

POORER NEUROCOGNITIVE PERFORMANCE ASSOCIATED WITH CSF HIV DNA DESPITE LONG-TERM ART ACTG HIV Reservoirs Cohort study A5321

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CONCLUSIONS

HIV Persistence in CSF

- HIV-infected cells persist in CSF in ~ half of donors despite long term suppressive 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?



BACKGROUND

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



NP OUTCOMES

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

N=65 HIV+ on ART

97% male

75% white

50 yrs median age

8.6 yrs median duration ART

**97% Plasma vRNA < 40 c/ml
(all <80 c/mL)**

CD4+ cells median

current 696/mm³

pre-ART 292/mm³

All ≥ 12 yrs education

NP medians

total z 0.2 (range -1.1, 1.5)

normal 0, SD 1

GDS 0.2 (range 0.0, 1.3)

normal 0, impaired ≥ 0.5

Detectable CSF HIV DNA (46%)

Associated with poorer

total z-score (p = 0.044)

GDS (p = 0.005)

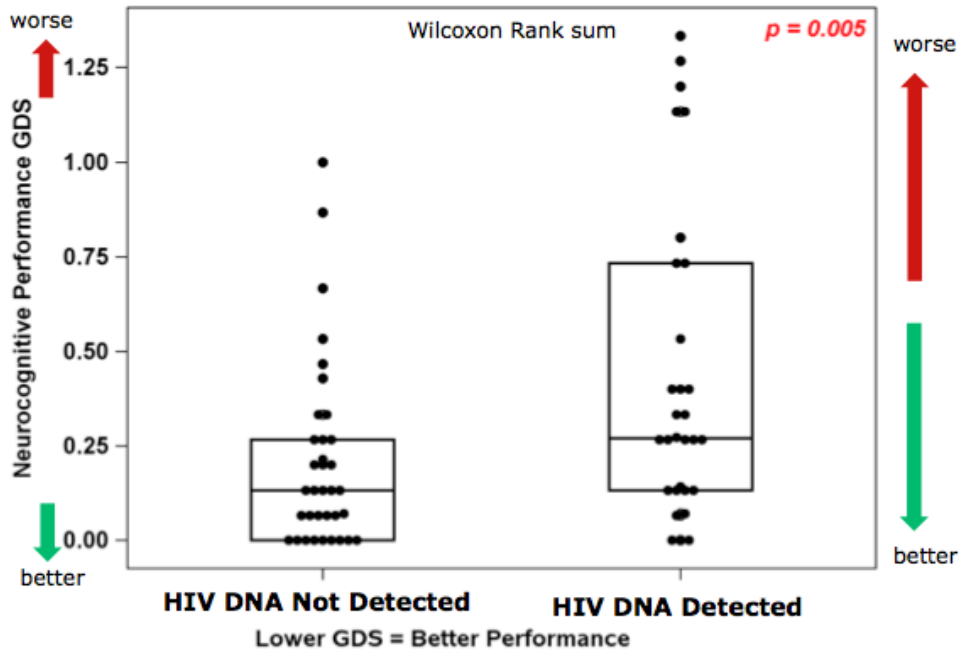
**Associations still present after
adjusted for pre-ART, current CD4,
and age**

CSF immune biomarkers

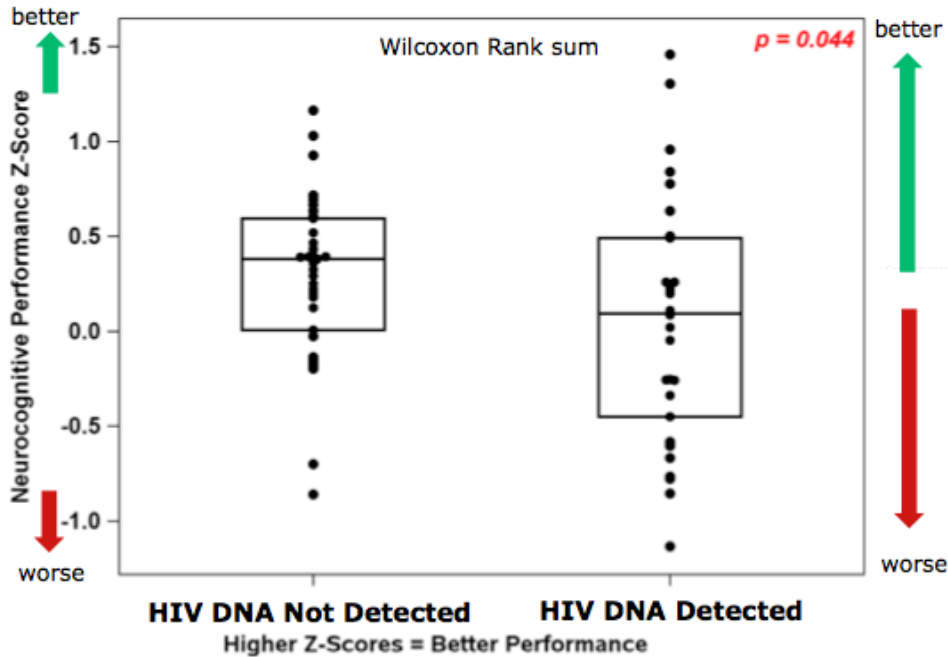
not associated with NP

RESULTS

Poorer NP by GDS in Detected CSF HIV DNA

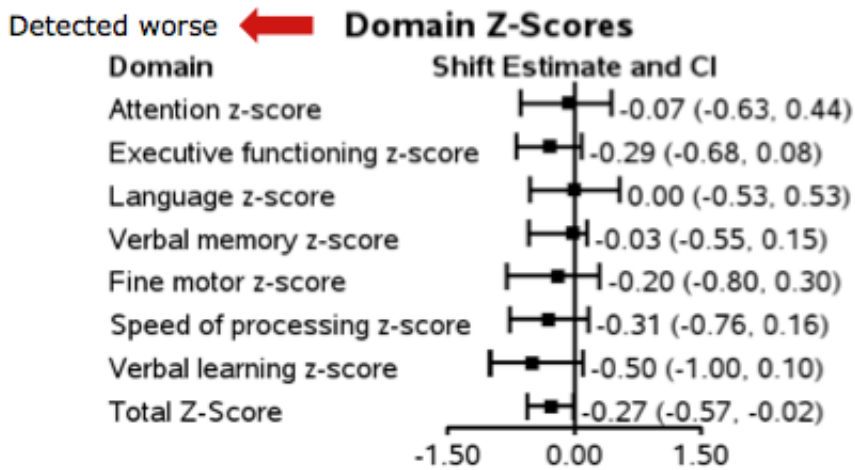
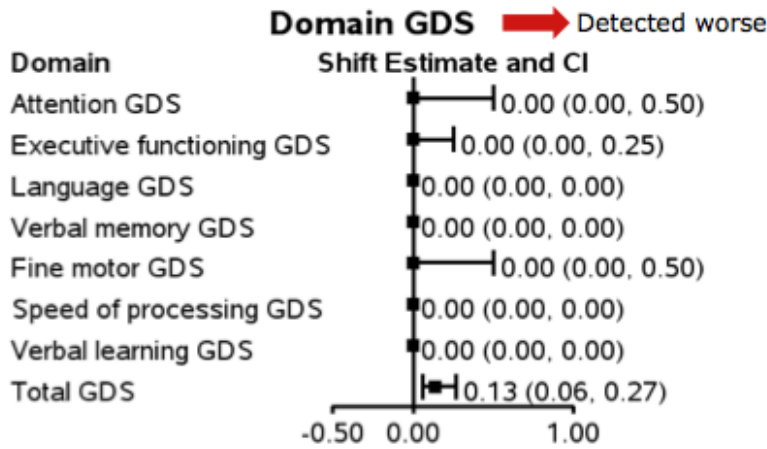


Poorer NP by total z in Detected CSF HIV DNA



RESULTS

Difference between CSF HIV DNA: Detected vs. Not



**Hodges-Lehmann method Shift Estimate
(Detected - Target Not Detected) and Confidence Intervals**