Brain HIV Latency Biomarkers

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BACKGROUND

- The presence and quantification of HIV in the brain is important for eradication as neuropathological studies suggest that latent brain HIV varies considerably amongst individuals.
- In virally-suppressed (VS) patients, both past and stable HAND is associated with brain latency and may serve as a latency biomarker discovery approach.
- We hypothesized that putative brain latency biomarkers would differ in VS past/stable HAND vs. non-HAND.

METHODS

- 24 HIV+ men VS in plasma and CSF (<100cpml) on cART underwent lumbar puncture and neuro-psychological testing.
- Patients with past HAND from which they had recovered and patients with chronic stable HAND (past/stable HAND group) were compared to patients with no known past or current CNS involvement (non-HAND group) for putative markers of HIV brain latency in CSF:
  - HIV RNA by single copy assay (SCA)
  - HIV tat
  - BCL11b
  - Neurofilament-light chain (NFL)
  - Neopterin
  - CCL2
  - CSF:serum albumin ratio (Q-Alb)
- Biomarkers were classified as normal/abnormal using normal references and a combined CSF latency biomarker risk score was created by summing the number of abnormal values.
- HAND status was defined using Global Deficit Score (GDS≥0.5). Past HAND was determined from medical record review.

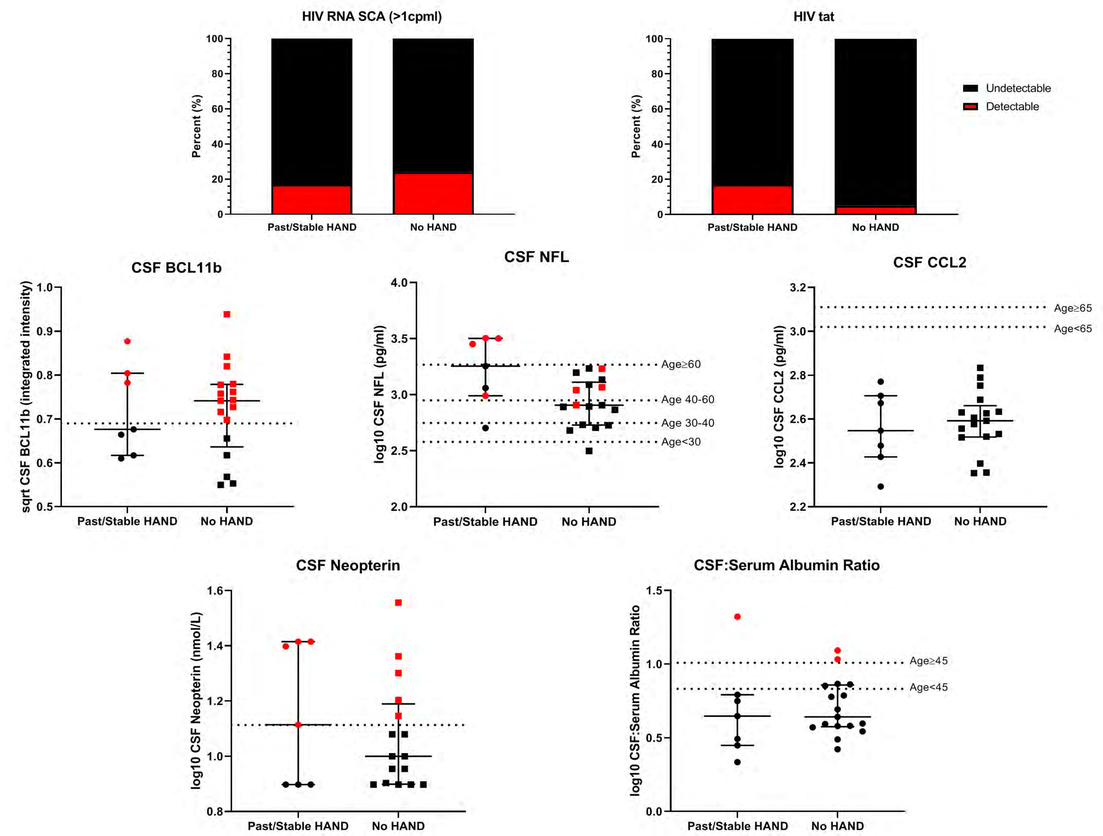


Figure 1. CSF biomarker ranges. Data presented as % detectable (top row) or median±IQR (middle and bottom rows). Age-adjusted normal reference range cut-offs are represented by dashed lines. Abnormal values used for latency biomarker risk score in red; normal values in black. Past/Stable HAND: *n*=7; No HAND: *n*=17.

RESULTS

- Viral persistence (CSF HIV RNA SCA >1-12.4cpml) and HIV tat were detected in CSF in both groups.
- BCL11b levels were abnormal in 43% of past/stable HAND and 71% of non-HAND patients (*p*=.20).
- NFL was higher in the past/stable HAND patients than non-HAND patients (*p*=.05).
- Neopterin was abnormal in 57% of past/stable HAND and 31% of non-HAND patients (*p*=.24).
- CCL2 and Q-Alb levels were largely normal and similar in both groups.
- **Consequently, the combined CSF latency biomarker risk score did not differ across groups (*p*=.58).**

Figure 2. CSF latency biomarker risk score (Med±IQR).

CONCLUSIONS

- Past/stable HAND is not a useful model for identifying brain latency biomarkers.
- Past/stable HAND remains an active virological immunological and degenerative process. The concept of a "legacy effect" from past HAND is not supported.
- Further studies in CSF and MRI are underway to quantify brain latency

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