

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



403LB

ACTG HIV Reservoirs Cohort study A5321

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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 \geq 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 \geq 0.5

Detectable CSF HIV DNA (46%)

Associated with poorer

total z-score (p = 0.044)

GDS (p = 0.005)

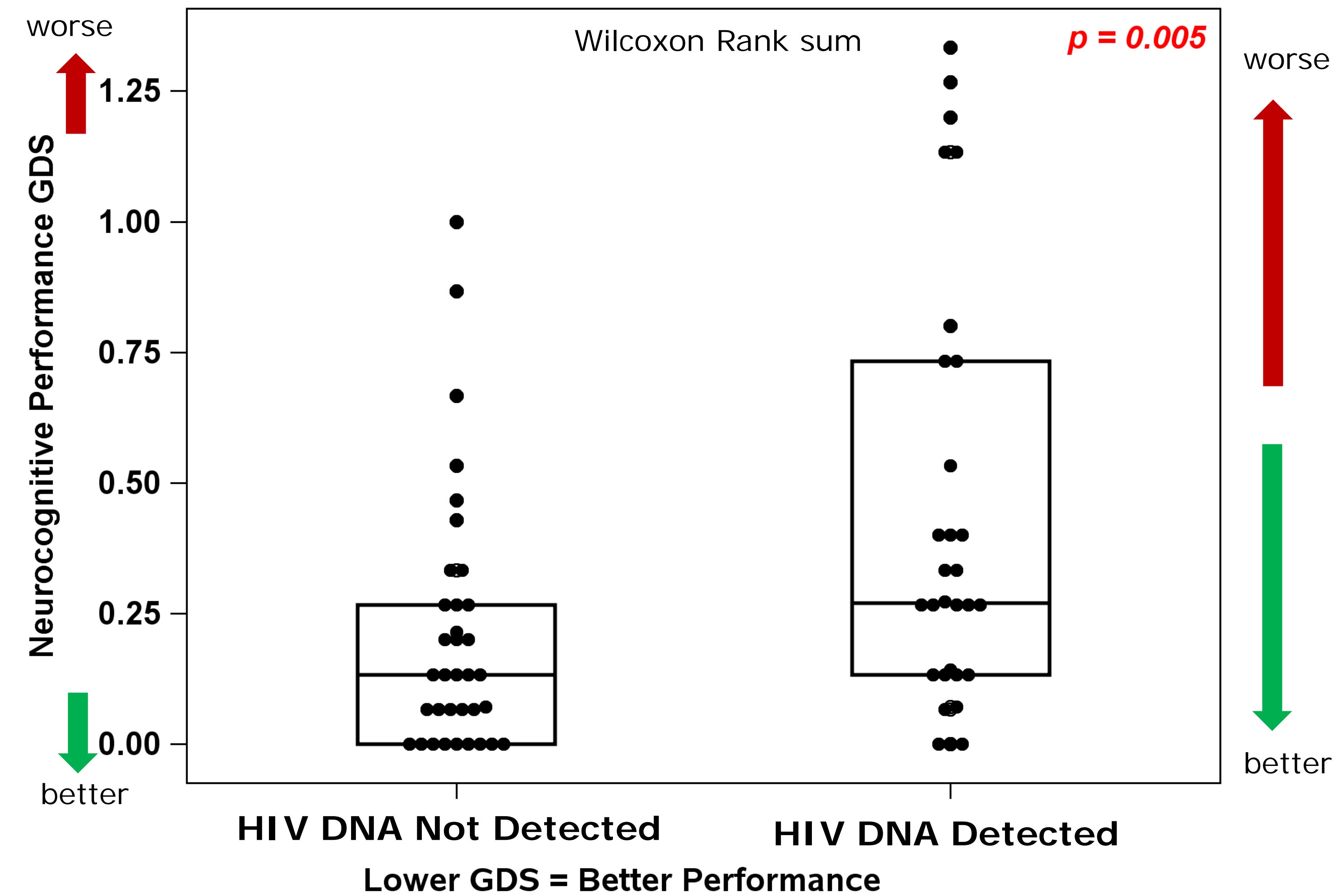
Associations still present after adjusted for pre-ART, current CD4, and age

CSF immune biomarkers

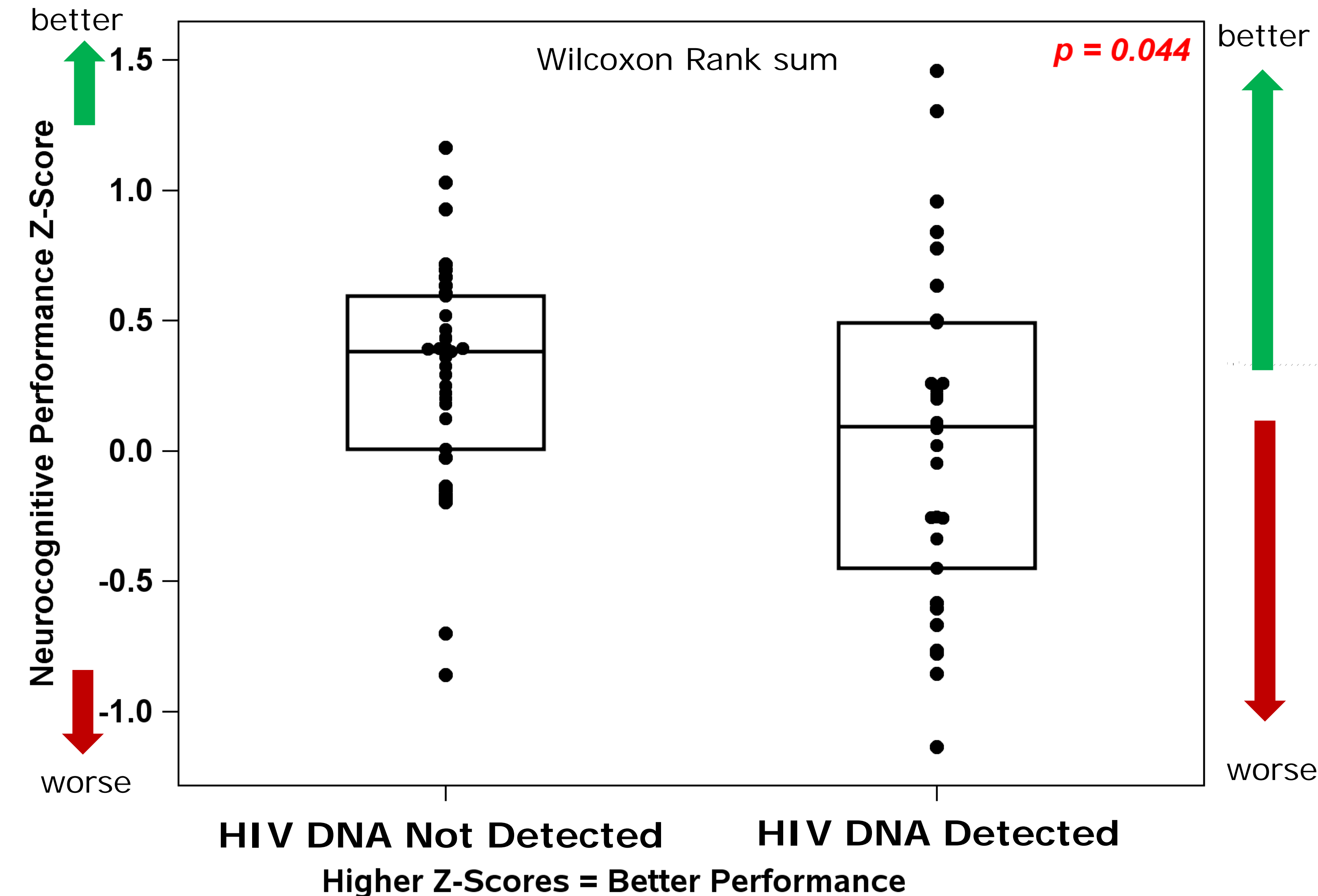
not associated with NP

RESULTS

Poorer NP by GDS in Detected CSF HIV DNA

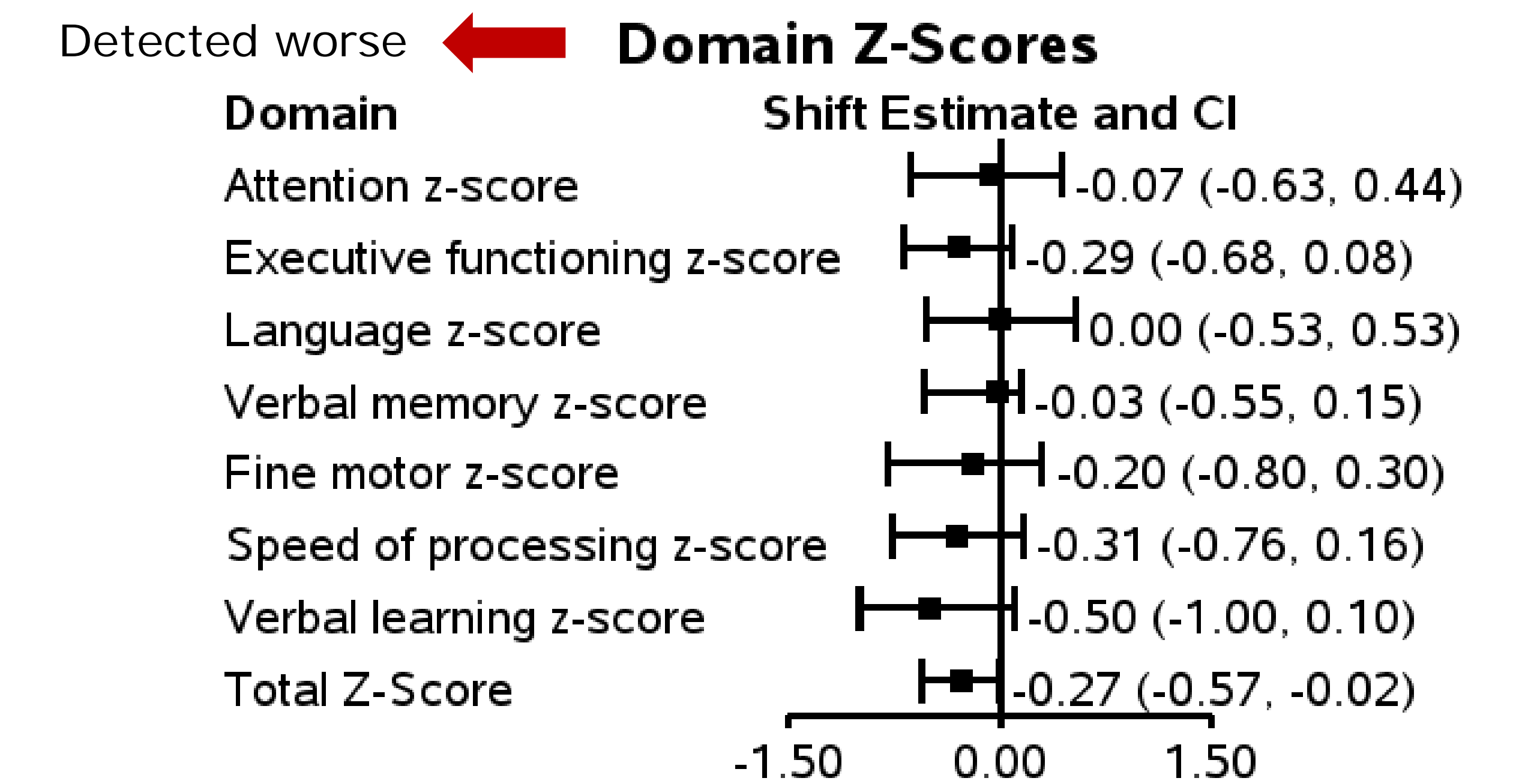
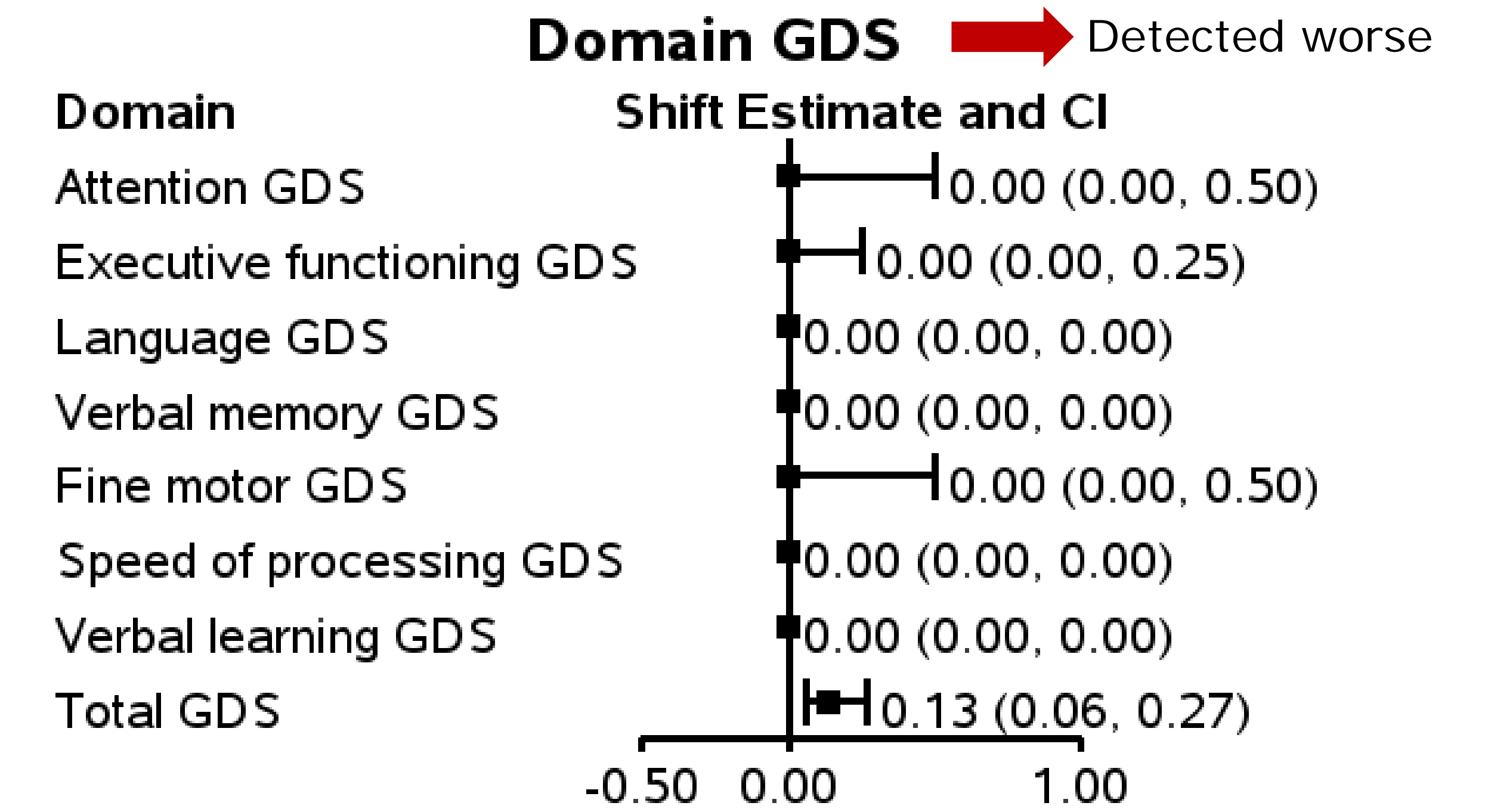


Poorer NP by total z in Detected CSF HIV DNA



RESULTS

Difference between CSF HIV DNA: Detected vs. Not



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

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?

See Oral: HIV Persists in CSF cells in Half of Individuals on Long-term ART
Spudich et al, 10 am March 7, CNS oral session #119 in ballroom B

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