

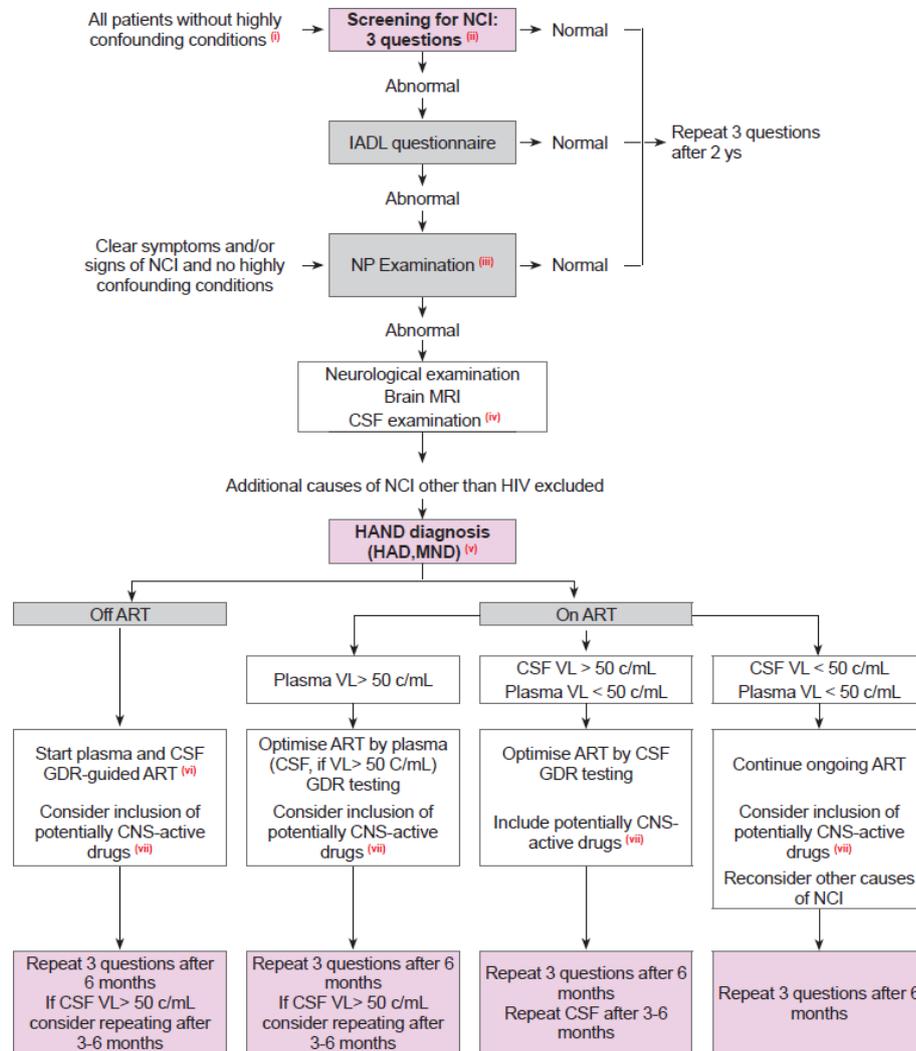
Screening for cognitive impairment in PLWHIV

The European AIDS Clinical Society (EACS)* recommend¹ that all HIV-infected people without any highly confounding conditions (severe psychiatric conditions, use of psychotropic drugs, alcohol abuse, sequela from previous opportunistic infections of the CNS or a current CNS infection) should be screened using three questions on comprehension, clarity and speed every 2 years.

- Do you experience frequent memory loss (e.g. do you forget the occurrence of special events even the more recent ones, appointments, etc.)?
- Do you feel that you are slower when reasoning, planning activities, or solving problems?
- Do you have difficulties paying attention (e.g. to a conversation, a book, or a movie)?

If abnormal or symptomatic use the following algorithm (Figure 1) for further assessment.

Figure 1. Algorithm for diagnosis and management of HIV-associated Neurocognitive Impairment (NCI)



ANI=Asymptomatic Neurocognitive Impairment; CSF=Cerebrospinal Fluid; GDR=genotypic drug resistance test; HAD=HIV-Associated Dementia; HAND=HIV-Associated Neurocognitive Disorder; IADL=Instrumental Activities of Daily Living; MND=Mild Neurocognitive Disorders; MRI=Brain Magnetic Resonance Imaging; NP=Neuropsychological

i **Highly confounding conditions** 1. Severe psychiatric conditions; 2. Abuse of psychotropic drugs; 3. Alcohol abuse; 4. Sequelae from previous CNS-OIs or other neurological diseases; 5. Current CNS-OIs or other neurological diseases.

ii **3 questions** (ref. Simioni et al., AIDS 2009). 1. Do you experience frequent memory loss (e.g. do you forget the occurrence of special events even the more recent ones, appointments, etc.)? 2. Do you feel that you are slower when reasoning, planning activities, or solving problems? 3. Do you have difficulties paying attention (e.g. to a conversation, a book, or a movie)? For each question, patients can answer: a) never, b) hardly ever, or c) yes, definitely. Patients are considered to have an “abnormal” result when answering “yes, definitely” on at least one question.

iii NP examination will have to include tests exploring the following cognitive domains: fluency, executive functions, speed of information processing, attention/working memory, verbal and visual learning, verbal and visual memory, motor skills (ref. Antinori et al., Neurology 2007).

iv **Brain MRI and CSF examination.** These are required to further exclude other pathologies and to further characterize HAND, by including assessment of CSF HIV-RNA level and, where appropriate, evidence for genotypic drug resistance (GDR) in a paired CSF and plasma sample.

v **HAD and MND definitions** (ref. Antinori et al., Neurology 2007).

- **HAD is defined in the presence of 1) marked** acquired impairment in cognitive functioning involving **at least 2** cognitive domains, as documented by performance of at least 2 SD below the mean for age-education appropriate norms on NP tests; 2) **marked** interference in daily functioning; 3) no evidence of another pre-existing cause for the dementia.
- **MND is defined in the presence of 1) acquired** impairment in cognitive functioning involving at least 2 cognitive domains, as documented by performance of **at least 1 SD** below the mean for age-education appropriate norms on NP tests; 2) **mild** interference in daily functioning; 3) no evidence of another pre-existing cause for the MND.

vi If GDR in CSF and/or plasma not available, store aliquots for possible future use.

vii **Definition of ‘potentially CNS-active’ drugs:** ARV drugs with either demonstrated clear CSF penetration when studied in healthy HIV-infected populations (concentration above the **IC90** in > 90 % examined patients) or with proven short-term (3-6 months) efficacy on cognitive function or CSF viral load decay when evaluated as single agents or in controlled studies in peer reviewed papers.

Agents with demonstrated clear CSF penetration:

- NRTIs: ZDV, ABC
- NNRTIs: EFV, NVP
- Boosted PIs: IND/r, LPV/r, DRV/r
- Other classes: MAR
- Drugs with proven “efficacy”:
- NRTIs: ZDV, d4T, ABC
- Boosted PIs: LPV/r

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References

1. European AIDS Clinical Society. [Guidelines. Version 6.0](#).* Accessed 4 July 2012.