasma NfL concentration vs Time relative to ART at Initiation, adjusting for Baseline age & CSF HIV-1 RNA. There was no significant change in CSF NfL pre- and post-ART (ß = 0.02, p = 0.35 and ß = -0.003, p = 0.099, respectively), while plasma NfL did not change before ART (ß = 0.0003, p = 0.75) but increased significantly post-ART (ß = -0.001, p = 0.037). However, the trend difference between the pre- and post-ART slopes was not significant in both CSF and plasma (ß=0.01, p=0.74 and ß=0.001, p=0.44, respectively).). *Figure A shows the 95% confidence intervals for the control group of people without HIV.

Table 1: Participants' Baseline Characteristics

Variable	Value (n=55)
Male, (n, %)	55 (100)
Age (years)	39 (32-46)
Estimated days of infection	106 (62-168)
CD4+ T cell count (cells/µL)	587 (421-735)
Plasma HIV-1 RNA, (log_{10} Copies/mL)	4.59 (3.96-5.02)
CSF HIV-1 RNA, (log_{10} Copies/mL)	2.56 (1.69-3.06)
ART-naïve (n, %)	54 (98.2)
CSF WBC count [cells/µL]	6.0 (3.0, 8.0)

Longitudinal correlation of CSF & Plasma NfL with NPZ-11 total z-scores and motor domain function

CSF and plasma NfL levels did not correlate longitudinally with NPZ-11 scores and average motor domain scores pre-ART.

CONCLUSIONS

- CSF NfL did not decline over time either pre- or post- ART suggesting that ART does not alter NfL concentration during early stages of HIV.
- Further studies with longer follow-up and larger sample sizes are needed to understand if neuronal injury is established during PHI and if there is any clinical significance associated with it if observed in PWH in early infection.

REFERENCES

1 Peluso MJ, Meyerhoff DJ, Price RW, Peterson J, Lee E, Young AC, et al. Cerebrospinal fluid and neuroimaging biomarker abnormalities suggest early neurological injury in a subset of individuals during primary HIV infection. J Infect Dis. 2013;207(11):1703-12.

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