12th International Symposium on Neuropsychiatry & HIV

14-15 / June / 2019

Barcelona, Catalonia, Spain

Neuropsychological Tests: Which, When, and How?

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Academic Editor - PLoS ONE

Question	*General Answer*	*Specific Answer*	*PROs*	*Limitations*	*Supporting Evidence*
WHICH?					
WHEN?					
HOW?					

Question	*General Answer*	*Specific Answer*	*PROs*	*Limitations*	*Supporting Evidence*
WHICH?	Comprehensive NP Testing	6-7 domains / 2 scores (Verbal Fluency, Learning, ...)	1) Experience/ updated information 2) Comparable data 3) Recommendations	1) Cost 2) Practice effect	NIMH, UNAIDS, Frascati, Mind Exchange, EACS, ...
WHEN?					
HOW?					

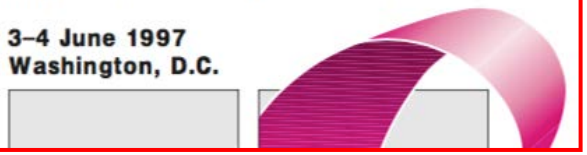
SPECIAL PRESENTATION

Assessment of Aids-Related Cognitive Changes: Recommendations of the NIMH Workshop on Neuropsychological Assessment Approaches*

Journal of Clinical and Experimental Neuropsychology
1990, Vol. 12, No. 6, pp. 963-978

UNAIDS Expert Consultation
on Cognitive and Neuropsychological impairment in Early HIV infection

3–4 June 1997
Washington, D.C.



UNAIDS
UNICEF • UNDP • UNFPA
UNESCO • WHO • WORLD BANK

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UNAIDS

Updated research nosology for HIV-associated neurocognitive disorders

A. Antinori, MD
G. Arendt, MD
J.T. Becker, PhD
B.J. Brew, MBBS, MD, FRACP
D.A. Byrd, PhD
M. Cherner, PhD
D.B. Clifford, MD
P. Cinque, MD, PhD
L.G. Epstein, MD
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M. Gisslen, MD, PhD
I. Grant, MD
R.K. Heaton, PhD
J. Joseph, PhD
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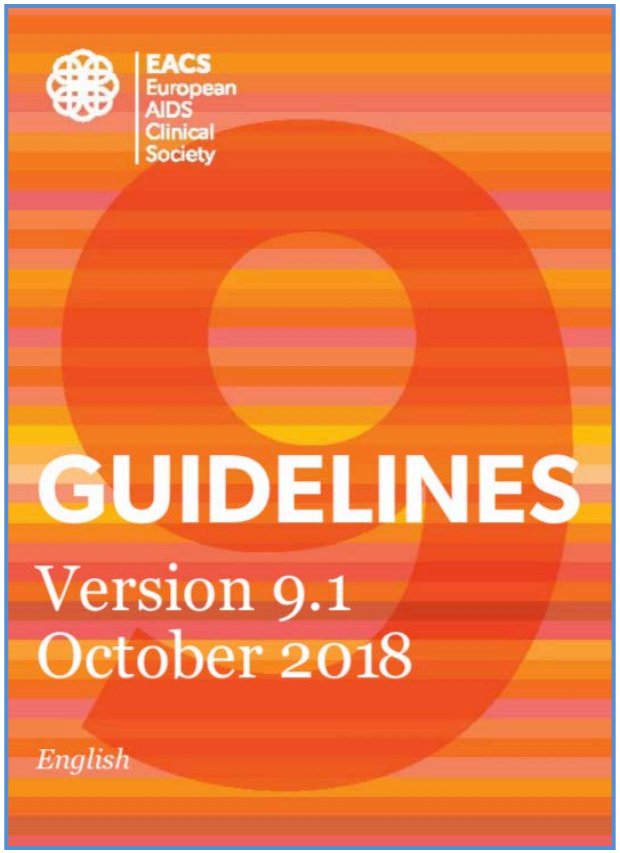
M. Nunn, PhD
R.W. Price, MD
L. Pulliam, PhD
K.R. Robertson, PhD
N. Sacktor, MD
V. Valcour, MD
V.E. Wojna, MD

Neurology 69 October 30, 2007

Assessment, Diagnosis, and Treatment of HIV-Associated Neurocognitive Disorder: A Consensus Report of the Mind Exchange Program

The Mind Exchange Working Group

HIV/AIDS • CID 2013:56 (1 April) • 1005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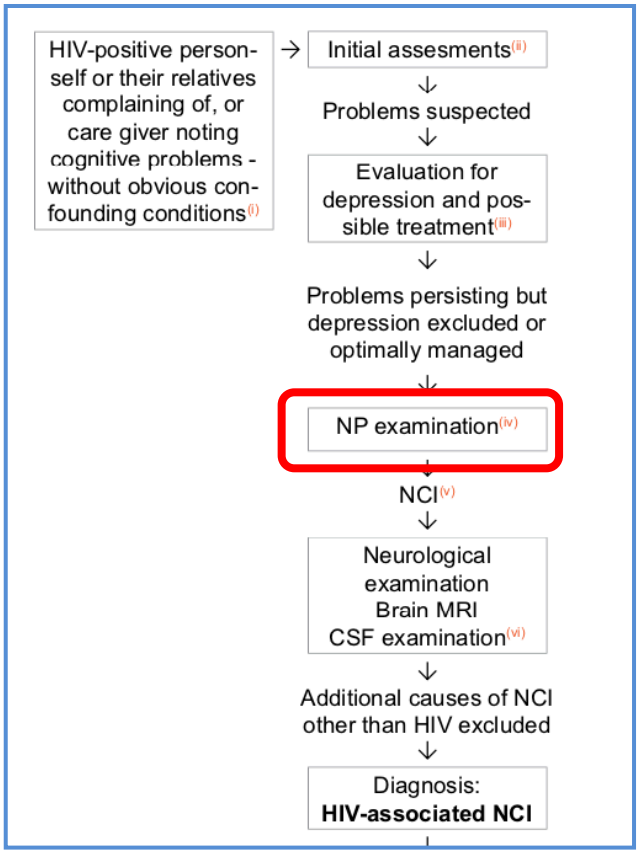
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Initial assesments(ii)
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Evaluation for depression and pos- sible treatment(iii)
Problems persisting but depression excluded or optimally managed
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NCI(v)
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Brain MRI
CSF examination(vi)
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Diagnosis:
HIV-associated NCI

A. Indication of Premorbid Intelligence
   1. *Vocabulary (WAIS-R)*
   2. National Adult Reading Test (NART)

B. Attention
   1. Digit Span (WMS-R)
   2. *Visual Span* (WMS-R)

C. Speed of Processing
   1. Sternberg Search Task
   2. Simple and Choice Reaction Times
   3. *Paced Auditory Serial Addition Test* (PASAT)

D. Memory
   1. *California Verbal Learning Test* (CVLT)
   2. Working Memory Test
   3. Modified Visual Reproduction Test (WMS)

E. Abstraction
   1. Category Test
   2. Trails Making Test, Parts A and B

F. Language
   1. Boston Naming Test
   2. Letter and Category Fluency Test

G. Visuospatial
   1. Embedded Figures Test
   2. Money's Standardized Road-Map Test of Direction Sense
   3. Digit Symbol Substitution

H. Construction Abilities
   1. Block Design Test
   2. Tactual Performance Test

I. Motor Abilities
   1. Grooved Pegboard
   2. Finger Tapping Test
   3. Grip Strength

J. Psychiatric Assessment
   1. Diagnostic Interview Schedule (DIS)
   2. *Hamilton Depression Scale*
   3. *State-Trait Anxiety Scale*
   4. Mini-Mental State Examination

Fluency
Controlled Oral Word Association Test (FAS) (1, 2)
Thurstone Word Fluency Test (3)
Category Fluency (4)
Action Fluency (5)
Design Fluency Tests (6, 7)

Executive Functions
Stroop Color and Word Test (8)
Trailmaking Test – Part B (3, 9)
Color Trails –II (10)
Wisconsin Card Sorting Test (11)
Halstead Category Test (3, 9)
Odd Man Out Test (12-14)
Tower Tests (15-17)
Delis-Kaplan Executive Function System (7)

Speed of Information Processing
WAIS-III Digit Symbol Subtest (18)
WAIS-III Symbol Search Subtest (18)
Symbol Digit Modalities Test (19)
Trailmaking Test – Part A (3, 9)
Color Trails – I (10)
Digit Vigilance Test (3, 20)
Stroop Color Naming (8)
Reaction Time Tests, e.g., California Computerized Assessment Battery (21)

Attention/Working Memory
WAIS-III Digit Span Subtest (18)
WAIS-III Letter-Number Sequencing Subtest (18)
WMS-III Spatial Span Subtest (22)
Paced Auditory Serial Addition Test (23)
Digit Vigilance Test (error component) (3, 20)

Verbal and Visual Learning
Verbal:
California Verbal Learning Test (Original and Revised; Total Learning) (24)
Rey Auditory Verbal Learning Test (Total Learning) (25)
Story Memory Test (Learning component) (3)
Hopkins Verbal Learning Test- Revised (Total Learning) (26)
Buschke Selective Reminding Test (27)
WMS-III Logical Memory I (22)
WMS-III Paired Associates I (22)

Visual:
WMS-III Visual Reproduction-I (22)
WMS-III Family Pictures-I (22)
Brief Visuospatial Memory Test – Revised (Total Learning) (28)
Figure Memory Test (Learning component) (3)
Rey-Osterreith Complex Figure Test (Immediate Recall) (29, 30)

Verbal and Visual Memory
Delayed recall scores of the 12 learning/memory tests listed above, with interpretation also guided by results on any normed, forgetting/savings scores and delayed recognition scores.

Motor Skills
Grooved Pegboard Test (3, 31)
Purdue Pegboard Test (32, 33)
Arendt Central Motor Test Battery (34, 35)
Finger Tapping Test (3)
Timed Gait (36)

Assessment, Diagnosis, and Treatment of HIV-Associated Neurocognitive Disorder: A Consensus Report of the Mind Exchange Program

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2. Comprehensive standard neuropsychological testing should be based on the following:

   a. A comprehensive test battery including at least 6 cognitive domains including verbal/language; attention/working memory; abstraction/executive function; memory functions (learning and recall); speed of information processing; and motor skills. CEBM 5; GOR D (Antinori et al., 2007)

   b. Standard computerised-based neuropsychological tests may be used by clinical neuropsychologists, or they may prefer paper and pencil version of the same tests. The importance is again in the use of standard and validated instruments for detection of HAND. See standard reference book Lezak et al., 2004

   c. Similar neuropsychological tests are recommended to be used for ANI, MND and HAD diagnosis, although a step-down battery is often more appropriate in patients with severe impairment. A standard assessment of independence in activities of daily living is needed to differentiate ANI, MND and HAD. CEBM 5; GOR D (Antinori et al., 2007; see also Al-Khindi et al., 2011; Cysique et al., 2010a; Muñoz-Moreno et al., 2008; Ellis et al., 2002; Heaton et al., 2010; Heaton et al., 2011; Robertson et al., 2007; Robertson et al. 2010; Vivithanaporn et al., 2010)

1. Verbal fluency
2. Executive functions
3. Processing speed
4. Attention
5. Learning
6. Verbal memory
7. Motor skills

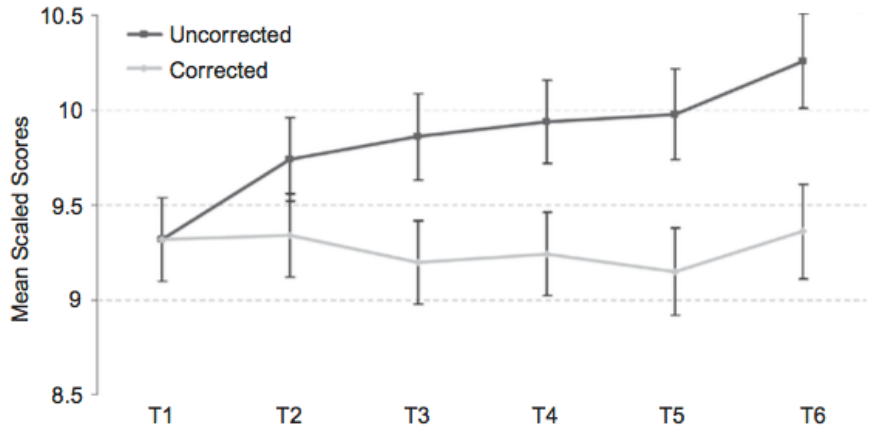
Normative data and validation of a regression based summary score for assessing meaningful neuropsychological change

Lucette A. Cysique[1,2], Donald Franklin, Jr[1], Ian Abramson[1], Ronald J. Ellis[1], Scott Letendre[1], Ann Collier[3], David Clifford[4], Benjamin Gelman[5], Justin McArthur[6], Susan Morgello[7], David Simpson[7], J. Allen McCutchan[1], Igor Grant[1], Robert K. Heaton[1], the CHARTER group, and the HNRC group

JOURNAL OF CLINICAL AND EXPERIMENTAL NEUROPSYCHOLOGY
2011, 33 (5), 505–522

TABLE 5
Median practice effect from baseline to follow-up on 15 NP measures

NP measure	*T2*	*T3*	*T4*	*T5 +*
Letter Fluency	0.0	0.5	1.0	1.0
Animal Fluency	0.0	0.0	0.0	0.0
PASAT-50	0.5	1.0	1.0	1.0
WAIS–III L–N Sequencing	0.0	0.0	0.0	0.0
WAIS–III Digit Symbol	0.0	0.5	1.0	1.0
WAIS–III Symbol Search	0.5	1.0	1.0	1.0
Trail Making Test A	0.5	1.0	1.0	1.0
WCST-64 Perseverative Errors	1.0	2.0	2.0	2.0
Trail Making Test B	1.0	1.0	1.0	1.0
HVLT–R Total Learning	0.0	1.0	0.5	0.5
HVLT–R Delayed Recall	0.5	0.5	0.5	0.5
BVMT–R Total Learning	1.0	1.0	0.0	1.0
BVMT–R Delayed Recall	0.5	0.0	0.0	0.5
Grooved Pegboard DH	0.5	0.0	1.0	1.0
Grooved Pegboard NDH	0.0	0.5	0.5	1.0
Sum	6.0	10.0	10.5	12.5



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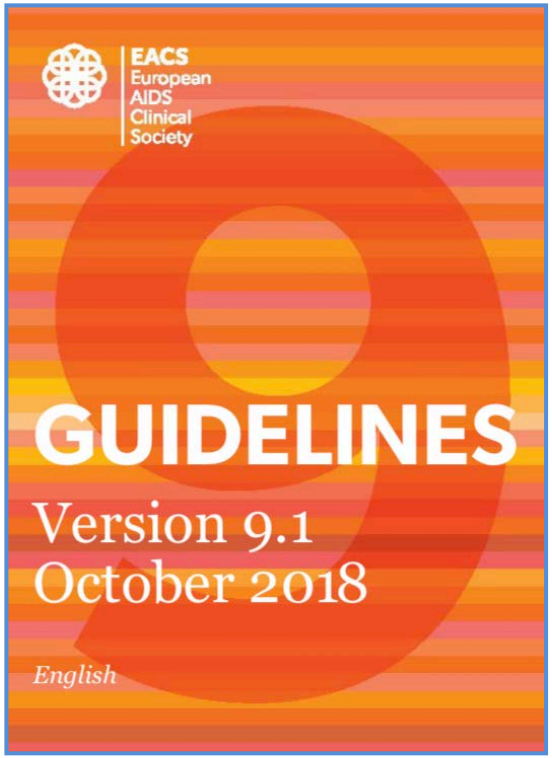
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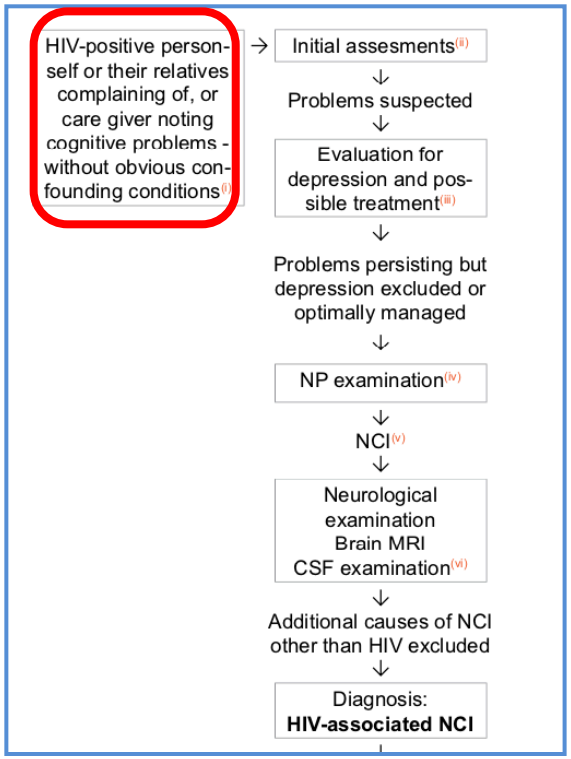
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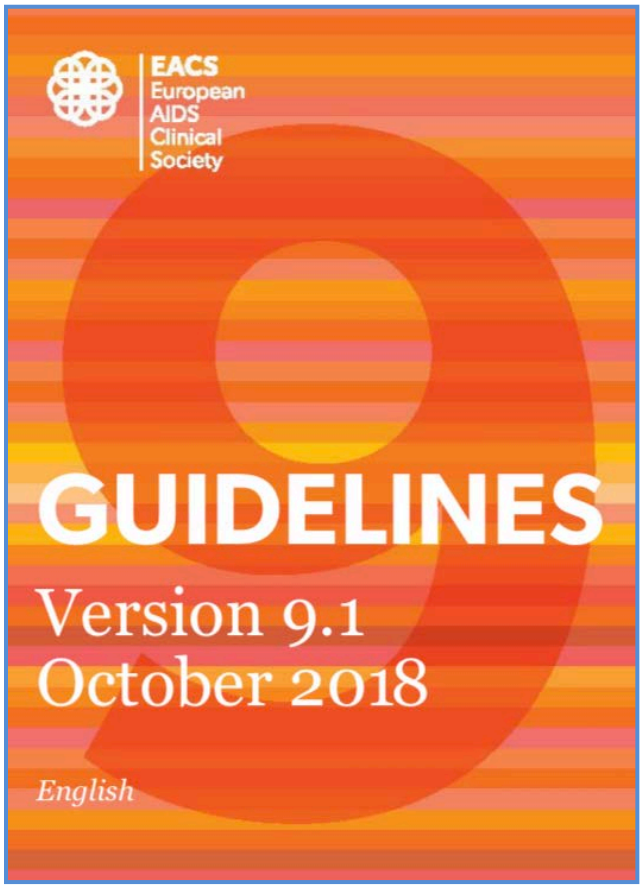

HIV-positive person- self or their relatives complaining of, or care giver noting cognitive problems - without obvious con- founding conditions[i]

→ Initial assesments[ii]

↓

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↓

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↓

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↓

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↓

NCI[v]

↓

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↓

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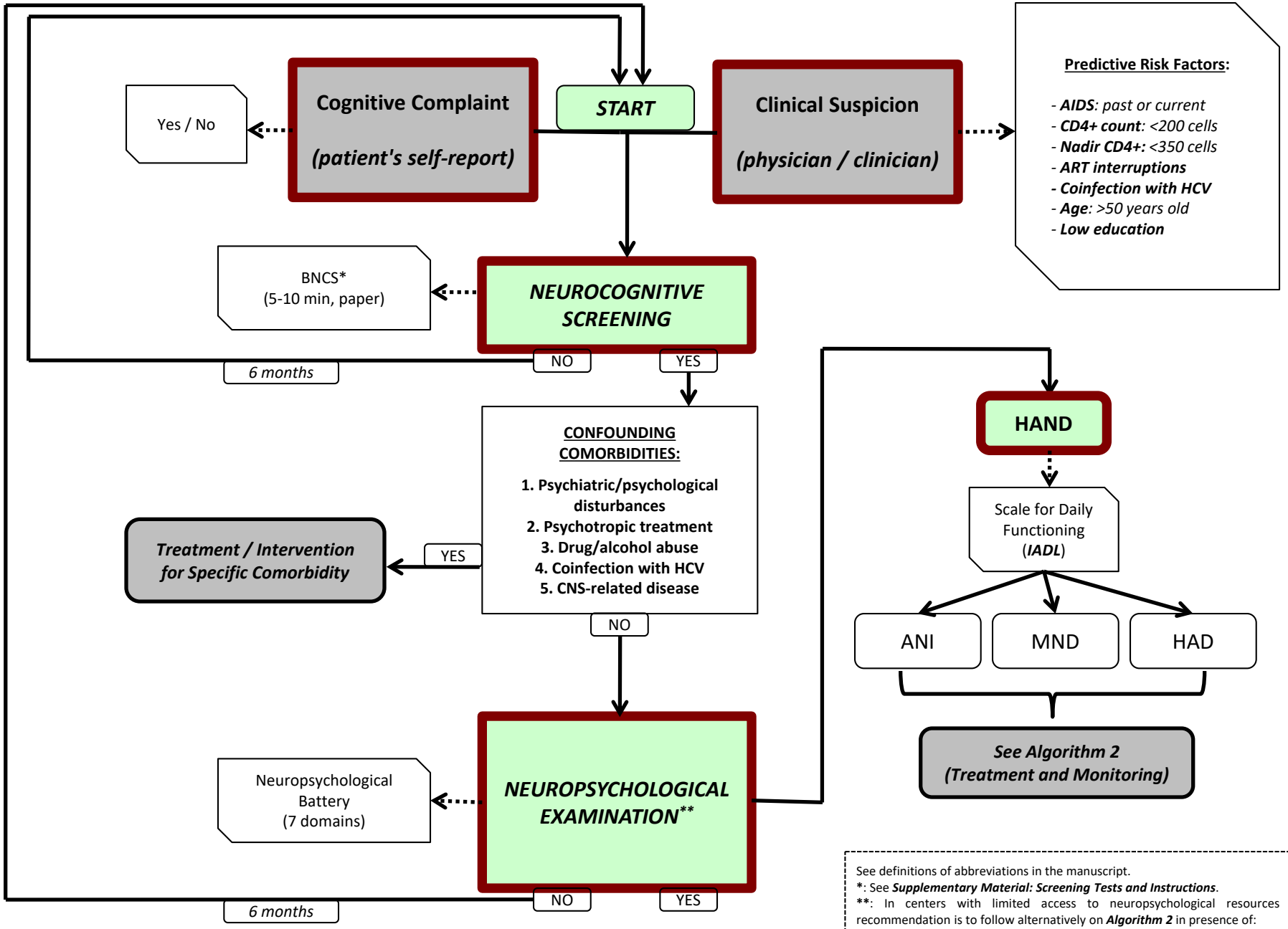
HIV-associated NCI

↓

ALGORITHM 1. Screening, assessment, and diagnosis of HIV-Associated Neurocognitive Disorders (HAND).



See definitions of abbreviations in the manuscript.
*: See ***Supplementary Material: Screening Tests and Instructions***.
: In centers with limited access to neuropsychological resources the recommendation is to follow alternatively on ***Algorithm 2* in presence of:
1) Cognitive Complaint + 2) Clinical Suspicion + 3) Positive Sreening.

Gisslén et al. BMC Infectious Diseases 2011, 11:356
http://www.biomedcentral.com/1471-2334/11/356

BMC Infectious Diseases

DEBATE Open Access

The definition of HIV-associated neurocognitive disorders: are we overestimating the real prevalence?

Magnus Gisslén[1*], Richard W Price[2] and Staffan Nilsson[3]

Torti et al. BMC Medicine 2011, 9:138
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BMC Medicine

COMMENTARY Open Access

Asymptomatic neurocognitive disorders in patients infected by HIV: fact or fiction?

Carlo Torti[1*], Emanuele Focà[1], Bruno M Cesana[2] and Francois X Lescure[3]

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AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 29, Number 6, 2013

DOI: 10.1089/aid.2012.0229

PATHOGENESIS

Deficits in Self-Awareness Impact the Diagnosis of Asymptomatic Neurocognitive Impairment in HIV

Stephanie Chiao,[1] Howard J. Rosen,[2] Krista Nicolas,[2] Lauren A. Wendelken,[2] Oscar Alcantar,[2] Katherine P. Rankin,[2] Bruce Miller,[2] and Victor Valcour[2,3]

Asymptomatic HIV-associated neurocognitive impairment increases risk for symptomatic decline

Neurology 82 June 10, 2014

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	Monitoring	- 3-6 Months ➔ ART start / Severe CI - 1-2 Years ➔ Mild CI	1) Close follow-up 2) Interventional options	1) Practice effect	- Mind Exchange - Cognitive improvement studies
HOW?					

1. Frequency of monitoring of patients who are receiving treatment (from the perspective of HAND, considering both efficacy and safety):

   a. Patients with HAD and MND commencing therapy should be monitored clinically, initially at 3 and 6 months, then 6 monthly until a plateau of response has been observed, and thereafter annually. If there is clearly no response - and especially if there is deterioration at these early time points - other causes of impairment should be re-evaluated. Among these is the possibility of immune reconstitution characterised by deterioration following an initial response.

   b. Patients with ANI commencing therapy should be monitored initially at 6 months and annually thereafter.

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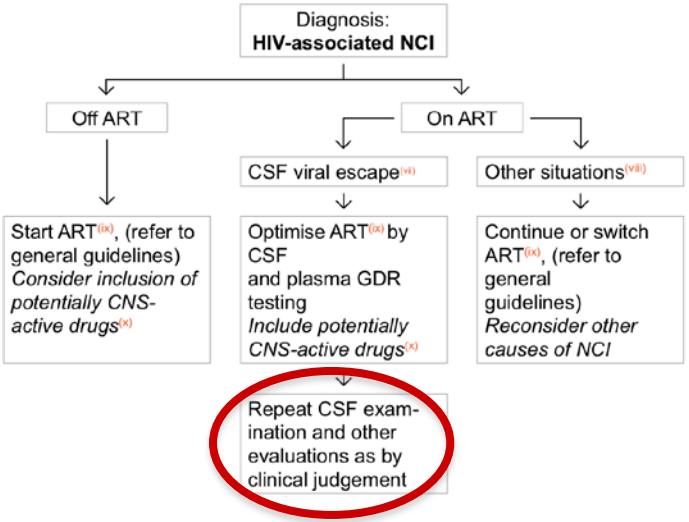
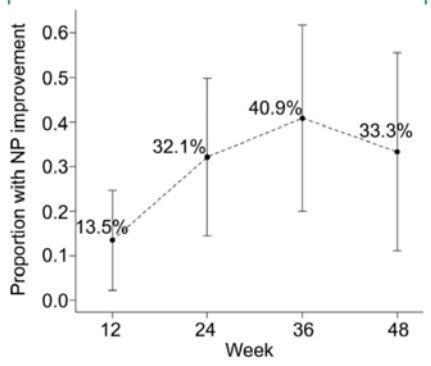


Dynamics of cognitive change in impaired HIV-positive patients initiating antiretroviral therapy

L.A. Cysique, PhD
F. Vaida, PhD
S. Letendre, MD
S. Gibson, BS
M. Cherner, PhD
S.P. Woods, PsyD
J.A. McCutchan, MD
R.K. Heaton, PhD
R.J. Ellis, MD, PhD

Neurology 73 August 4, 2009

Figure 1 Proportion of HIV+ individuals with neuropsychological improvement from baseline



Central Nervous System (CNS) Effects of Therapy Initiation with Integrase Inhibitors

Anna Prats[1], Ignacio Martínez-Zalacaín[2], Beatriz Mothe[3], Eugènia Negredo[1], Maite Garolera[4], Sira Domènech-Puigcerver[5], Michael Meulbroek[6], Carmina R. Fumaz[1], Maria J. Ferrer[1], Bonaventura Clotet[3], Carles Soriano-Mas[2], **Jose A. Muñoz-Moreno[1]**; on behalf of the ***ARBRE Study Group***

Abstract #439

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Conference on Retroviruses and Opportunistic Infections
March 3 -7, 2019
Seattle, WA

Figure 2a. *BL NPZ-12.*

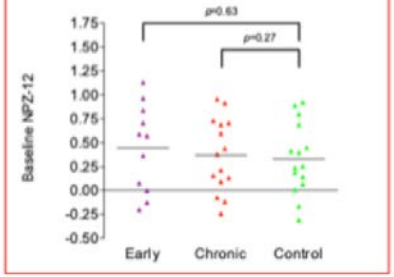
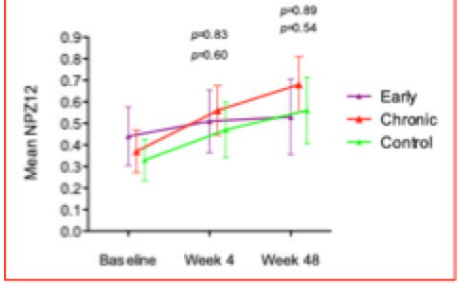


Figure 2b. *Mean NPZ-12.*



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HOW?	Trained Neuropsychologist	- HIV Unit - Neurology/ Neuropsychological Units	1) Individualized management 2) Close collaboration (eg, comorbidities assessment, ...) 3) Oriented to treatment	1) Cost 2) Practice effect	NIH, UNAIDS, Frascati, Mind Exchange, EACS, ...

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	Physician/ Clinician	- Screening	1) Time 2) Cost	1) Scarce information 2) Poor differential diagnosis 3) Difficulty to treat	- - -

Screening Tools

Name	Ref	Duration	Advantages	Limitations
CogState®	*Cysique et al, J Int Neuropsych Soc, 2006*	10-15 min	- 4 areas covered - Low practice effect	- Economical cost - Feasibility (computerized)
CAMCI® (Computer Assessment of Mild Cogn. Impairm.)	*Becker et al, AIDS Patient Care and STDs, 2011*	20 min	- 4 areas covered - Low practice effect	- Economical cost - Feasibility (computerized)
HNRC Screen	*Carey et al, Clin Neuropsychol, 2004*	5-10 min	- Good accuracy (78%, 85%) - Only 2 measures	- Economical cost - Instrumental requirements (pegboard)
IHDS (International HIV Dementia Scale)	*Sacktor et al, AIDS, 2005*	5-10 min	- Quantitative score - Extensively used	- Designed for HAD - Limited accuracy
BNCS (Brief NeuroCognitive Screen)	*Ellis et al, J Neurovirol, 2005*	5-10 min	- Paper-based use - Extensively used	- Economical cost - Limited sensitivity (65%)
MoCA® (Montreal Cognitive Assessment)	*Koski et al, HIV Medicine, 2011*	5-10 min	- Quantitative score - 4 areas covered	- Designed for aging - Limited specificity (42%)
NEU Screen	*Muñoz-Moreno et al, JAIDS, 2013*	5-10 min	- Good accuracy (74%, 81%) - No copyright restrictions	- Limited to Spanish speakers - No formal validation

Question	*General Answer*	*Specific Answer*	*PROs*	*Limitations*	*Supporting Evidence*
WHICH?	Comprehensive NP Testing	6-7 domains / 2 scores (Verbal Fluency, Learning, ...)	1) Experience/ updated information 2) Comparable data 3) Recommendations	1) Cost 2) Practice effect	NIMH, UNAIDS, Frascati, Mind Exchange, EACS, ...
	Brief NP Assessment	Brief battery (eg, CogState, NEU battery, ...)	1) Time 2) Cost	1) Scarce information 2) Necessity of neuropsychologist	ACTGs, CogState studies, Other studies, ...
WHEN?	Cognitive Symptoms/Complaints	- Patient's report - EACS questions - Other tests (eg, PAOFI, ...)	1) Clinical impact confirmed 2) Chance to HAND	-	NIH, UNAIDS, Frascati, Mind Exchange, EACS, ...
	Clinical Suspicion	- Specific reason - Suspected risk factor	1) Widespread covering 2) Potential decline anticipated	1) Overestimated frequency? 2) Unclear clinical relevance	- Valcour, 2013 (*AIDS Res&Hum Retro*) - Grant, 2014 (*Neurology*)
	Monitoring	- 3-6 Months ➔ ART start / Severe CI - 1-2 Years ➔ Mild CI	1) Close follow-up 2) Interventional options	1) Practice effect	- Mind Exchange - Cognitive improvement studies
HOW?	Trained Neuropsychologist	- HIV Unit - Neurology/ Neuropsychological Units	1) Individualized management 2) Close collaboration (eg, comorbidities assessment, ...) 3) Oriented to treatment	1) Cost 2) Practice effect	NIH, UNAIDS, Frascati, Mind Exchange, EACS, ...
	Physician/ Clinician	- Screening	1) Time 2) Cost	1) Scarce information 2) Poor differential diagnosis 3) Difficulty to treat	- - -