DETERMINANTS OF COGNITIVE FUNCTION DIFFER IN A EUROPEAN AND A KOREAN COHORT

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BACKGROUND

HIV-associated cognitive impairment (CI) remains relevant in people living with HIV (PLWH) treated with combination antiretroviral therapy (cART). However, risk factors for CI may differ in populations of PLWH of different ethnicity.

AIMS

- To compare the prevalence and determinants of CI in a Northern European and a Korean cohort of PLWH.
- To assess the ability of individual cognitive tests to discriminate between those with and without CI.

METHODS

The COBRA collaboration (the Netherlands and the UK)

The COBRA cohort recruited **134 PLWH** aged ≥45 years, on cART and with a plasma HIV viral load <50 copies/mL for ≥12 months, from HIV outpatient clinics in Amsterdam (Netherlands) and London (UK). Exclusion criteria included current depression, history of neurological diseases and substance abuse.

The Korean NeuroAIDS project (South Korea)

194 PLWH aged ≥18 years (90% on cART, 79% with HIV RNA <50 copies/mL) were recruited from two hospitals in Seoul (South Korea). Exclusion criteria were current psychotic disorder, history of neurological diseases, central nervous system infection and substance abuse.

Neuropsychological assessment

Cognitive performances were assessed using a comparable battery covering 6 cognitive domains [1,2]. Scores were standardised into T-scores (mean=50, standard deviation=10) using population-specific normative scores and averaged to obtain an overall score where higher scores indicate better cognitive function.

CI was defined by an overall T-score ≤45 (i.e. ≥0.5 standard deviations below the mean normative score).

Statistical analysis

- Determinants of overall cognitive function were evaluated separately in the two cohorts using linear regression. In univariate analysis factors were considered one at the time. Those factors that were associated with cognitive function in univariate analyses (p≤0.05) were selected for simultaneous inclusion in a multivariable model.
- The discriminative ability of individual cognitive tests to detect CI was assessed using the area under the receiver operating characteristic (AUROC) curve.

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ACKNOWLEDGEMENTS

Academisch Medisch Centrum, Universiteit van Amsterdam - *Department of Global Health and Amsterdam Institute for Global Health and Development (AIGHD):* P. Reiss, J. Schouten, K.W. Kooij, R.A. van Zoest, E. Verheij, S.O. Verboeket, B.C. Elsenga, F.R. Janssen, W. Zikkenheiner. *Department of Experimental Immunology:* N.A. Kootstra, A.M. Harskamp-Holwerda, I. Maurer, M.M. Mangas Ruiz, A.F. Girigorie. *Department of Neurology:* P. Portegies, B.A. Schmand, G.J. Geurtsen. *Department of Radiology:* C.B.L.M. Majoie, M.W.A. Caan, T. Su. *Department of Psychiatry:* I. Visser. **Stichting HIV Monitoring** - F.W.N.M. Wit, S. Zaheri, M.M.J. Hillebregt, Y.M.C. Ruijs, D.P. Benschop. **Imperial College of Science, Technology and Medicine** - *Department of Medicine, Division of Infectious Diseases:* A. Winston, J. Underwood, L. Tembo, L. McDonald, M. Stott, K. Legg, N. Doyle, C. Kingsley. *Department of Medicine, Division of Brain Sciences, The Computational, Cognitive & Clinical Neuroimaging Laboratory:* D.J. Sharp, R. Leech, J.H. Cole. **University College London** - *Research Department of Infection and Population Health:* C. Sabin, D. De Francesco. **GGD Amsterdam/Public Health Service Amsterdam** - *Cluster of Infectious Diseases, research department:* M. Prins, M.F. Schim van der Loeff, J. Berkel, T. Kruijer. **Stichting Katholieke Universiteit Nijmegen** - D. Burger, M. de Graaff-Teulen. **Erasmus Universitair Medisch Centrum Rotterdam** -*Department of Genetics:* J. Hoeijmakers, J. Pothof. **Vlaams Instituut voor Biotechnologie** - *Inflammation research center:* C. Libert, S. Dewaele. **Universität Konstanz** -*Department of Biology:* A. Bürkle, T. Sindlinger, S. Oehlke. **Alma Mater Studiorum Università di Bologna** - *Department of Experimental, Diagnostic and Specialty Medicine:* C. Franceschi, P. Garagnani, C. Pirazzini, M. Capri, F. Dall'Olio, M. Chiricolo, S. Salvioli. **Göteborgs Universitet** - M. Gisslén, D. Fuchs, H. Zetterberg. **Università degli studi di Modena e Reggio Emilia** - *Department of Medical and Surgical Sciences for Children & Adults:* G. Guaraldi. The COBRA collaboration has received funding from the European Union's 7th Framework Programme (FP7/2007-2013) under grant agreement n° 305522.

The Korean NeuroAIDS project was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number : HI16C1705).

RESULTS

Characteristics of the two cohorts (Table 1)

Median (IQR) or n (%)	COBRA (n=134)	NeuroAIDS (n=194)	*p*
Age [years]	56 (51, 62)	45 (37, 52)	<0.01
Male	125 (93%)	182 (94%)	0.85
Black-African	16 (12%)	0 (0%)	<0.01
Likely route of HIV transmission			<0.01
MSM	115 (86%)	102 (53%)	
Heterosexual sex	15 (11%)	53 (27%)	
Years of education	14 (13, 16)	13 (12, 16)	0.23
BMI [kg/m^2]	24.6 (22.6, 27.4)	22.5 (20.5, 24.4)	<0.01
Anemia	11 (8%)	37 (19%)	<0.01
Hepatitis B co-infection	7 (3%)	9 (5%)	0.81
Hepatitis C co-infection	5 (2%)	6 (4%)	0.75
CD4 count [cells/µL]	618 (472-806)	477 (323, 607)	<0.01
CD4:CD8 ratio	0.84 (0.60, 1.12)	0.55 (0.35, 0.85)	<0.01
Time since HIV diagnosis [years]	15.0 (9.1, 20.0)	5.8 (2.3, 8.2)	<0.01
Prior AIDS	42 (31%)	55 (28%)	0.56
Nadir CD4 count [cells/µL]	180 (90, 250)	169 (69, 273)	0.78

Table 1 Characteristics of study participants [MSM: men who have sex with men; IQR: interquartile range; BMI: body-mass index; Anemia: haemoglobin ≤13 g/dL].

Prevalence of CI

The prevalence of CI was similar in the two cohorts: 18.8% in COBRA PLWH and 18.0% in NeuroAIDS PLWH (p=0.86). The median (IQR) overall cognitive score was 51.2 (46.0, 54.8) and 50.7 (47.1, 54.0), respectively (p=0.21).

Determinants of cognitive function – univariate analysis (Table 2)

In univariate analysis, anemia was significantly associated with poorer overall cognitive scores in both COBRA and NeuroAIDS PLWH while few factors were associated in one but not the other cohort (Table 2).

Risk factor	COBRA (n=134)		NeuroAIDS (n=194)	
	coefficient (95% CI)	p	coefficient (95% CI)	p
Age [per 10 years]	0.3 (-1.2, 1.7)	0.73	1.2 (0.6, 1.6)	**<0.01**
Male vs Female	6.1 (1.9, 10.3)	**0.01**	-1.4 (-3.8, 1.1)	0.28
Black-African vs white	-10.9 (-13.6, -8.1)	**0.01**	N/A	N/A
Likely route of HIV transmission				
Heterosexual vs MSM	-5.8 (-9.1, -2.5)	**<0.01**	-0.4 (-1.8, 1.0)	0.54
Other vs MSM	-1.8 (-7.9, 4.3)	0.56	-0.2 (-1.9, 1.7)	0.82
Years of education [per year]	0.2 (-0.2, 0.6)	0.37	0.2 (0.04, 0.4)	**0.01**
BMI [per 5 kg/m2]	-1.3 (-2.6, -0.04)	**0.04**	0.4 (-0.4, 1.2)	0.43
Anemia (yes vs no)	-5.0 (-8.9, -1.2)	**0.01**	-1.5 (-2.9, -0.03)	**0.05**
CD4 count [per 100 cells/µL]	0.2 (-0.4, 0.7)	0.55	-0.03 (-0.3, 0.2)	0.80
CD4:CD8 ratio	-0.2 (-2.4, 2.0)	0.84	0.2 (-0.6, 1.1)	0.84
Time since HIV diagnosis [per 10 years]	0.1 (-0.03, 0.2)	0.12	0.1 (-0.1, 0.3)	0.43
Prior AIDS (yes vs no)	-1.9 (-4.2, 0.4)	0.11	-0.2 (-1.5, 1.1)	0.75
Nadir CD4 count [per 100 cells/µL]	0.5 (-0.2, 1.3)	0.15	-0.1 (-0.6, 0.3)	0.55

Table 2 Estimates from univariate regression (one factor at the time) in the two cohorts.

Determinants of cognitive function – multivariate analysis (Figure 1)

In multivariate analysis, being of black-African descent was the main determinant of cognitive function among COBRA PLWH with on average 11.0 (7.6, 14.4) point lower scores compared to PLWH of white ethnicity (p<0.01).

In the NeuroAIDS cohort, other than age and years of education (both p-values <0.01), anemia was the main risk factor for CI; this factor was, however, of only marginal statistical significance (p=0.12).

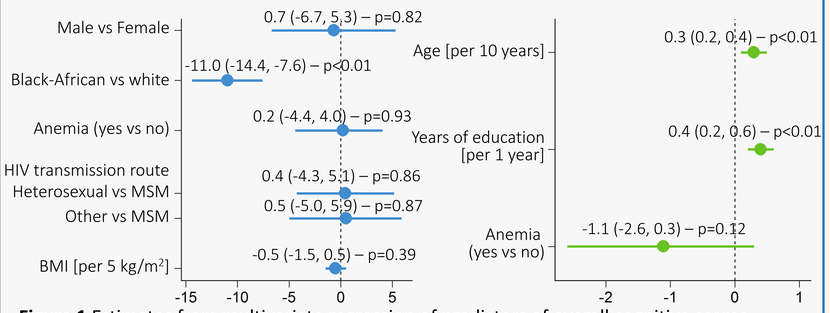

Figure 1 Estimates from multivariate regression of predictors of overall cognitive scores.

Screening for CI (Table 4)

The discriminative ability of CI screening was highest for tests of attention (AUROC of 0.81 to 0.84) and executive function (0.80-0.88) in COBRA PLWH and for tests of processing speed (0.73-0.80) and motor function (AUROC=0.78) in NeuroAIDS PLWH.

Domain	Test	COBRA (n=134)	NeuroAIDS (n=194)
Attention	PASAT 3	0.84 (0.79, 0.90)	N/A
	WAIS-III LN sequencing (C)/Digit span (K)	0.81 (0.75, 0.87)	0.75 (0.66, 0.83)
Exec. function	Trail Making Test-B	0.88 (0.82, 0.93)	0.71 (0.62, 0.80)
	Wisconsin CST - No of total errors	0.81 (0.71, 0.90)	0.74 (0.65, 0.83)
	Wisconsin CST - No of perseverative errors	0.80 (0.71, 0.89)	0.70 (0.61, 0.79)
	Wisconsin CST - No of perseverative resp.	0.81 (0.73, 0.89)	0.73 (0.65, 0.82)
Language	Category Fluency - Animals	0.82 (0.74, 0.91)	N/A
	Category Fluency - Occupations	0.81 (0.71, 0.90)	N/A
	Letter Fluency (C)/WAIS III Vocabulary (K)	0.68 (0.57, 0.78)	0.78 (0.71, 0.84)
Memory	RAVL - Recall	0.72 (0.63, 0.82)	0.73 (0.65, 0.80)
	RAVL - Delayed recall	0.74 (0.64, 0.84)	0.73 (0.66, 0.80)
	WMS-IV Visual Reproduction - Recall	0.73 (0.63, 0.83)	0.73 (0.64, 0.81)
	WMS-IV Visual Reproduction - Delayed R	0.76 (0.69, 0.84)	0.71 (0.63, 0.80)
Motor function	Grooved pegboard	0.67 (0.57, 0.77)	0.78 (0.71, 0.86)
	Finger tapping	0.68 (0.58, 0.79)	N/A
Processing speed	Trail Making Test-A	0.73 (0.63, 0.82)	0.73 (0.65, 0.81)
	WAIS-III Digit Symbol	0.82 (0.72, 0.91)	0.80 (0.73, 0.86)
	Stroop colour-word test	0.71 (0.64, 0.78)	N/A

Table 4 AUROC (95% CI) of individual cognitive tests for CI screening

CONCLUSIONS

- Despite similar rates of CI in two cohorts of PLWH from different geographic regions, determinants of cognitive performance differ considerably with ethnicity and anaemia being important determinants in one but not the other cohort.
- Differences in ethnicity and other diseases should be taken into consideration when comparing CI rates in different geographic regions.
- Also cognitive domains mainly affected by HIV-associated CI may vary in PLWH from different geographic regions.