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Asymptomatic neurocognitive impairment in People Living With HIV infection (PLWH): are we misdiagnosing for someone?

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Background

HIV-Associated Neurocognitive Disorders (HAND) include a spectrum of cognitive, motor and mood problems affecting People Living With HIV (PLWH). For a comprehensive neurocognitive assessment, at least 2 tests for each cognitive domain should be administered. Although in accordance with guidelines a comprehensive neurocognitive assessment should be periodically performed, in several clinical setting this good clinical practice is just occasionally performed . Aim of this study was to examine the prevalence of neurocognitive impairment (NCI) in neurocognitive asymptomatic PLWH attending our outpatient clinics.

Methods

116 subjects without a previous diagnosis of psychiatric or cerebrovascular events, aged over 18 years, on Antiretroviral treatment (ARV) with an undetectable HIV RNA viremia from more than 1 year, were screened by the same doctor, after a specific training, during last autumn routine check-up visits. Attention, concentration, executive functions, memory, language, visuoconstructive skills, abstraction, calculation, and orientation were assessed with an italian version of Montreal Cognitive Assesment (MoCA) test (fig.1). The estimated administration time for the MoCA test is around 10 minutes; the maximum score is 30 points; a total score ≥26/30 is considered normal. Moreover, the following parameters were analyzed: sex, age, CD4 cells count, CD4 nadir, HIV RNA viremia, lenght of time of ARV treatment, antiretroviral regimen (INSTI based or not, 2DR vs 3DR, NUC sparing), years of schooling.

Fig 1 Montreal cognitive assessment (MoCA test) Italian version


Results

Among the 116 examined subjects, 85 (73%) were male, median age 52 (IQR 42-60) years, median lenght of exposition to antiretroviral treatment 10 (IQR 4,7-20.2) years. All of them had HIV RNA viremia below 200 copies/ml: 109 (94%) <50 copies/ml, 67 (58%) TND. Median CD4 nadir was 252 (IQR 107-457) cells/µl. Median CD4 cell count was 781 (IQR 540-996) cells/µl. Median years of schooling 13 (IQR 8-13) years. The median MoCA score was 24 (IQR 21-26) (Tab. 1). Thirty one (27%) subjects had a normal value (fig. 2). When we analyzed the distribution of **MoCA score, a Spearman correlation** was detected with **age** (r=-0.26; two tailed p=0.0048); **schooling** (r=0.335; two tailed p=0.0002); **CD4 nadir** (r=0.216; two tailed p= 0.02); **years ot treatment** (r=0.233; two tailed p=0.012) (Tab. 2 and fig. 3,4,5).

No statistical differences were seen regarding normal MoCa score with last CD4 cell count, HIV RNA viremia, current ARV regimen, therapeutic strategy (anchor drug and 2DR vs 3DR).

Tab.1 Demographic and Clinical Characteristics of Examined Subjects

| Characteristics	Value
Total subjects examined	116
Male subjects	85 (73%)
Median age (IQR) (years)	52 (42-60)
Median length of antiretroviral treatment (IQR) (years)	10 (4.7-20.2)
HIV RNA viremia < 200 copies/ml	116 (100%)
HIV RNA viremia < 50 copies/ml	109 (94%)
HIV RNA viremia TND (target not detected)	67 (58%)
Median CD4 nadir (IQR) (cells/µl)	252 (107-457)
Median CD4 cell count (IQR) (cells/µl)	781 (540-996)
Median years of schooling (IQR)	13 (8-13)
Median MoCA score (IQR)	24 (21-26)

Fig.2 Percentage Distribution of MoCA (Montreal Cognitive Assessment) Test Scores (normal score >26/30)

MoCa test ≥26/30 27%
MoCa test <25/30 73%

- MoCa test ≥26/30
- MoCa test <25/30
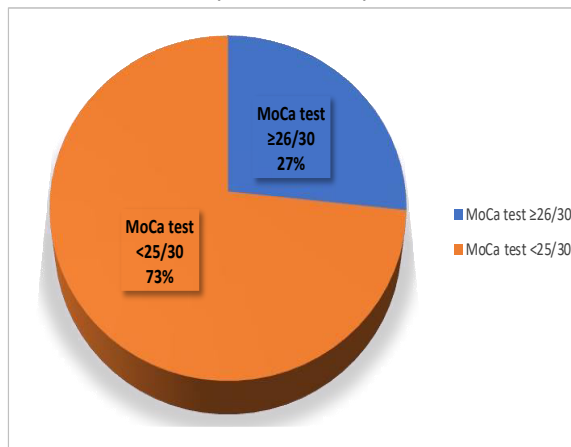
Tab.2 Spearman Correlation between MoCA Score and some examined parameters

Variable	Correlation (r)	p-value
Age	-0.26	0.0048
Schooling	0.335	0.0002
CD4 nadir	0.216	0.0200
Years of treatment	0.233	0.0120

Fig. 3,4.5 Correlation of MoCA (Montreal Cognitive Assessment) Test Scores with Age, years of treatment and schooling

SLR Age-MOCA result

SLR YiA-MOCA

SLR Years of schooling - MOCA Results
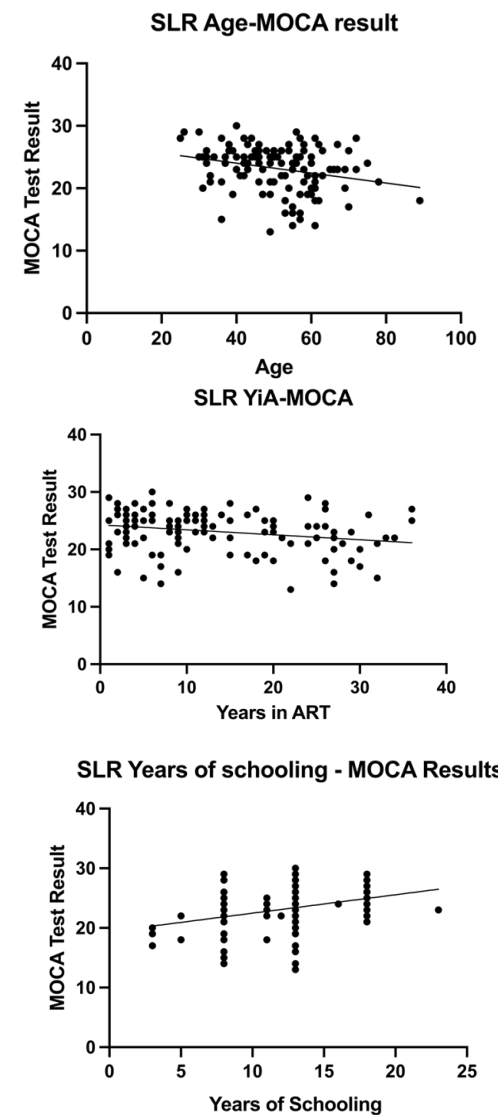
Discussion and Conclusions

Just a quarter of PLWH, screened in this cross sectional analysis, performed a normal MoCA score. Age, schooling, longer exposition to ARV treatment and lower CD4 cell count nadir were observed to be potentially associated with patological score. Noteworthy, cognitive test performances and relative scores could be strongly influenced by complex educational, cultural and socioeconomic factors which can interact with HIV risk. As a consequence, Frascati criteria could mis-classify over 20% of cognitively healthy individuals as having any impairment. In the era of the effective ARV treatment and ageing for PLWH, cognitive impairment is frequently multifactorial and, hence, is not inevitably a result of the direct effect of HIV on the brain. Nevertheless, a comprehensive neurocognitive assessment should be periodically performed in clinical setting to prevent or early recognize any undesirable impairment.