Novel Method for More Reliably Estimating the Burden of Cognitive Impairment in HIV

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Background

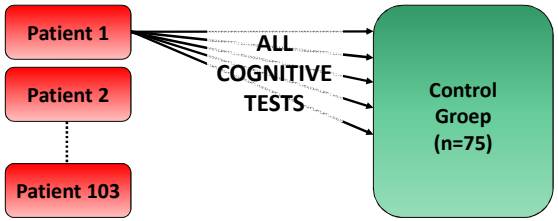
A high but varying prevalence (15-69%) of cognitive impairment has been reported among HIV-1-infected individuals.[1,2]
To classify HIV-1 associated neurocognitive disorders (HAND), a set of diagnostic criteria (Frascati criteria) has been developed.[3]
Frascati criteria have high sensitivity for HAND, possibly resulting in a high false-positive rate and overestimation of HAND prevalence.
Gisslén proposed modified criteria to increase specificity.[4]
Multivariate normative comparison (MNC) is a new statistical method specifically designed to control false-positive rate while retaining sensitivity.[5]

1 Simioni S, Cavassini M. AIDS. AIDS. 2010 Jun 1;24(9):1243-50. 2 Heaton RK, Clifford DB. Neurology 2010 Dec 6;75(23):2087–96.
3 Antinori A, Arendt G. Neurology 2007 Oct 30;69(18):1789–99. 4 Gisslén M, Price RW. BMC Infectious Diseases 2011;11(1):356.
5 Huizenga HM, Smeding H. Neuropsychologia 2007 Jun 18;45(11):2534–42.

Objectives

- To determine the prevalence of HAND among HIV-1-infected men with suppressed viraemia on cART, aged ≥45.
- To assess whether MNC improves the detection of HAND as compared to Frascati and Gisslén's criteria.

Multivariate normative comparison



MNC may be seen as a multivariate version of Student's t-test for one sample.
It compares multiple characteristics (in this case cognitive test scores) of each subject against the distributions of the same characteristics in a control sample, taking the covariance between all variables into account.
The test statistic is Hotelling's T^2.
The false positive rate is the level of significance (alpha), which in this study was set at 5% one-tailed, resulting in a specificity of at least 95%.

Methods

The AGE$_h$IV Cohort Study investigates aging-associated comorbidities among HIV-1-infected individuals and highly comparable HIV-uninfected controls, all aged ≥45. HIV-1-infected participants are recruited at the HIV outpatient clinic of the Academic Medical Center in Amsterdam, The Netherlands, and HIV-uninfected controls from the ongoing Amsterdam Cohort Studies on HIV/AIDS and among Amsterdam Public Health Service sexual health clinic attendants. AGE$_h$IV Cohort Study participants were consecutively invited to participate in a nested cognitive substudy. Additional eligibility criteria for the substudy were: male gender, no history of severe neurological disorders, no alcohol abuse or daily illicit drug use, and for the HIV-1-infected group: sustained suppression of HIV viremia on antiretroviral treatment (plasma HIV-RNA <40 copies/mL) for ≥12 months.

103 HIV-1-infected and 75 highly comparable HIV-uninfected participants were enrolled in the cognitive substudy.
They underwent neuropsychological assessment covering six cognitive domains: fluency, attention, information processing speed, executive function, memory, and fine motor function.
Prevalence of cognitive impairment was assessed by Frascati and Gisslén's criteria, as well as by MNC.

Demographic and HIV-related characteristics

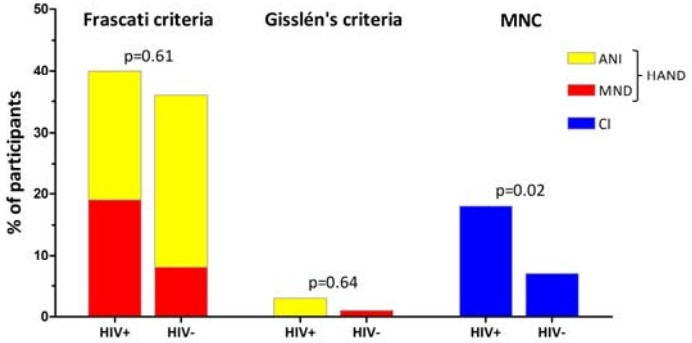
Data presented as % or median (IQR)	HIV-positives (n=103)	HIV-negatives (n=75)	P-value
Age (years)	52.8 (48.0-60.8)	53.3 (49.0-60.7)	0.65
Men having sex with men (MSM)	93.2%	90.4%	0.50
Dutch origin	86.4%	89.0%	0.60
Education (ISCED level)*	6 (5-6)	6 (5-6)	0.43
Premorbid intelligence (IQ)	102 (95-111)	103 (97-112)	0.29
Depressive symptoms (BDI score)#	4 (2-8)	3 (1-5)	0.09
Known duration of HIV-infection (years)	13.5 (7.4-17.1)	-	-
CD4 count at enrolment (cells/mm^3)	625 (475-800)	-	-
Nadir CD4 count (cells/mm^3)	170 (60-250)	-	-
Duration undetectable viral load (years)	8.3 (3.5-11.2)	-	-
Duration since start of first ART (years)	11.6 (4.9-14.9)	-	-
ART-naïve at start cART	79.6%	-	-
Prior AIDS	35.0%	-	-

* Educational level was defined using the International Standard Classification of Education (ISCED) 2011.
# Depressive symptoms were assessed using the Beck Depression Inventory (BDI).

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Results: cognitive impairment



HAND = HIV-associated neurocognitive disorder
ANI = Asymptomatic neurocognitive impairment
MND = Mild neurocognitive disorder
CI = Cognitive impairment

Conclusions

- HAND by Frascati criteria was highly prevalent in HIV-positives but also in controls, confirming low specificity of this method.
- Gisslén's criteria showed improved specificity, but sensitivity was reduced, resulting in a low HAND prevalence.
- MNC identified cognitive impairment in 18% of HIV-infected men and in 7% of uninfected controls.

Acknowledgements

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