Mitochondrial DNA Haplogroups and Cognitive Function in Black and Hispanic Women with HIV

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BACKGROUND

- Mitochondria are important in cellular processes, particularly for high-energy tissues of the nervous system.
- Mitochondrial DNA (mtDNA) variation has been shown to be related to cognitive impairment in non-White persons with HIV, but prior analyses studied primarily men with HIV.
- We studied these haplogroup-cognition associations in Black and Hispanic women with HIV (WWH).

METHODS

- Study Design: Cross-sectional analysis.
- Participants were Black and Hispanic WWH enrolled in the Women's Interagency HIV Study (WIHS; now part of the MACS/WIHS Combined Cohort Study [MWCSS]) with neuropsychological and mtDNA haplogroup data.
- Outcomes were continuous T-scores (TS) and clinical rating scores (1-9; scores ≥4=impairment) in 7 cognitive domains.
- Ordinary least squares and logistic regression models were used. Models were adjusted for CD4 T-cell nadir, current plasma HIV RNA, current antiretroviral drug use, body mass index (BMI), and hepatitis C virus (HCV) status. Small sample sizes for Hispanic WWH precluded logistic regression models.

RESULTS

- 571 Black and 120 Hispanic WWH were included in analyses. Selected baseline factors are summarized in the **Table**.
- **Black WWH and haplogroup L2a were less likely to have impairment in motor performance and speed of information processing (SIP)** than other haplogroups (15 vs. 23%, *p*=0.05; 19 vs. 30%, *p*=0.03, respectively). Adjusted odds ratios (aOR) are shown in **Figure 1**. There were no statistically significant associations with performance TS (*not shown*).
- In unadjusted analyses, **Hispanic WWH and haplogroup B had less impairment** (0-17% vs. 13-28%) in all cognitive domains except verbal memory. In adjusted models, **WWH and haplogroup B had significantly higher motor TS** (*better* performance; *p*=0.04; **Figure 2**). Adjusted point estimates for all other domain TS were consistent with better performance but were not statistically significant.

mtDNA haplogroups L2a and B are associated with better domain-specific cognitive performance in Black and Hispanic women with HIV, respectively.

Table. Baseline adjustment factors and specific mtDNA haplogroups of interest in WWH, by self-reported race/ethnicity

	Black WWH (N=571)	Hispanic WWH (N=120)	Combined (N=691)
Age, median (IQR)	46 (41-52)	48 (43-53)	46 (41-52)
CD4 nadir, median (IQR)	297 (185-429)	311 (196-417)	304 (187-425)
Combination ART, %	80	85	81
BMI (kg/m^2), median (IQR)	30 (25-36)	28 (25-33)	30 (25-35)
HCV RNA positive, %	17	19	18
Haplogroup L2a, N (%)	114 (20)	-	-
Haplogroup B, N (%)	-	12 (10)	-

WWH = women with HIV; ART = antiretroviral therapy; BMI = body mass index; HCV = hepatitis C virus infection

Figure 1. Forest plot of adjusted OR for Domain Impairment by African mtDNA Haplogroup L2a in Black WWH

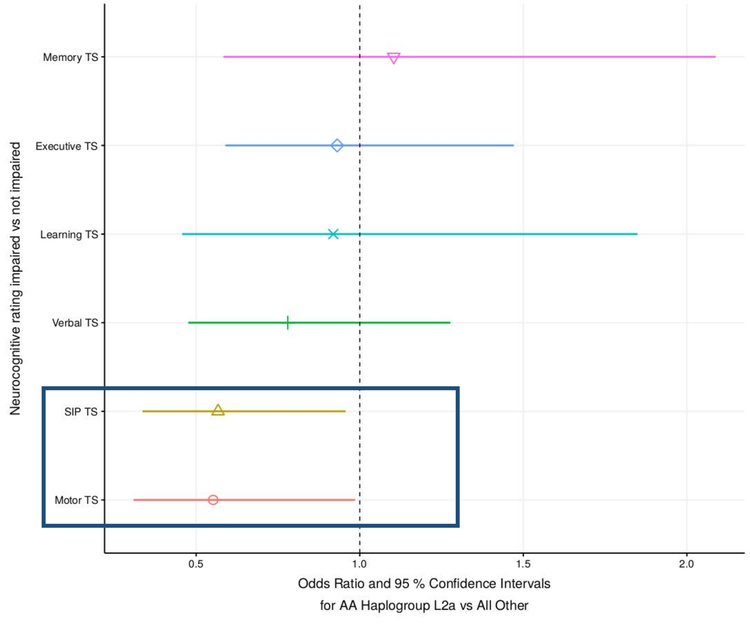
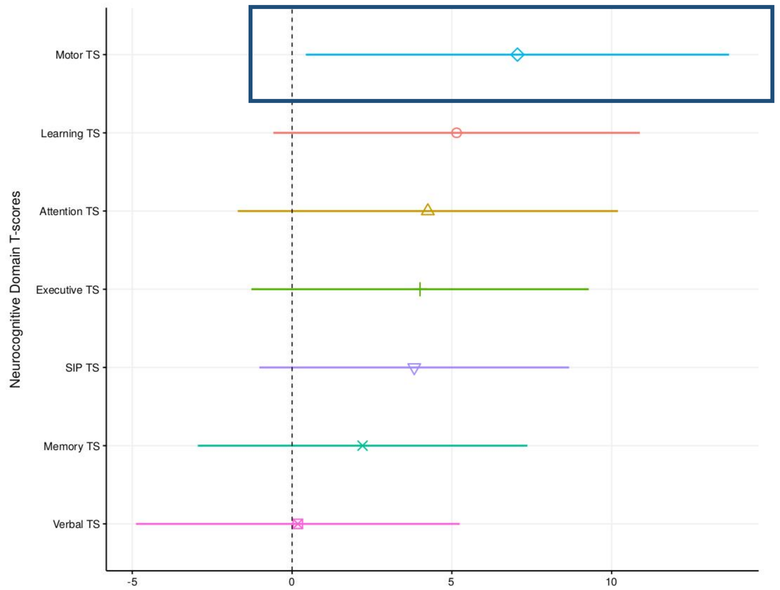


Figure 2. Forest plot of Beta (CI) for Domain T-scores by Hispanic mtDNA Haplogroup B in Hispanic WWH



CONCLUSIONS

- **Domain-specific cognitive function was associated with mtDNA haplogroups in Black and Hispanic WWH.**
  - **Black WWH and haplogroup L2a had less domain-specific cognitive impairment (different from prior studies in men).**
  - **Hispanic WWH and haplogroup B had better cognitive performance (consistent with prior studies in men).**
- **This suggests possible sex-related differences in genetic risk.**
- **Associations with motor performance in both groups suggest neuromuscular mechanisms that deserve further study.**
- **Analyses of longitudinal cognitive performance in WWH in relation to mtDNA haplogroups are ongoing.**

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