Assessing depression's impact on neurocognitive performance in the NAMACO study

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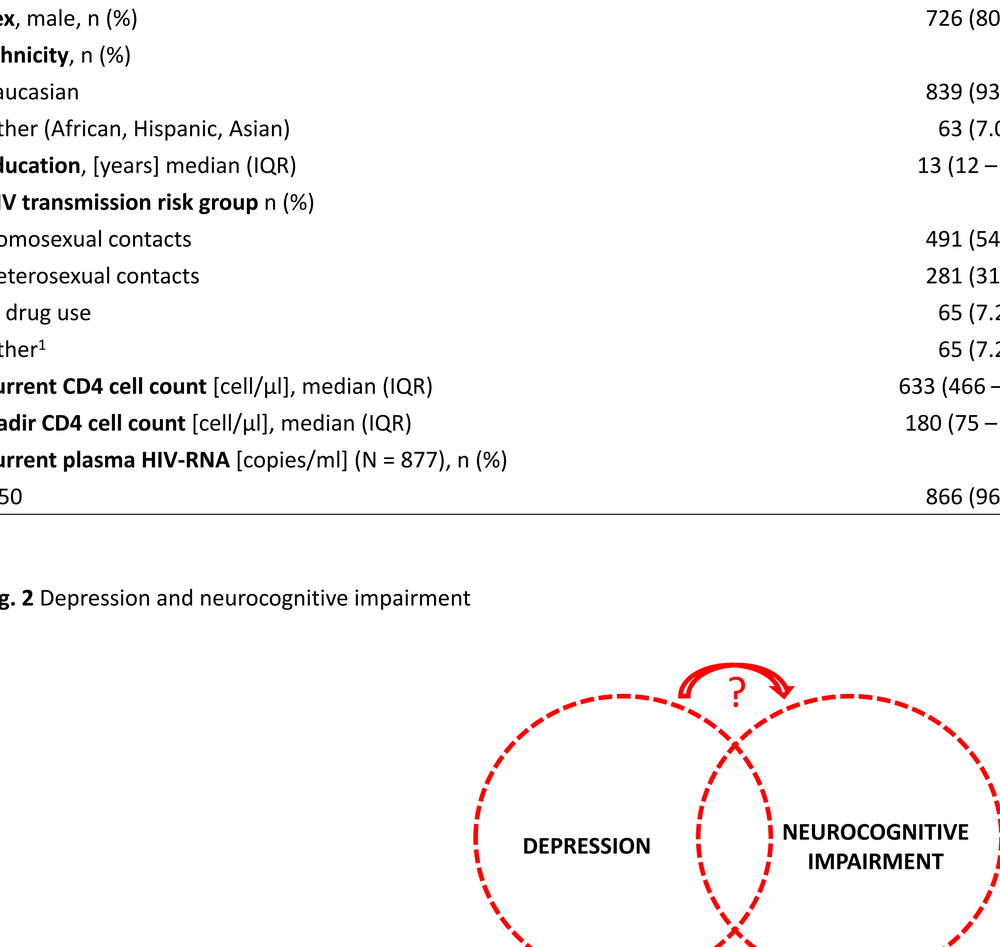
BACKGROUND

- In the era of potent antiretroviral therapy with suppressed blood HIV replication, HIV-associated neurocognitive disorders (HAND) remain a concern.
- This study aimed to analyze the link between depressive symptoms and neurocognitive impairment among well-treated HIV-positive patients.

METHODS

- Neurocognitive Assessment in the Metabolic and Ageing COhort (**NAMACO**) of the Swiss HIV Cohort Study (SHCS) is an ongoing prospective observational cohort study.
- Recruitment of 981 HIV-infected **SHCS** participants aged ≥ 45 years old from eight Swiss hospital centres between January 2013 and November 2016.
- Comprehensive and standardized neurocognitive assessment by neuropsychologists.
- Neurocognitive impairment classification based on the revised **American Academy of Neurology diagnostic criteria** for HAND diagnosis (Antinori et al.) without taking depressive symptoms into account.
- Depressive symptoms were assessed using the **Centre for Epidemiologic Studies Depression (CES-D) scale** (0–60).
- CES-D ≥ 16: depression; CES-D ≥ 27: severe depression
- Using the Wilcoxon-Mann-Whitney test, cross-sectional associations between CES-D scale and several factors were analysed.
- **Univariate and multivariate analyses** were performed on baseline data using regression models controlling for demographics, HIV infection characteristics and comorbidities, after exclusion of individuals with known neurological conditions increasing the risk of cognitive impairment.
- Depressive symptoms according to **the CES-D scale** were studied as **potential predictors of the presence of neurocognitive impairment**.

Fig. 1 Flowchart of patients analysed



RESULTS

Tab. 1 Patient demographics, HIV infection characteristics
[1] Transfusion, perinatal transmission, uncertain cause.

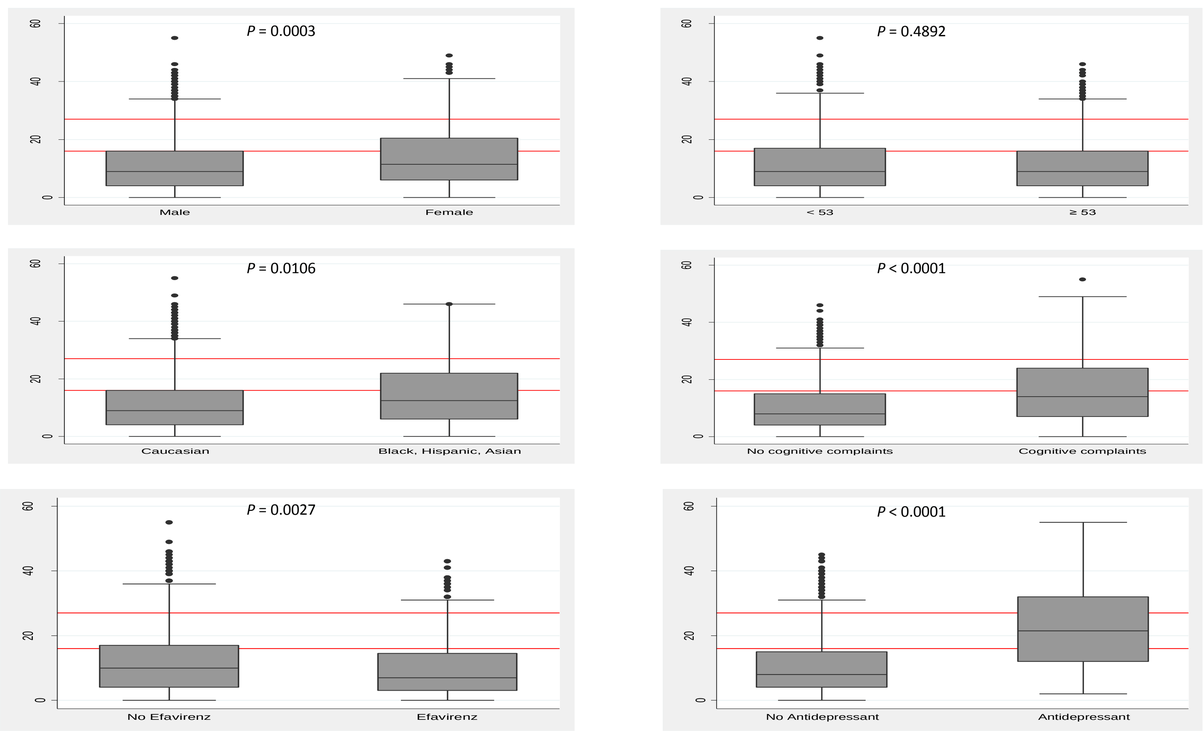
	N = 902
Age, [years] median (IQR)	53 (49 – 59)
Sex, male, n (%)	726 (80.5)
Ethnicity, n (%)	
Caucasian	839 (93.0)
Other (African, Hispanic, Asian)	63 (7.0)
Education, [years] median (IQR)	13 (12 – 14)
HIV transmission risk group n (%)	
Homosexual contacts	491 (54.4)
Heterosexual contacts	281 (31.2)
IV drug use	65 (7.2)
Other[1]	65 (7.2)
Current CD4 cell count [cell/µl], median (IQR)	633 (466 – 820)
Nadir CD4 cell count [cell/µl], median (IQR)	180 (75 – 272)
Current plasma HIV-RNA [copies/ml] (N = 877), n (%)	
< 50	866 (96.1)

Fig. 2 Depression and neurocognitive impairment

Tab. 2 Neurocognitive impairment, Centre for Epidemiologic Studies Depression (CES-D) score and drug use history among NAMACO study participants
[1] Answer "Yes definitely" to at least one of three screening questions.

Neurocognitive impairment (NCI) (N = 888) n (%)	
Normal neurocognitive examination	574 (64.6)
Asymptomatic neurocognitive impairment	279 (31.4)
Mild neurocognitive disorder	19 (2.1)
Dementia	16 (1.8)
Cognitive complaints[1] (N = 897) n (%)	213 (23.8)
CES-D score, (N = 895) median (IQR)	9 (4 – 16)
< 16	643 (71.8)
≥ 16, < 27	167 (18.7)
≥ 27	85 (9.5)
Antidepressant, (N = 902) n (%)	84 (9.3)
Actual / past IV drug use, (N = 898) n (%)	117 (13.0)
Cocaine consumption, (N = 901) n (%)	16 (1.8)
Cannabis consumption, (N = 901) n (%)	90 (10.0)

Fig. 3 Several factors statistically significantly associated with the CES-D scale (Wilcoxon-Mann-Whitney test)

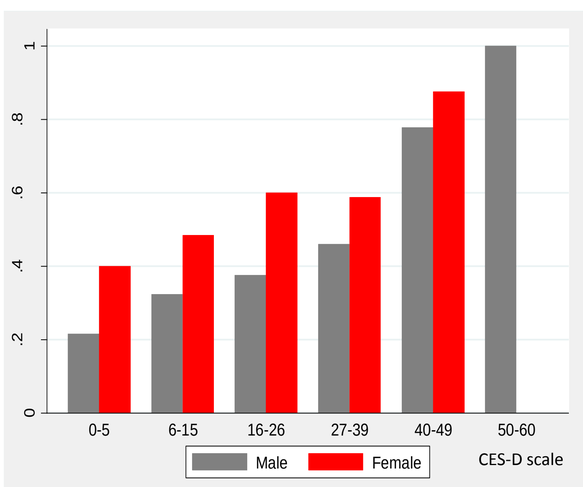


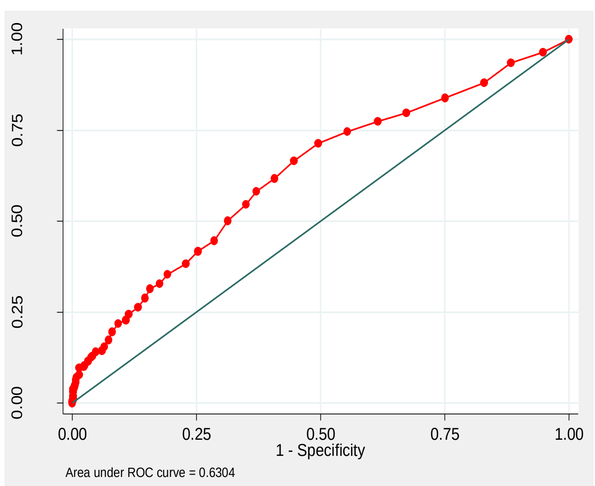
Upper red line: CES-D scale 27 (severe depression) - lower red line CES-D scale 16 (depression)

Tab. 3 CES-D scale and neurocognitive impairment
Adjustment variables: age, age^2, sex, ethnicity, education [years], time since cART initiation, time since cART initiation^2, HIV transmission risk group, nadir CD4 cell count (< 200, ≥ 200 cells/µl), haemoglobin (categorical variable, according to sex: < lower limit of reference range, within reference range, > upper limit of reference range), platelet count, diabetes, arterial hypertension, antecedent of cardiovascular events, cannabis consumption, cocaine consumption, past and/or actual IV drug use, efavirenz prescription, positive Hepatitis C serology (exposure), positive Hepatitis B serology (exposure), positive syphilis serology (exposure).

CES-D scale		Crude effect			Adjusted effect	
Continuous	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
N		*885*			*857*	
Total	1.05	1.04 – 1.06	< 0.001	1.05	1.04 – 1.07	< 0.001
N		*635*			*613*	
< 16	1.08	1.04 – 1.12	< 0.001	1.08	1.03 – 1.13	0.002
N		*250*			*244*	
≥ 16	1.06	1.03 – 1.10	< 0.001	1.07	1.02 – 1.12	0.002
Dichotomized	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
N		*885*			*857*	
≥16	2.10	1.55 – 2.83	< 0.001	2.28	1.60 – 3.26	< 0.001
≥ 27	2.65	1.68 – 4.17	< 0.001	2.85	1.68 – 4.83	< 0.001

Fig. 4 CES-D scale and neurocognitive impairment, frequency distribution and ROC curve
CES-D scale categories:





CONCLUSION

- Depression is an important potential confounding factor when assessing neurocognitive performance in HIV-infected individuals, even with moderate depressive symptoms.
- The CES-D scale is a poor predictor of neurocognitive impairment.
- CES-D scale: the relationship between depressive symptoms and neurocognitive impairment is not characterized by a threshold; a cutoff at 16 predicts the presence of NCI with a sensitivity of 38.3% and a specificity of 77.2%.
- Better addressing depressive symptoms might potentially improve the neurocognitive outcome of HIV-infected patients.

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