The Course of Neurocognitive Performance Over Four Years in Well-Treated PLWH

461

José Damas[1], Bruno Ledergerber[2], Mélanie Bieler-Aeschlimann[3], Philip E. Tarr[4], Marcel Stoeckle[5], Anna Hachfeld[6], Alexandra Calmy[7], Frederic Assal[8], Patrick Schmid[9], Thomas Hundsberger[10], Caroline Di Benedetto[11], Barbara Hasse[2], Katharine E.A. Darling[1], Renaud Du Pasquier[3], Matthias Cavassini[1], *the NAMACO study group and the Swiss HIV Cohort Study*

[1]Service of Infectious Diseases, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland, [2]Department of Infectious Diseases and Hospital Epidemiology, Zurich University Hospital, University of Zurich, Zurich, Switzerland, [3]Service of Neurology, Department of Clinical Neurosciences, Lausanne University Hospital, University of Lausanne, Lausanne, Switzerland, [4]University Department of Medicine, Kantonsspital Bruderholz, University of Basel, Basel, Switzerland, [5]Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, University of Basel, Basel, Switzerland, [6]Department of Infectious Diseases, University Hospital Bern, University of Bern, Bern, Switzerland, [7]Division of Infectious Diseases, University Hospital Geneva, University of Geneva, Geneva, Switzerland, [8]Service of Neurology, University Hospital Geneva, University of Geneva, Geneva, Switzerland, [9]Memory Clinic, Felix Platter Hospital University Centre for Medicine of Aging, Basel, Switzerland, [10]Department of Neurology, Kantonsspital St. Gallen, St. Gallen, Switzerland, [11]Division of Infectious Diseases, Regional Hospital Lugano, Lugano, Switzerland

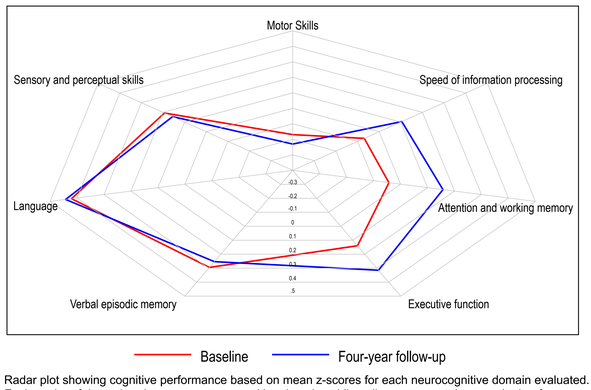
BACKGROUND

Among people living with HIV (PLWH) enrolled in the Neurocognitive Assessment in the Metabolic and Aging Cohort (NAMACO) study, we observed a neurocognitive impairment (NCI) prevalence of 40% by Frascati criteria. However, most patients had asymptomatic neurocognitive impairment (ANI), and analysed trajectories at two-years follow-up showed no signs of decline[1]. In the current study, we examined neurocognitive performance (NP) after four years, and its associated characteristics.

METHODS

- The NAMACO study is an ongoing prospective, longitudinal, multicentre and multilingual (French, German, Italian) study embedded within the Swiss HIV Cohort.
- PLWH ≥ 45 years old were recruited and assessed with standardized neuropsychological tests performed by neuropsychologists at baseline (between 2013 and 2016) and then at two- and four-years follow-up. NP was described by Frascati criteria, and by global and per cognitive domains z-scores.
- To evaluate factors associated with changes in NP over time, we defined our outcome as mean yearly changes in global mean z-scores from baseline. Uni- and multivariable linear regression models were performed and subsequently weighted for the inverse probability of dropping out of the study.
- Probabilities of dropping out of the study were obtained by multivariable logistic regression adjusted for all baseline characteristics with a ROC AUC of 0.68.

Figure 1. Mean z-score by neuropsychological domain at baseline and 4-year follow-up



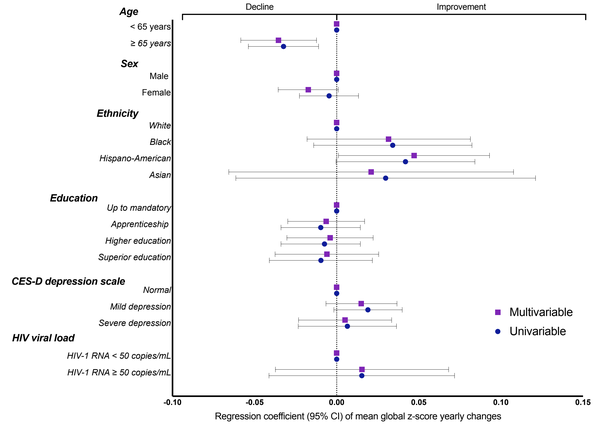
Radar plot showing cognitive performance based on mean z-scores for each neurocognitive domain evaluated. Each spoke of the radar plot represents a cognitive domain, while spikes represent the magnitude of mean z-score per domain. Points closer to the centre (-0.4) represent lower cognitive performance.

In a *well-treated* population of **PLWH**, we observed *stability or improvement in* **neurocognitive performance** after four years of follow-up.
Age ≥ 65 years was the only main factor associated with cognitive decline.

RESULTS

- A total of 981 participants were enrolled at baseline.
- Out of them, 540 (55.1%) were assessed at two-year and four-year follow-up.
- Participants were predominantly male (80.8%), MSM (56.1%), highly educated (87.9%) and employed (65.7%). Rest of demographic and clinical characteristics are presented in **table 1**.
- PLWH lost to follow-up were more likely to have Asymptomatic Neurocognitive Impairment (ANI) at baseline, mild or severe depression, being smokers, and to have moderate to severe alcohol consumption.
- We observed an increase in cognitive performance among the executive function domain, and among sensory and perceptual skills. (**Figure 1, table 1**).
- Overall, after adjusting for confounders, age ≥65 years was the only factor associated with cognitive decline among our population over the course of four years (**Figure 2**).

Figure 2. Clinical and demographic factors associated with neurocognitive change as measured by annualized mean z-scores changes between baseline and 4-year follow-up in univariable and multivariable linear regression models



	Baseline (N = 540)	Four-year follow-up (N = 540)	p-value
Age	53 (49; 58)	55 (52; 60)	**< 0.001**
HIV-1 RNA > 50 copies/mL	17 (3.2%)	2 (0.4)	**0.001**
CD4⁺ cell count nadir	180 (75; 270)	180 (75; 270)	1
CD4⁺ cell count (cells/µl)	615 (466; 796)	661 (509; 867)	**0.007**
Current smoker	176 (32.6)	167 (30.5)	0.6
Alcohol consumtpion	95 (17.6)	75 (13.7)	0.07
On anti-depression treatment	59 (10.9	65 (11.9)	0.6
Cardiovascular disease	68 (12.6)	75 (13.9)	0.5
Metabolic Disease	43 (7.9)	43 (7.9)	1
Liver disease	12 (2.2)	13 (2.4)	0.8
Kidney disease	10 (1.9)	9 (1.7)	0.8
Bone disease	93 (17.2)	101 (18.7)	0.5
Hepatitis B (HBV DNA)	10 (1.9)	10 (1.9)	1
Hepatitis C (HCV RNA)	40 (7.4)	21 (3.9)	**0.01**
Toxoplasmosis (IgG+)	277 (51.9)	278 (52.1)	0.9
Cytomegalovirus (IgG+)	469 (87.2)	469 (87.2)	1
Syphilis (VDRL)	116 (21.6)	118 (22.1)	0.8
Depressive symptoms by CES-D scale			0.02
No symptoms	368 (68.2)	404 (75.2)	
Mild depressive symptoms	118 (21.9)	82 (15.3)	
Severe depressive symptoms	54 (10.0)	51 (9.50)	
IADL	37 (6.9)	27 (5.0)	0.2
Neurocognitive domain affected			
Attention and working memory	151 (27.9)	146 (26.4)	0.6
Executive function	111 (20.6)	78 (14.3)	**0.006**
Language	29 (5.4)	17 (3.1)	0.06
Verbal episodic memory	68 (12.6)	81 (14.8)	0.2
Motor skills	199 (36.9)	191 (34.9)	0.4
Sensory and perceptual skills	18 (3.3)	5 (0.9)	**0.006**
Speed of information processing	156 (28.9)	137 (25.0)	0.1

*Lawton's Instrumental Activities of Daily Living

CONCLUSIONS

- In a well-treated population of predominantly male, white and well-educated PLWH, neurocognitive performance remained stable or improved over the course of four years.
- Executive functions and sensory and perceptual skills appeared to significantly improve over the study period.
- Comorbidities were not associated with cognitive changes over four years of follow-up.
- Depression, smoking and alcohol consumption were factors associated with not continuing the study, limiting our knowledge on the course of cognitive performance among this sub-population.

ACKNOWLEDGEMENTS

We would like to thank all the participants in our study, and all the members of the NAMACO study group, the Metabolic and Aging cohort, and the Swiss HIV Cohort Study.
This project was funded by The Swiss National Science Foundation Grant #324730_19777/1.

[1]Damas J, Ledergerber B, Nadin I, Tarr PE, Stoeckle M, Kunze U, Hauser C, Gutbrod K, Calmy A, Assal F, Schmid P, Hundsberger T, Di Benedetto C, Rossi S, Hasse B, Schlosser L, Du Pasquier R, Darling KEA, Cavassini M; NAMACO study group. Neurocognitive course at 2-year follow-up in a Swiss cohort of people with well-treated HIV. AIDS. 2021 Dec 1;35(15):2469-2480. doi: 10.1097/QAD.0000000000003057. PMID: 34411034; PMCID: PMC8631148.

Contact information:
Jose.Damas-Fernandez@chuv.ch