Poster # 471

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HIV-Associated Neurocognitive Disorder is Associated with HIV-1 Dual Infection

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CHARTER
CNS HIV Anti-Retroviral Therapy Effects Research

Objective

To investigate the relationship between HIV-1 dual infection (DI) and HIV-associated neurocognitive impairment (HAND).

Background & Significance

- HIV-1 DI (re-infection of an individual with a second strain from a different source partner) has been associated with decreased CD4 T-cell counts and increased viral loads.
- Same markers are associated with the development of HAND, a common problem among HIV-infected individuals in the era of antiretroviral therapy (ART).
- Despite this, the neurological sequelae of DI are poorly characterized.
- Next generation sequencing (NGS) was utilized to measure the prevalence of DI among CHARTER participants on ART and examine the relationship between HAND and DI.

Methods

- CHARTER participants were selected who had > 4 years of follow-up while on ART (*N*=34).
- NGS (454 FLX and Junior) was performed on PBMC-derived HIV-1 DNA populations using four PCR-amplified coding regions (*env* C2-V3, *gag* p24, *pol* RT, and *pol* PR).
- Samples were classified as DI when, in any coding region:
  - (i) maximal genetic divergence exceeded >5% in *env* and >2.5% in *gag* and *pol*,
  - (ii) longitudinal phylogenetic reconstruction showed divergent populations supported with bootstrap values ≥90%,
  - (iii) BLAST against laboratory database did not yield contamination checks.
- All participants underwent neurocognitive, substance use, and neuromedical assessments at each study visit.
- A global deficit score indicative of neurocognitive impairment (≥0.5) was derived from a well-established comprehensive battery of neuropsychological tests adjusted for demographics and corrected for practice effect over time.
- Participants with comorbidities confounding HAND were excluded.

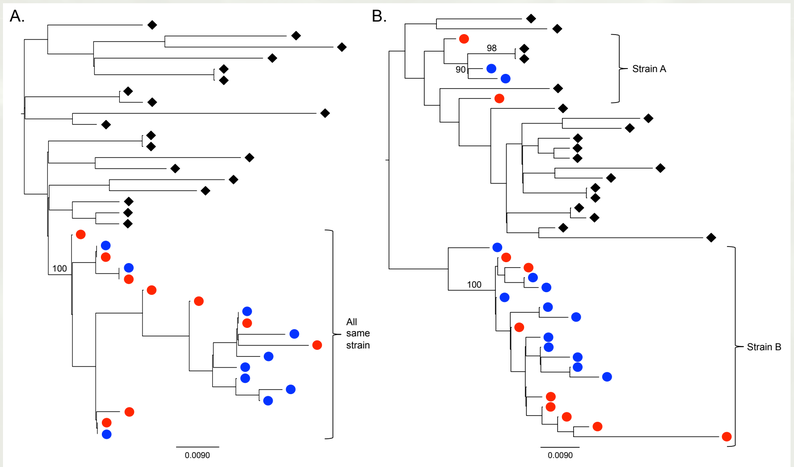
Results

- Of 34 participants, 18 had neurocognitive impairment measured in at least one study visit.
- 8 out of 34 subjects had DI in at least one HIV-1 coding region (prevalence 23.5%, 95%CI 11.6%-39.8%).
- 7 out of 18 (39%) impaired subjects had DI, while 1 out of 16 (6%) normal subjects had DI (p = 0.042).

Table 1. Characteristics of normal and neurocognitively impaired participants.

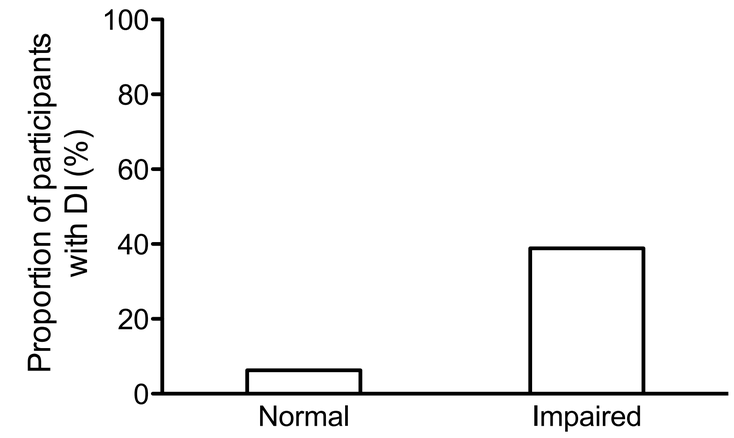
	Normal (*N*=16)	Impaired (*N*=18)	*p*-value
Age, median (IQR)	52 (49.3–58.3)	58 (46–60)	*NS*
Education years, median (IQR)	13 (11.5–15)	13 (11.5–14)	*NS*
% Male	94%	78%	*NS*
Viral load median $\log_{10}$ copies/mL (IQR)	<1.70 (1.70–2.16)	<1.70 (1.70–2.17)	*NS*
CD4 T-cell count median cells/μL (IQR)	668 (431–941)	510 (207–813)	*NS*

Figure 1. Phylogenetic trees illustrating HIV-1 (A) monoinfection and (B) dual infection.



Maximum likelihood trees of longitudinal *gag* sequences from two different participants. Colored circles represent consensus haplotypes from different timepoints and black diamonds indicate heterologous background sequences. Blue circles: timepoint 1; red circles: timepoint 2.

Figure 2. Proportion of participants with DI and neurocognitive impairment.



	Monoinfection	Dual Infection	Total
Normal	15	1	16
Neurocognitively Impaired	11	7	18
Total	26	8	34

p =0.042, Chi-Square Test

Conclusions

- Using NGS, we identified a high prevalence of DI (23.5%) in a population of HIV-infected individuals on ART.
- Neurocognitive impairment was associated with DI.
- DI may play a role in the development of HAND.

Selected References

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