POORER NEUROCOGNITIVE PERFORMANCE ASSOCIATED WITH CSF HIV DNA DESPITE LONG-TERM ART

ACTG HIV Reservoirs Cohort study A5321

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CONCLUSIONS

HIV persists despite antiretroviral therapy (ART)
- HIV reservoirs not well defined
- Central nervous system (CNS) likely harbors a special HIV reservoir
- protected, blood brain barrier
- HIV RNA is often detected in cerebrospinal fluid (CSF) off ART
- but rare on ART (CSF escape)
- Neurocognitive Performance (NP)
- in some, HIV can lead to poor NP, HIV associated neurocognitive dysfunction (HAND)
- even on ART ~20%

Is HIV persistence related to NP?
Does HIV persistence on ART impact neurocognition?

METHODS

ACTG HIV Reservoirs Cohort/A5321
HIV+ on long-term ART
Cross-sectional
Blood, lumbar puncture,
Neurocognitive assessments

HIV Persistence
Cell-associated (CA) HIV DNA
Cell-associated (CA) HIV RNA
CSF and in PBMC (Hong, JCM 2016).
Cell-free (CF) HIV RNA
Single copy assay (SCA)
CSF supernatant, blood plasma (Cillo, JCM 2014)

BIOMARKERS

Inflammatory
CSF and Plasma
IL-6
IP-10
Neopterin
MCP-1
sCD14
sCD163
TNF-α

RESULTS

Total z scores
Global Deficit Score (GDS)
- Average of 15 scores in 7 domains:
  1. Language/Premorbid
  2. Fine Motor
  3. Verbal Learning
  4. Verbal Memory
  5. Speed of Processing
  6. Executive Functioning
  7. Attention/Working Memory

RESULTS

NP OUTCOMES

RESULTS

HIV DNA Not Detected
HIV DNA Detected

LOWER GDS = BETTER PERFORMANCE

POORER NP by GDS in Detected CSF HIV DNA

WILCOXON RANK SUM

POORER NP by total z in Detected CSF HIV DNA

WILCOXON RANK SUM

CONCLUSIONS

HIV Persistence in CSF
- HIV-infected cells persist in CSF in ~ half of individuals on long-term ART
- Associated with worse neurocognitive performance

Inflammatory Biomarkers in CSF
- Not associated with NP
- Inflammation may not be driving injury
- Legacy of prior inflammation?

CNS Is An Important Site of HIV Persistence
- Future research to assess:
  - Longitudinal clinical significance?
  - Obstacle to HIV cure?