12° INTERNATIONAL SYMPOSIUM ON
NEUROPSYCHIATRY & HIV

Example of comprehensive neurocognitive assessment in a HIV population in Northern Italy

Barcelona – June 14th 2019

Dott. C.Bolla

Division of Infectious Diseases, SS.Antonio e Biagio e Cesare Arrigo, Alessandria, Italy

HIV neuro psychiatry

BACKGROUND

HAND is a common disease with variable reported prevalence in different populations (20–69%)

It is most commonly seen in advanced stages of HIV/AIDS; however, HAND can also occur in asymptomatic HIV infection.

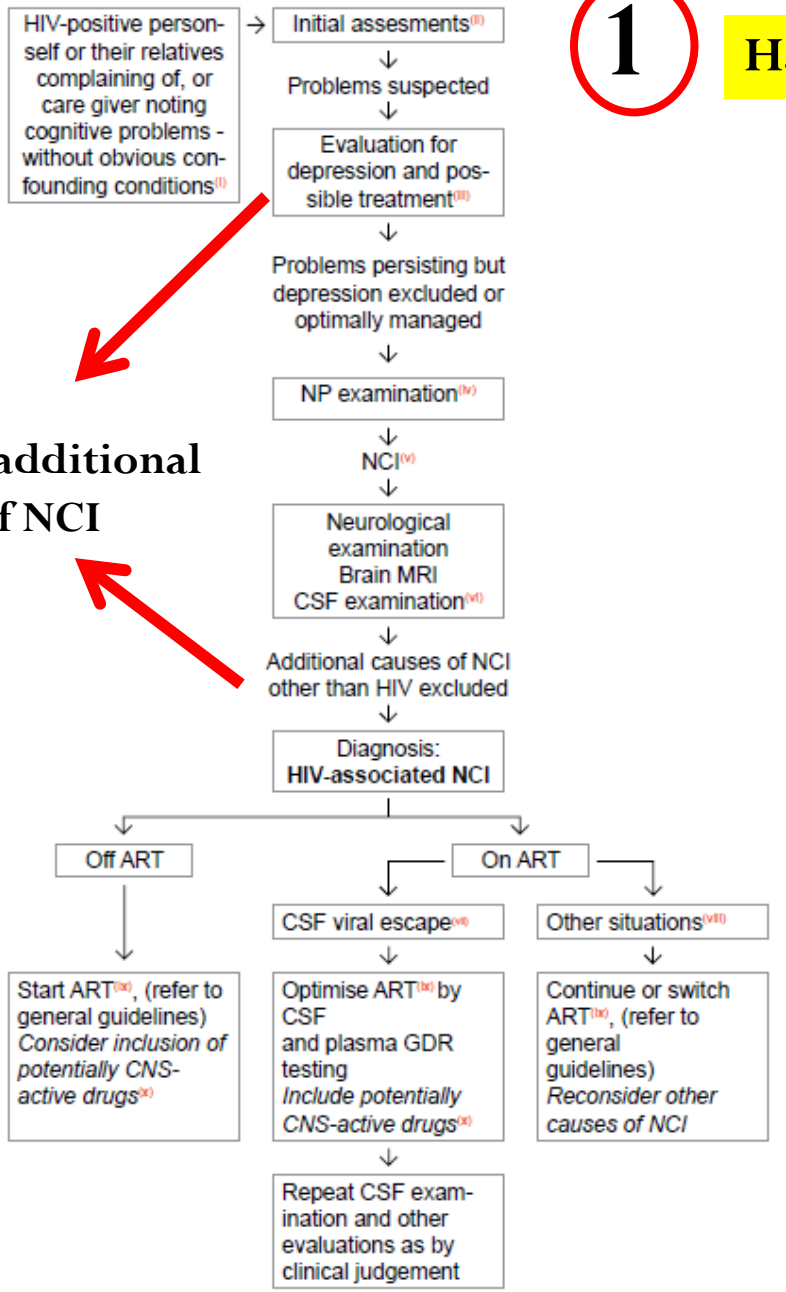
It is critically important, though, to recognize that HAND occurs in only *some* patients – the majority of patients who are virally suppressed on HAART will not develop HAND.

Antonia Carroll et al. HIV-associated neurocognitive disorders: recent advances in pathogenesis, biomarkers, and treatment F1000 Research 2017

HIV neuro psychiatry

1

Has the patient a real HAND?



Exclusion of additional causes of NCI

- Drugs with demonstrated clear CSF penetration:
  - —NRTIs: ZDV, ABC*
  - —NNRTIs: EFV**, NVP
  - —PI/r: LPV/r, DRV/r*
  - —INSTI: DTG
  - —Other classes: MVC
- Drugs with proven clinical efficacy:
  - —NRTIs: ZDV, ABC
  - —PI/r: LPV/r

2 Risk factors assessment

RISK FACTORS AND COMORBIDITIES IN HAND (Smail and Brew 2018)
Low CD4+
Longer duration of infection
History of AIDs defining illness
High plasma HIV viral load
HIV-related infections
cART-related toxicity
Alcohol or drug abuse
Metabolic (e.g., anemia, low hematocrit, thrombocytopenia, renal failure)
Cardiovascular and cerebrovascular disease
Previous immune deficiency
Diabetes, hyperlipidemia, carotid atherosclerosis
Epilepsy
Depressive symptoms (Heaton et al. 2015; Malaspina et al. 2011)
Lower education or cognitive reserve
Hepatitis C (Ciccarelli et al. 2013)

Jacqueline Rosenthal et al. Aging, comorbidities, and the importance of finding biomarkers for HIV-associated neurocognitive disorders
Journal of NeuroVirology December 2018

HIV neuro psychiatry

3 What is the best performer?

Screening for Neurocognitive Impairment in HIV Individuals: The Utility of the Montreal Cognitive Assessment Test

Rodrigo Hasbun[1,*], Jairo Eraso[1], Sweeya Ramireddy[1], D' Arcy Wainwright[1], Lucrecia Salazar[1], Richard Grimes[1], Michele York[2], and Adriana Strutt[2]

The International HIV Dementia Scale: a new rapid screening test for HIV

Ned C. Sacktor[a], Matthew Wong[b], Noeli
Skolasky[a], Ola A. Selnes[a], Seggane M
Justin C. McArthur[a], Allan Ronald

Screening for Neurocognitive Impair
aged 50 and Older: Montreal Cogniti
Self-Reported and Clinician Rated Everyday Functioning

P. L. Fazeli[1,3], K. B. Casaletto[2], E. Paolillo[2], R. C. Moore[3,4,5], D. J. Moore[3], and the HNRP Group

Accepted Manuscript

Utility of the Montreal cognitive assessment (MoCA) and its subset in HIV-associated neurocognitive disorder (HAND) screening

Woo Jung Kim, Nam Su Ku, Young-Joon Lee, Jin Young Ahn, Sun Bean Kim, Hye-Won Ahn, Kyung-Wook Hong, Joon Young Song, Hee Jin Cheong, Woo Joo Kim, June Myung Kim, Kee Namkoong, Jun Yong Choi,

AIDS. 2010 Jun 1;24(9):1243-50. doi: 10.1097/QAD.0b013e3283354a7b.

Cognitive dysfunction in HIV patients despite long-standing suppression of viremia.

Simioni S[1], Cavassini M, Annoni JM, Rimbault Abraham A, Bourquin I, Schiffer V, Calmy A, Chave JP, Giacobini E, Hirschel B, Du Pasquier RA.

Department of Neurology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

None identifies nature of cognitive disorders and , especially ANI diagnosis is particularly difficult.

HIV neuro psychiatry

OUR CLINICAL PATHWAY

HIV clinic: 450 patients

Staff: 2 MD and 2 nurses

- Consecutive HIV positive adults prospectively enrolled since May 2018 until May 2019

- Screening for HAND:

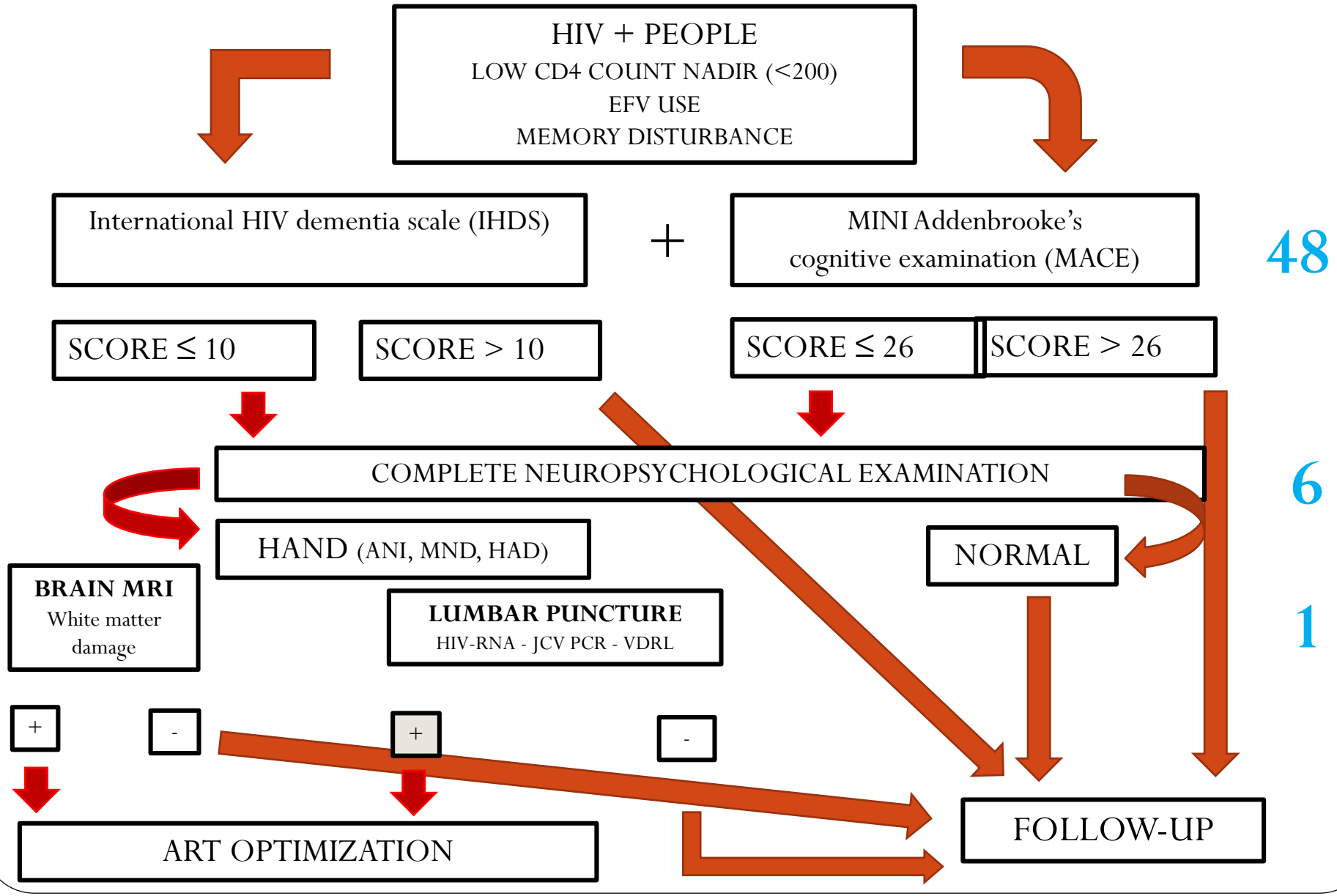
- CD4 nadir <200 cell/mmc and/or
- EFV use and/or
- Symptoms of NC impairment

Azienda Ospedaliera Nazionale
SS. Antonio e Biagio e Cesare Arrigo
Alessandria

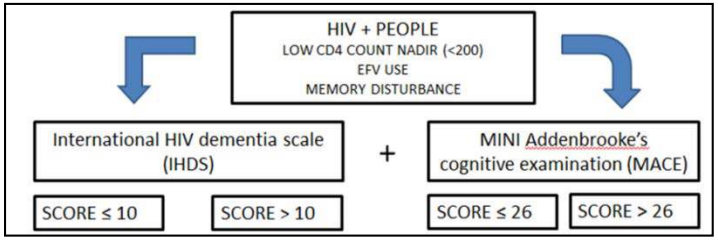
CHARACTERISTIC	N (%)
Patient number	**48**
Male Sex	35 (72,7%)
Caucasian	46 (93,7%)
Age (median)	50 (28-68)
HIV-RNA <20cp/ml	89,5%
On ART	48 (100%)
Mild symptoms of NCI	**38 (79%)**
CD4 Nadir (median)	254 (5-1250)
< 200/mmc	**5 (10,5%)**
Median year of diagnosis	2004 (1986-2018)
Previous IDU	13 (27%)
Mild controlled psy.disease	15 (31,2%)
HCV+	13 (27%)
Vascular encephalopathy	5 (10,5%)
Previous EFV use	**5 (10.5%)**

HIV neuro psychiatry

FLOW CHART



HIV neuro psychiatry



IHDS

- Rapid and easy administration by phisician without specific neurological training
- Language and culturally neutral
- 3 main cognitive domains assessed: motor speed, psychomotor speed and memory
- Maximum score: 12
- IHDS has variable sensitivity and specificity according to the cutoff
- Lack of accuracy due to a low specificity when screening for the milder forms of HAND (ANI and MND)

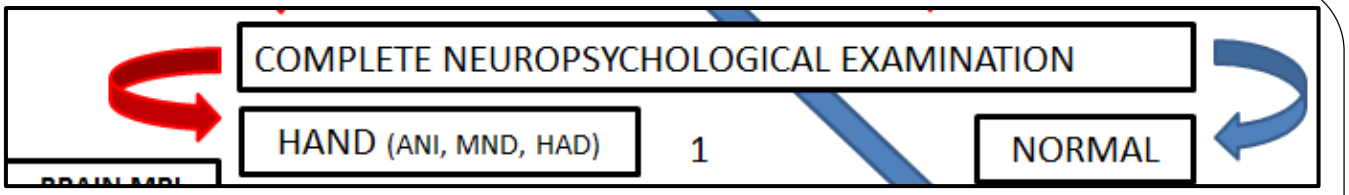
MACE

- Very brief and sensitive cognitive screening tool for NC Impairment
- 4 main cognitive domains assessed: orientation, memory, language and visuo-spatial function.
- Maximum score of 30 (higher scores = better cognitive function)
- Two cut-offs (21 and 25) are recommended
- Higher specificity at lower cut-off (21/30)

Haddow LJ, Floyd S, Copas A, Gilson RJ. A systematic review of the screening accuracy of the HIV Dementia Scale and International HIV Dementia Scale. PLoS One. 2013; 8(4):e61826. doi: 10.1371/journal.pone.0061826 PMID: 23613945

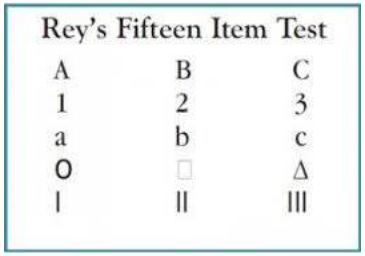
Sharpley Hsieh et al. The Mini-Addenbrooke's Cognitive Examination: A New Assessment Tool for Dementia. Dementia and Geriatric Cognitive Disorder 2015;39:1–11

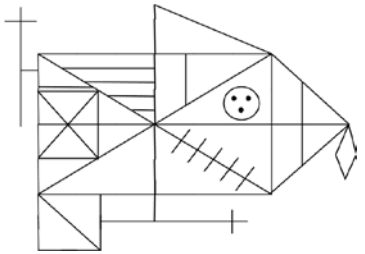
HIV neuro psychiatry

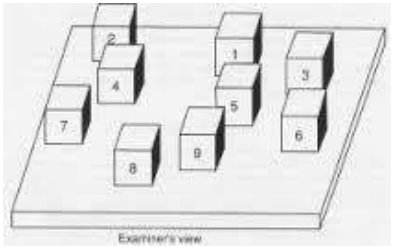


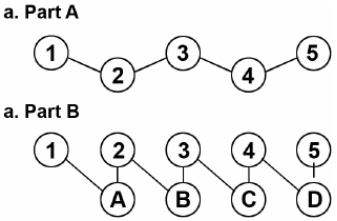
Patients with MACE < 26 and IHDS < 10 underwent a complete NPE by a NP of our Hospital Psycological Unit

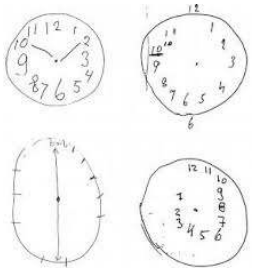
- FAB - Frontal Assessment Battery
- Activity of Daily Living (ADL-IADL)
- Digits span Forward
- Corsi's test
- Prose memory
- Rey's 15 item test
- Rey's complex figure test
- Stroop's test
- Trail Making Test A-B
- Lexical recall for phonemic categories (F,P,L)
- Clock test
- Test for costructive apraxia
- Cipher from WAIS-IV
- BDI-II Beck Depression Inventory
- HAM-A Hamilton Anxiety Rating Scale

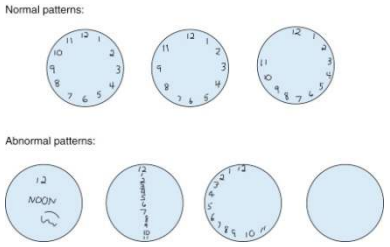






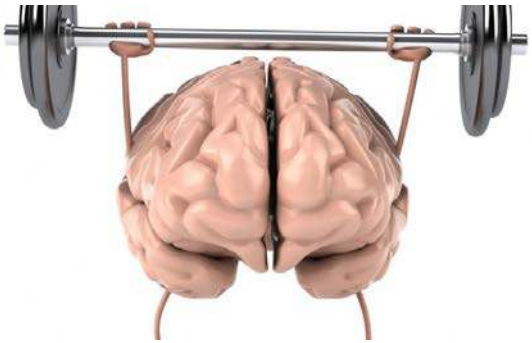






HIV neuro psychiatry

NEUROPSYCHOLOGICAL EVALUATION

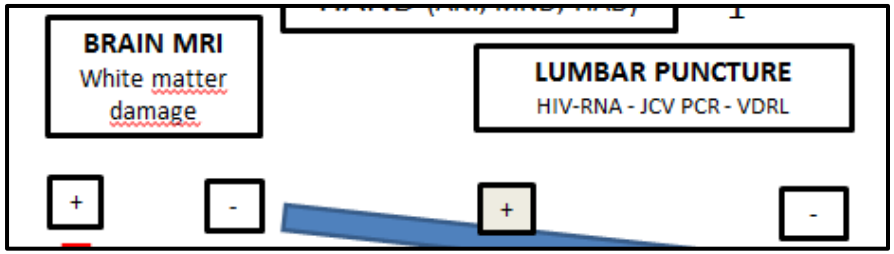


Four inquiry areas:

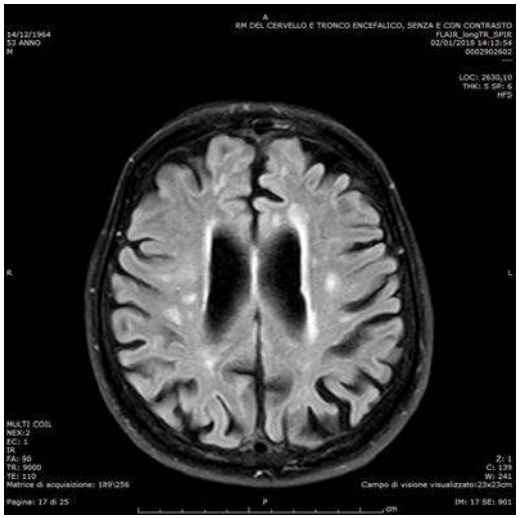
1. MEMORY
2. ATTENTIVE FUNCTION
3. PRAXIA/VISUO-SPATIAL FUNCTION
4. ELABORATION SPEED

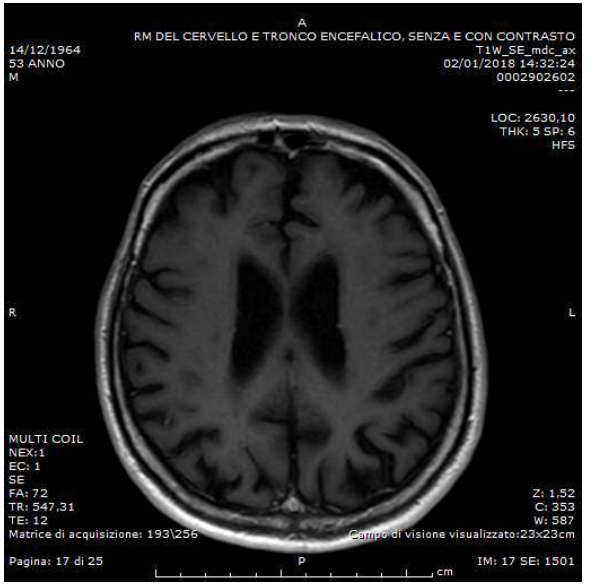
Final comment of NP and HAND diagnosis in accordance to Frascati criteria

HIV neuro psychiatry



MRI



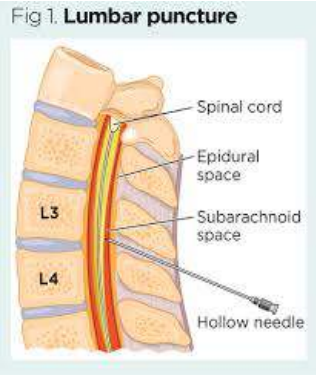


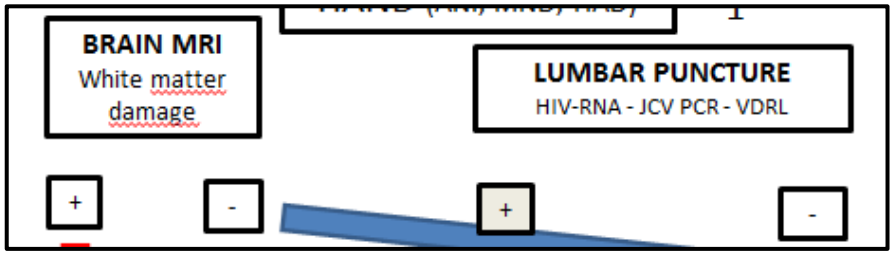
- Magnetic resonance spectroscopy (MRS), volumetric MRI
- Diffusion tensor imaging (DTI)
- Functional MRI (fMRI)

Beau M. Ances. Neuroimaging of HIV Associated Neurocognitive Disorders (HAND) Curr Opin HIV AIDS. Nov 2014

Mary C. Masters. Role of Neuroimaging in HIV Associated Neurocognitive Disorders (HAND) Semin Neurol. 2014

HIV neuro psychiatry





- **ROUTINE TESTS**

- wbc, glucose and protein
- HIV-RNA
- JCV PCR
- Syphilis
- CSF GDR testing

- **ADDITIONAL TESTS**

- Viral tropism testing
- CSF and blood isoelectric focusing
- Markers of neuro-inflammation and neuronal damage (neopterin, tau protein, etc)

EACS guidelines 9.1 2018
Cerebrospinal fluid biomarkers in patients with central nervous system infections: a retrospective study. Di Stefano A, et al. CNS Spectr. 2019 May 27:1-7
Blood brain barrier impairment is associated with cerebrospinal fluid markers of neuronal damage in HIV-positive patients.
A.Calcagno. J Neurovirol. 2016 Feb;22(1):88-92

HIV neuro psychiatry

ART OPTIMIZATION

Man, 54 years old

2016: admission for wasting syndrome, oral candidiasis and molluscum contagiosium. Dx of AIDS.

Baseline: Cd4 151 cells/mmc, VL HIV 4.271.000

HAART: DTG/ABC/3TC

Progressive neurological impairment.

2019: MACE 12, IHDS 6 → complete NP assessment

(**HAD diagnosis**)

→ MRI: T2 hyper and T1 hypointensity in superficial and periventricular supratentorial white matter

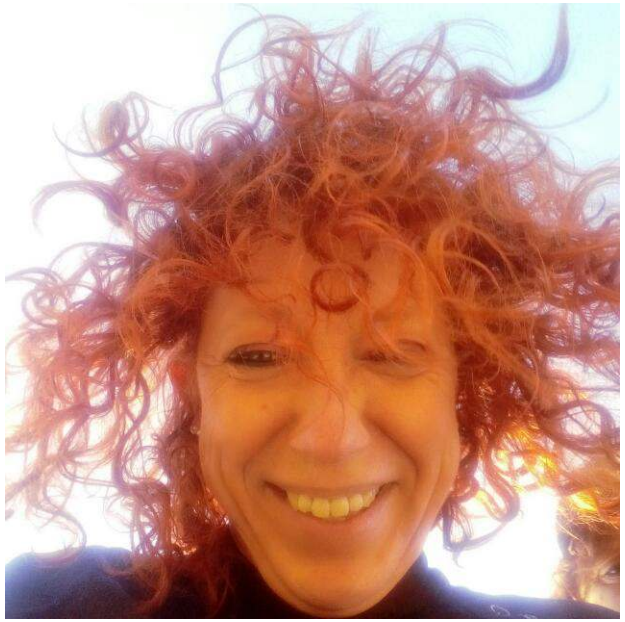
Lumbar puncture: HIV viral load 70 cp/mmc (blood VL <20)

↓

ART switch: from DTG/ABC/3TC to DRV/cobi + TAF/FTC + MVC

HIV neuro psychiatry

CONCLUSIONS

- Dedicated pathway for neurological assessment of HIV patients
- Specific depression pre-screening
- Cardiovascular risk factors
- Is the combination of 2 tests the solution?
- Collaboration with referral Centres

ACKNOWLEDGEMENTS