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Subtype Associations with HIV Associated Neurocognitive Disorders

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Background

- HIV causes neurocognitive impairment in infected individuals, even with effective antiretroviral treatment [1].
- HIV associated neurocognitive dysfunction (HAND) has been associated with HIV-1 subtype, CD4 count and nadir, HIV-1 proteins *env* and *tat*, and blood and cerebrospinal fluid (CSF) viral loads [2,3].
- Studies linking HIV-1 subtype with HAND have been performed in heterogeneous populations and therefore may not have accounted for the influence of ethnic host genetics [4].
- Here we investigated the role of HIV-1 subtype with HAND in China.

Objective

To characterize the association between HIV-1 subtype and HAND in a homogeneous ethnic population of China.

Methods

- We used population-based sequencing to generate HIV-1 *tat* and *env* sequences from the blood plasma of HIV-1-infected subjects from 2 different locations of China: Anhui (n=116) and Yunan (n=184).
- We determined HIV-1 subtype based on both *tat* and *env* using tools available through the Los Alamos National Laboratory (LANL).
- We determined the mixed-based index (MBI) based on the number of mixed bases normalized to the sequence length.
- Neuropsychological assessment was performed and normalized to the Global Deficit Score (GDS) [5]. Neurocognitive impairment (NCI) was defined as having a GDS ≥ 0.5.
- All statistical analyses were done in R statistical software.

Figure 1. Electropherogram containing a mixture (MBI)

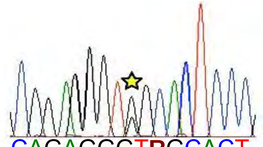


Figure 1. Color peaks represent nucleotides in the DNA sequence. Multiple color peaks at a site may result in an ambiguous base call. In this figure **R** could be either adenine (A) or guanine (G).

References

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Results

Table 1. Participant Demographics and Clinical Data

Characteristic	Normal (n=226)	Impaired (n=82)	*P-value**
Age	36 (33 - 36.75)	36 (31 - 39.75)	0.53
Education	9 (6 - 8)	9 (4 - 7.3)	**0.09**
AIDS Status (% with)	84 (37%)	47 (57.3%)	**<0.01**
Sex, no. (%) male	148 (65%)	51 (62%)	0.59
MBI	0.1742 (0.16 - 0.19)	.1774 (0.17 - 0.19)	**0.05**
CD4 nadir	287.0 (185.5 - 451.5)	197.5 (117.5 - 265.3)	**<0.01**
CD4 count	407.5 (270.0 - 5362.2)	359.5 (199.8 - 515.8)	**0.03**
HIV RNA levels	4.00 (2.66 - 4.51)	3.59 (1.77 - 4.35)	0.19
Estimated Duration of Infection (Years)	7.4 (3.3 - 12.3)	9.329 (5.4 - 12.6)	**0.06**
Time Since 1st HIV Test (Years)	1.69 (0.70 - 2.92)	2.14 (0.96 - 3.11)	0.11

Table 1. Median values with interquartile range are shown for the entire cohort and by study groups (Normal vs. Impaired). *Represent the p-value of a double-tailed Mann-Whitney or Fisher test. Impaired individuals had significantly lower CD4 Nadir and CD4 Counts, slightly higher MBI, and longer duration of infection. Additionally neurocognitive impairment was associated with AIDS status.

Table 2. HIV-1 subtype is not associated with neurocognitive impairment.

Subtype	Normal (n=217)	Impaired (n=81)
B	68.2% (75)	31.8% (35)
B/C	74.7% (56)	25.3% (19)
C	76.1% (86)	23.9% (27)

Table 2. Distribution of normal and impaired patients for each occurring subtype. The distribution of HIV-1 subtype was not linked with NCI (p=0.4, 3x2 Fisher Exact test).

Table 3. MBI, CD4 count and nadir significant correcting for HIV-1 subtype.

Variable	*P-value*
MBI	**0.01**
CD4 nadir	**0.04**
CD4 count	0.10
HIV RNA levels	0.33
Estimated Duration of Infection	0.62
Time Since 1st HIV Test	0.74

Table 3. After correcting for HIV-1 subtype and correlating with GDS as a measure of NCI, MBI and CD4 nadir remained statistically significant, and CD4 count became a trend.

Figure 2. Poorer neurocognitive function is associated with higher viral diversity, and lower CD4 nadir and counts.

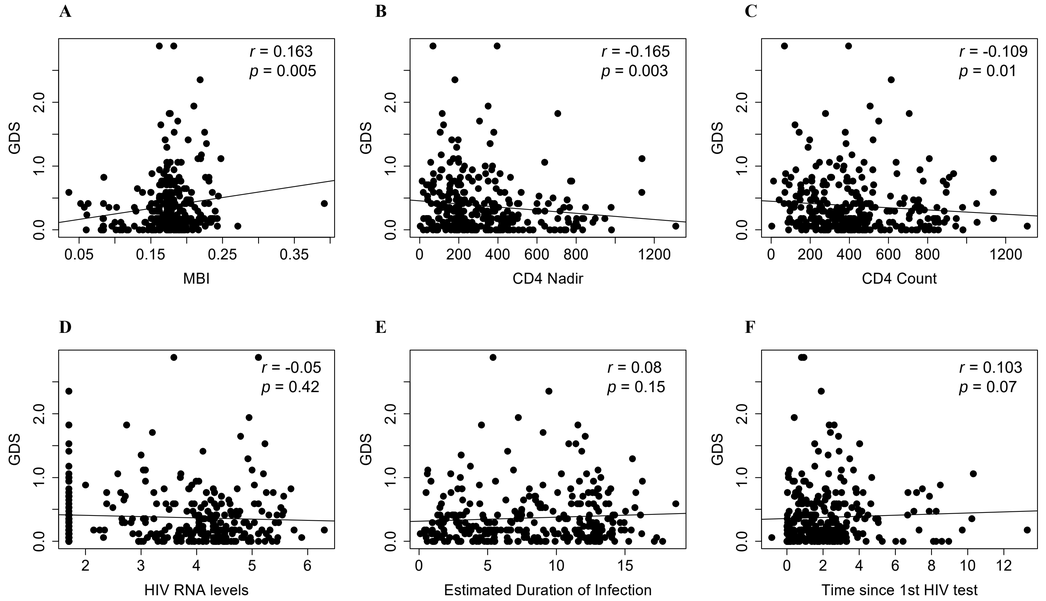


Figure 1. Poorer neurocognitive performance was associated with higher HIV diversity, lower CD4 counts and lower CD4 Nadir. There was no association of neurocognitive performance with HIV RNA levels, estimated duration of infection and years after the first HIV test.

Conclusions

- Individuals with impairment had significantly lower nadir and absolute CD4 counts and slightly higher MBI than those without impairment (**Table 1**).
- Poorer neurocognitive performance was associated with higher viral population diversity, lower CD4 nadir counts, and lower CD4 counts, and there was no association with HIV-1 subtype (**Figure 1 and Table 2**).
- AIDS was significantly associated with impairment (**Table 1**).
- Viral diversity and CD4 nadir remained significantly associated with NCI after adjusting for HIV-1 subtype (**Table 3**).
- Our results suggest that HIV-1 subtype does not have a significant impact on the development of HAND, and previous findings linking HIV-1 subtype and HAND might be confounded by heterogeneity of the study populations that were compared.

Acknowledgments

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