Assessment of adults living with HIV infection (PLHIV) and neurocognitive symptoms

M. Harris[1,3], S. Guillemi[1,3], A. Yamamoto[2,3], L. Tiamiyu[1], W. Zhang[1], M. Hull[1,3], P. Ross[1], J. Montaner[1,3], G.-Y. R. Hsiung[3]

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1. B.C. Centre for Excellence in HIV/AIDS, 2. Providence Health Care, 3. University of British Columbia, Vancouver, B.C.

Background

Neurocognitive symptoms are common among antiretroviral-treated adults and can affect quality of life.

We examined neurocognitive function in a prospective cohort of PLHIV undergoing assessment in an HIV outpatient neurology referral clinic.

Methods

Study participants

HIV positive adults (≥19 years) with cognitive complaints not readily explained by another diagnosis (e.g. cerebral trauma, stroke)

Procedures

- Comprehensive evaluation by a neurologist, including
  - history of HIV, comorbid conditions, and substance use
  - physical examination including neurological examination
  - plasma HIV RNA (pVL) and CD4 cell count
  - serum apolipoprotein B and high-sensitivity C-reactive protein
- Neurocognitive function was categorized by a neuropsychologist as normal for age, mild neurocognitive impairment (NCI), or dementia.
- Study protocol and informed consent were approved by the UBC/Providence Health Care Research Ethics Board (H10-00762).

Cognitive screening tests

- Montreal Cognitive Assessment (MoCA) (www.mocatest.org) – a score ≤25 is considered indicative of possible cognitive impairment [1]
- HIV Dementia Scale (HDS) – a score ≤10 or ≤14 is considered indicative of possible cognitive impairment [2,3]

CSF viral load (VL) and biomarkers

A subset of participants who had lumbar puncture performed for clinical assessment had the following measured in CSF:

- HIV RNA – lower limit of detection 40 copies/mL
- T tau and p tau – markers of neuronal degeneration; elevated levels seen in Alzheimer Disease (AD), stroke, brain trauma [4]
- Beta amyloid – lower levels seen in association with amyloid plaques in AD [4]

White Matter Densities (WMD)

A subset of participants who had brain MRI performed for clinical assessment had WMD (a marker of ischemic changes) scored using established visual scales. Higher scores are associated with more extensive WMD.

- Age-Related White Matter Changes (ARWMC) [5] – a single score from 0 (no lesions) to 3 (diffuse lesions)
- Fazekas Visual Scale [6] – a modified score was used which assesses all 4 brain quadrants, each on a scale from 0 (no lesions) to 4 (severe/diffuse lesions)

Statistical analysis

- Categorical variables were compared using Cochran-Mantel-Haenszel Mean Score test
- Continuous variables were compared using Kruskal-Wallis test

References

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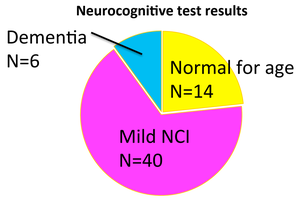
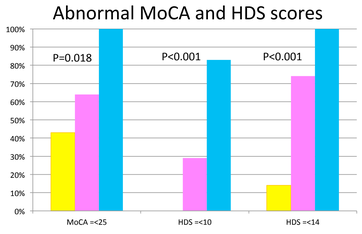
2. Power C et al. *JAIDS* 1995; 8: 273-8.
3. Simioni S et al. *AIDS* 2010; 24:1243-50.
4. Blennow K et al. *Nat Rev Neurol* 2010; 6: 131-44.
5. Wahlund L et al. *Stroke* 2001: 32:1318-22.
6. Zimmerman RD et al. *AJR* 1986; 146:443-50.

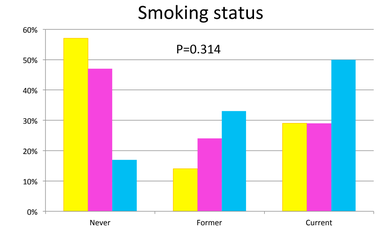
Results

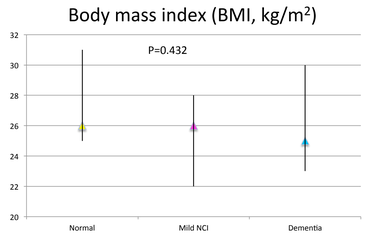


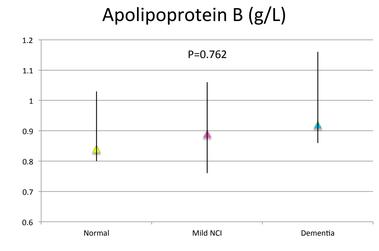
Demographics of study population (N = 60)

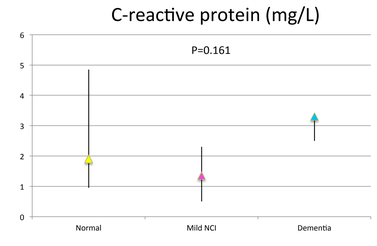
	Normal for age	Mild NCI	Dementia	P value
N (%)	14 (23%)	40 (67%)	6 (10%)	
Gender, N (%)				0.143
Male	14 (100%)	38 (95%)	5 (83%)	
Female	0 (0%)	2 (5%)	1 (17%)	
Caucasian ethnicity, N (%)	11 (78%)	26 (65%)	6 (100%)	0.711
Age, years, median (Q1-Q3)	53 (49-59)	52 (47-58)	55 (48-62)	0.863
Time since HIV diagnosis, years, median (Q1-Q3)	10 (6-21)	8 (4-17)	5 (5-25)	0.649



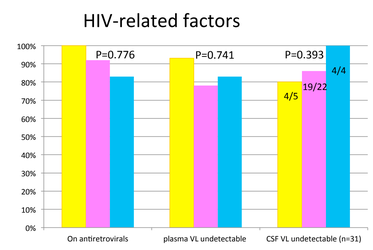




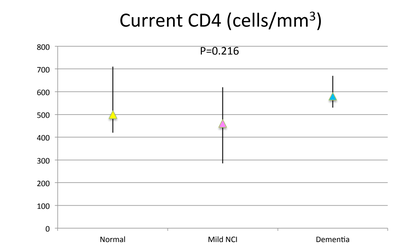




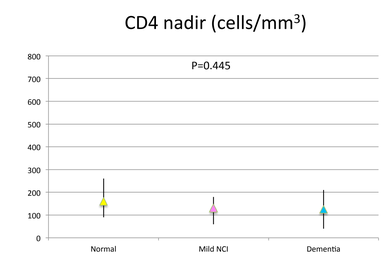
HIV-related factors



Current CD4 (cells/mm³)



CD4 nadir (cells/mm³)



CSF VL and biomarkers

- 4 participants had detectable CSF VL: 3 had pVL <40 copies/mL and CSF VL 52, 162, and 328 copies/mL; one had pVL 84,000 copies/mL and CSF VL >1.4 million (before starting antiretroviral therapy)
- CSF t tau, p tau, and beta amyloid were measured in 25 participants (3 normal for age, 18 mild NCI, and 4 dementia). No significant differences were observed among groups (p>0.1 for all).

White Matter Densities (WMD)

MRI was performed and white matter changes assessed in 26 participants. ARWMC tended to be higher (indicating more extensive WMD) in those with mild NCI.

	Normal for age	Mild NCI	Dementia	P value
N with MRI	9	15	2	
ARWMC score, median (Q1-Q3)	1 (0-2)	2 (1-3)	0 (0-0)	0.067
Fazekas score, median (Q1-Q3)	5 (4-5)	7 (2-9)	4 (1-6)	0.440

Limitations

- This is a cross-sectional analysis of the first study visit
- Small number of participants with dementia limits the interpretation of between-group comparisons, especially for the CSF biomarkers and white matter changes

Conclusions

- Among PLHIV with neurocognitive complaints, nearly one-quarter had normal neurocognitive function for their age. While a decline from a high-functioning baseline is a possible explanation in some cases, this information may offer reassurance to concerned patients.
- Neurocognitive function was not consistently related to CSF viral load, other HIV disease-associated factors, or to vascular risk factors in this cross-sectional analysis.
- Thresholds of 25 for MoCA and 14 for HDS identified all participants with dementia, but also some who were normal for age; these screening tests should be interpreted with caution
- These data highlight the value of a comprehensive assessment in PLHIV experiencing cognitive symptoms.

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