4th International

Barcelona, May 5th and 6th 2011

4rd Symposium on Psychiatry and HIV

- - -

Barcelona, May 6th 2010

Neurocognitive Testing in HIV Infection:

How to Implement this Assessment in the Clinical Practice?

Jose A. Muñoz-Moreno

- - -

Lluita contra la SIDA Foundation

Germans Trias i Pujol University Hospital

- - -

Barcelona, Catalonia, Spain

www.flsida.org

Why to Assess?

Which Tools?

Which Patients and When Monitoring?

Why to Assess?

Main Reasons

- ☑ High and Unexpected Incidence and Prevalence
- ☑ Associated with Several Negative Consequences
- ☑ Significant Lack of Effective Treatments!

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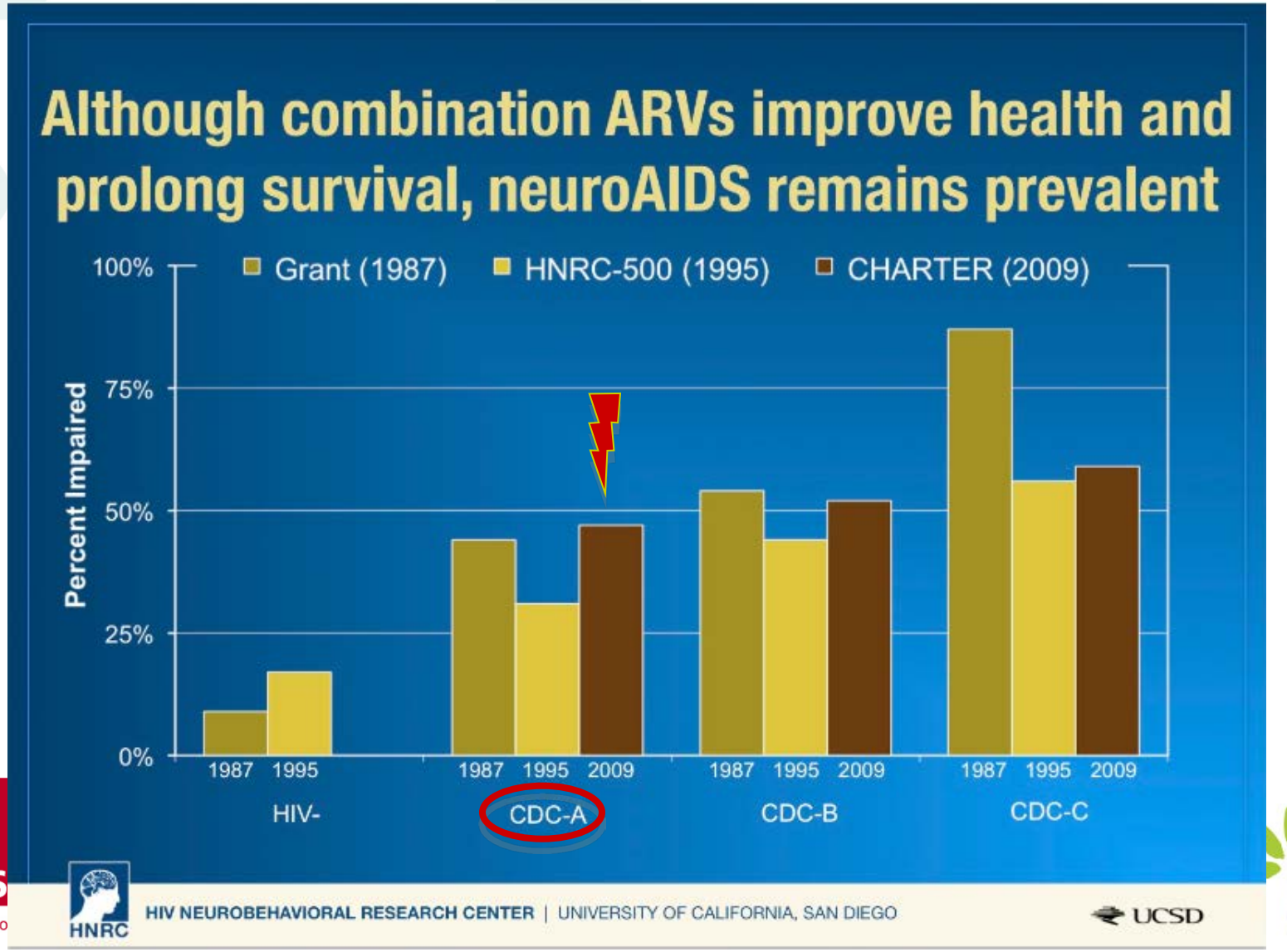
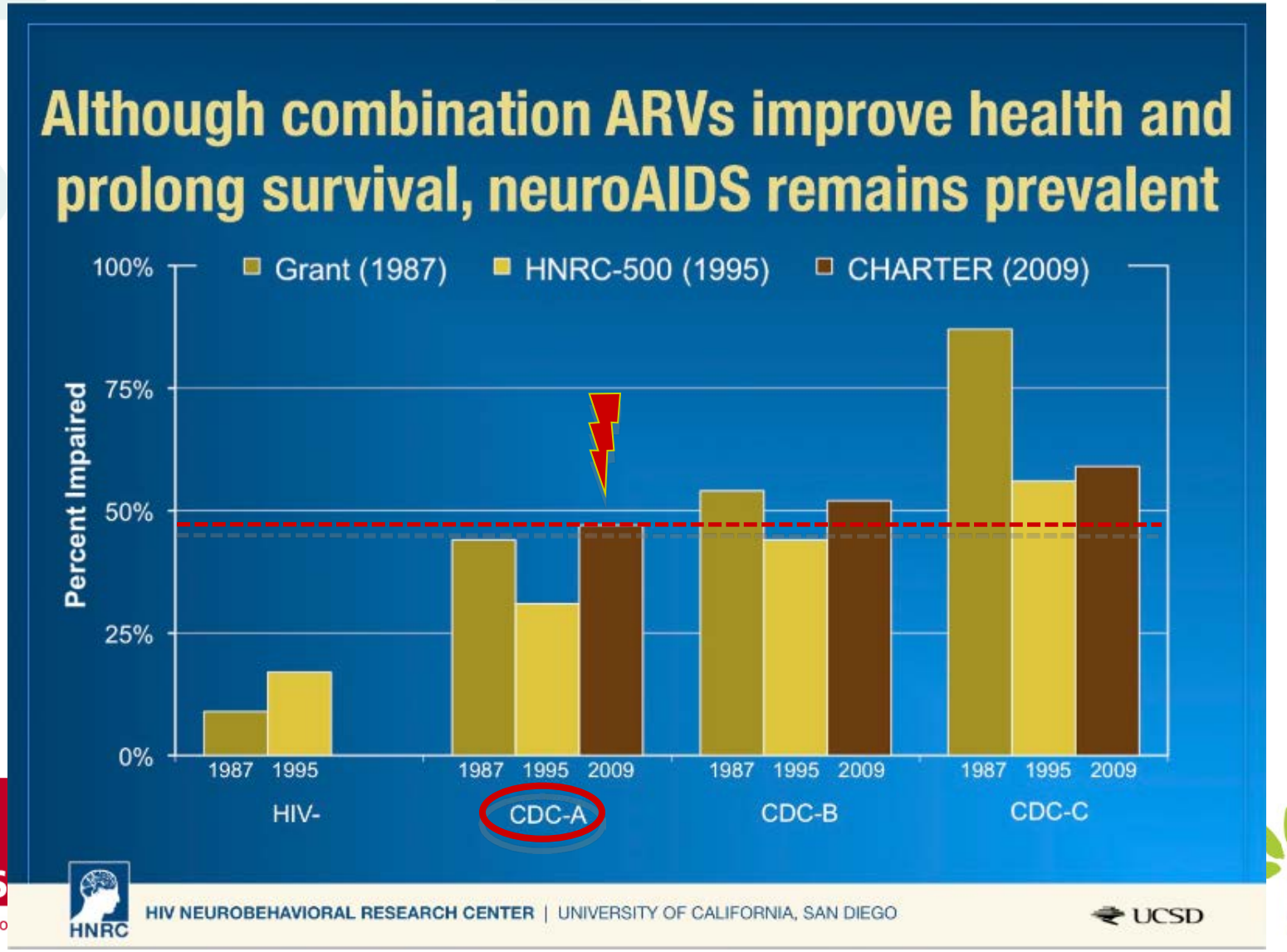
Prevalence of HIV-Associated NCI



Prevalence of HIV-Associated NCI



And in Spain??

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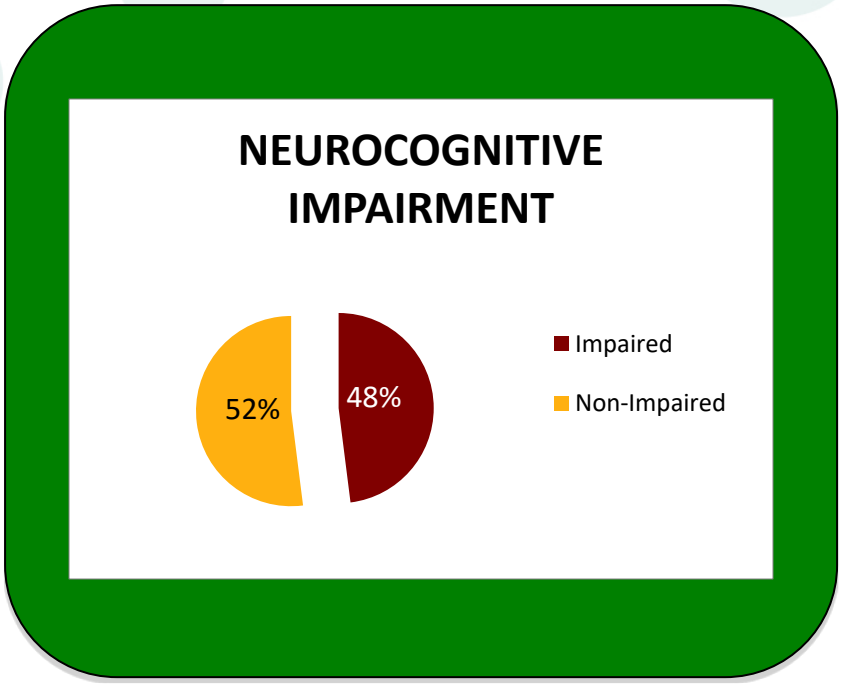
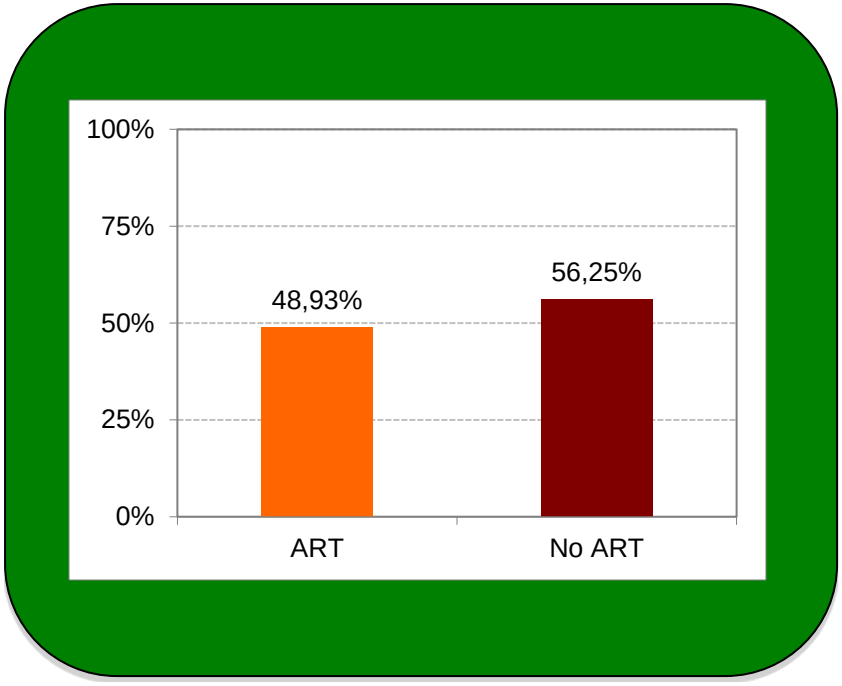


Muñoz-Moreno et al, 10th International Symposium on Neurovirology, Milan, 2010

N=142



Muñoz-Moreno et al, Mid-Year INS, Helsinki, 2009

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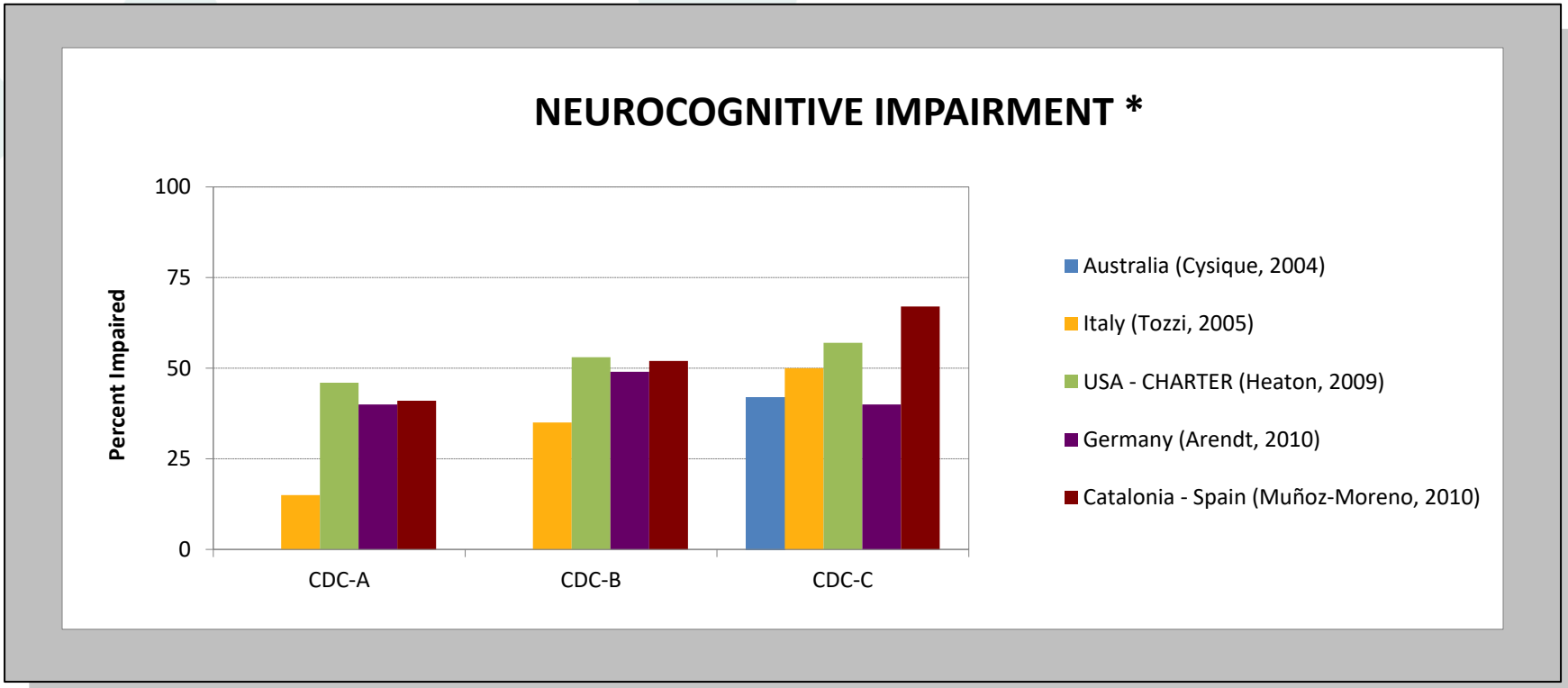
Confirming Data



Muñoz-Moreno et al, 10th International Symposium on Neurovirology, Milan, 2010

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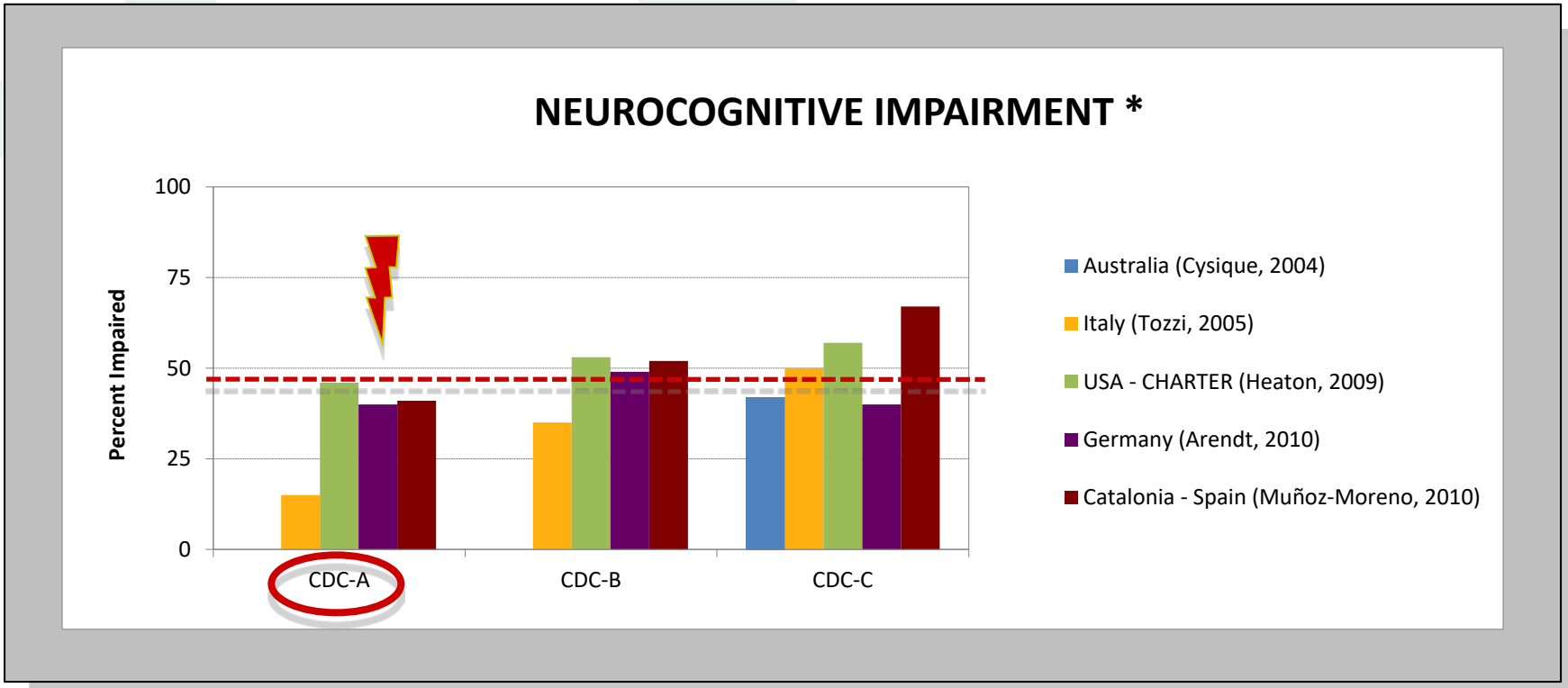
Confirming Data



Muñoz-Moreno et al, 10th International Symposium on Neurovirology, Milan, 2010

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Leading to Negative Consequences...

- Worse Quality of Life — *Tozzi, 2003*
- Interference on Daily Living Activities — *Heaton, 2004*
- Worse Adherence to Antiretroviral Treatment — *Woods, 2009*
- More Frequent Virological Failure — *Tozzi, 2003*
- Predictor of Higher Death Rates — *Sevigny, 2007*

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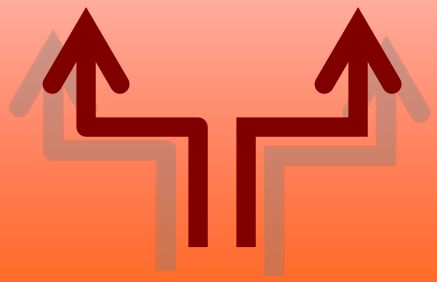
Interventions

NEUROACTIVE ARV DRUGS

NON-NEUROACTIVE ARV DRUGS



Letendre et al, Enhancing ART for HIV Cogntive Disorders, Ann Neurol, 2004

Giancola et al, Neuroactive ART Drugs Do Not Influence NC Performance, JAIDS, 2006

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Insufficient Although Growing Evidence...

	Cysique	Tozzi	Ellis	Marra
Study	*UCSD CIT*	*NIID*	*ALLRT*	*ACTG 736*
Sample Size	*37*	*185*	*2,636*	*26*
Prospective	*Yes*	*Yes*	*Yes*	*Yes*
Controlled	*No*	*No*	*No*	*No*
Number of NP Tests	*6*	*15*	*3*	*4*
CPE: CSF VL	***Lower VL***	*No CSF*	*No CSF*	***Lower VL***
CPE: NP Tests	***Better***	***Better***	***Better***	***Worse***
Used Norms for NP Change	***Yes***	*No*	*No*	*No*

Cysique et al, Neurology 2009, 73(5):342-8; Tozzi et al, J Acquir Immune Defic Syndr 2009;52:56–63; Ellis et al, Annual Meeting American Neurological Association 2009; Marra et al, AIDS 2009, 23(11):1359-66

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*: Courtesy of Dr. Letendre

Other ARV Approaches

Nadir CD4 Cell Count Predicts Neurocognitive Impairment in HIV-Infected Patients

Jose A. Muñoz-Moreno,[1,2] Carmina R. Fumaz,[1,2] Maria J. Ferrer,[1,2] Anna Prats,[1,2] Eugènia Negredo,[1,2] Maite Garolera,[3] Núria Pérez-Álvarez,[1,4] José Moltó,[1,2] Guadalupe Gómez,[4] and Bonaventura Clotet[1,2,5]

Muñoz-Moreno, et al, 2008

TABLE 2. NEUROCOGNITIVE IMPAIRMENT BY NADIR CD4 CELL COUNT CUTOFF

	No. of patients	*% of impaired patients* (n)	p *value*
Nadir CD4 cutoff 200 cells/ml			
Nadir ≤200	26	73.1 (19)	0.12
Nadir >200	38	52.6 (20)	
Nadir CD4 cutoff 250 cells/ml			
Nadir ≤250	33	66.7 (22)	0.31
Nadir >250	30	53.3 (16)	
Nadir CD4 cutoff 300 cells/ml			
Nadir ≤300	36	63.9 (23)	0.59
Nadir >300	23	56.5 (13)	
Nadir CD4 cutoff 350 cells/ml			
Nadir ≤350	35	57.1 (20)	0.76
Nadir >350	16	62.5 (10)	

Other ARV Approaches

Nadir CD4 Cell Count Predicts Neurocognitive Impairment in HIV-Infected Patients

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Poster # 429

Ronald J. Ellis | 220 Dickinson St., Suite B, MC 8231 | San Diego, CA 92103 | Phone: 619-543-5079 | Fax: 619-543-4744 | roellis@ucsd.edu

Higher CD4 Nadir is Associated with Reduced Rates of HIV-Associated Neurocognitive Disorders in the CHARTER Study: Potential Implications for Early Treatment Initiation

Ronald J. Ellis, M.D., Ph.D.[1], Robert K. Heaton, Ph.D.[1], Scott Letendre, M.D.[1], Jayraan Badiee, M.P.H.[1], Jose A. Muñoz-Moreno, M.S.[1], Florin Vaida, Ph.D.[1], David B. Clifford, M.D.[2], Benjamin B. Gelman, M.D., Ph.D.[3], David M. Simpson, M.D.[4], Igor Grant, M.D.[1], for the CHARTER Group
[1]University of California, San Diego; [2]Washington University, St. Louis; [3]University of Texas Medical Branch, Galveston; [4]Mount Sinai School of Medicine

CHARTER
CNS HIV ANTI-RETROVIRAL THERAPY EFFECTS RESEARCH

Muñoz-Moreno, et al, 2008

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Ellis, CROI, 2010

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Other ARV Approaches

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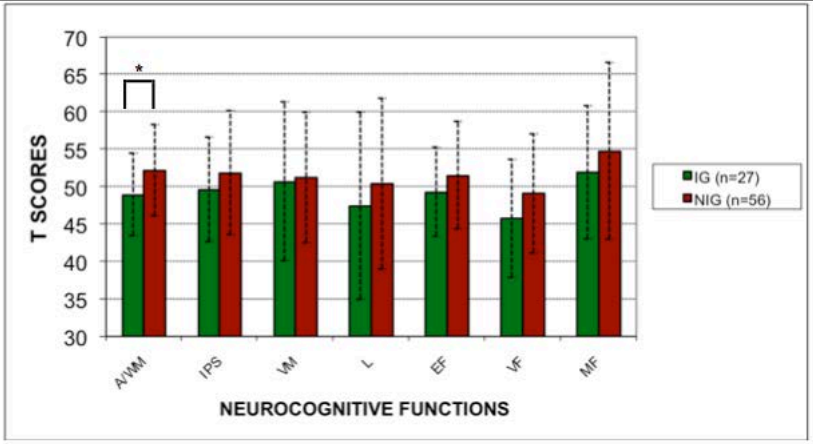
DOI: 10.3109/13550281003767710

informa
healthcare

Interruptions of antiretroviral therapy in human immunodeficiency virus infection: are they detrimental to neurocognitive functioning?

Jose A. Muñoz-Moreno,[1,2] Carmina R. Fumaz,[1,2] Anna Prats,[1,2] Maria J. Ferrer,[1,2] Eugènia Negredo,[1,2] Núria Pérez-Álvarez,[1,3] José Moltó,[1,2] Guadalupe Gómez,[3] Maite Garolera,[4] and Bonaventura Clotet[1,2,5]

[1]Lluita contra la SIDA Foundation, Germans Trias i Pujol University Hospital, Badalona, Barcelona, Catalonia, Spain; [2]Autònoma de Barcelona University, Barcelona, Catalonia, Spain; [3]Politècnica de Catalunya University, Barcelona, Catalonia, Spain; [4]Consorci Sanitari de Terrassa Hospital, Terrassa, Barcelona, Catalonia, Spain; and [5]IrsiCaixa Foundation, Badalona, Barcelona, Catalonia, Spain



* : p<0.05.

Muñoz-Moreno, et al, 2010

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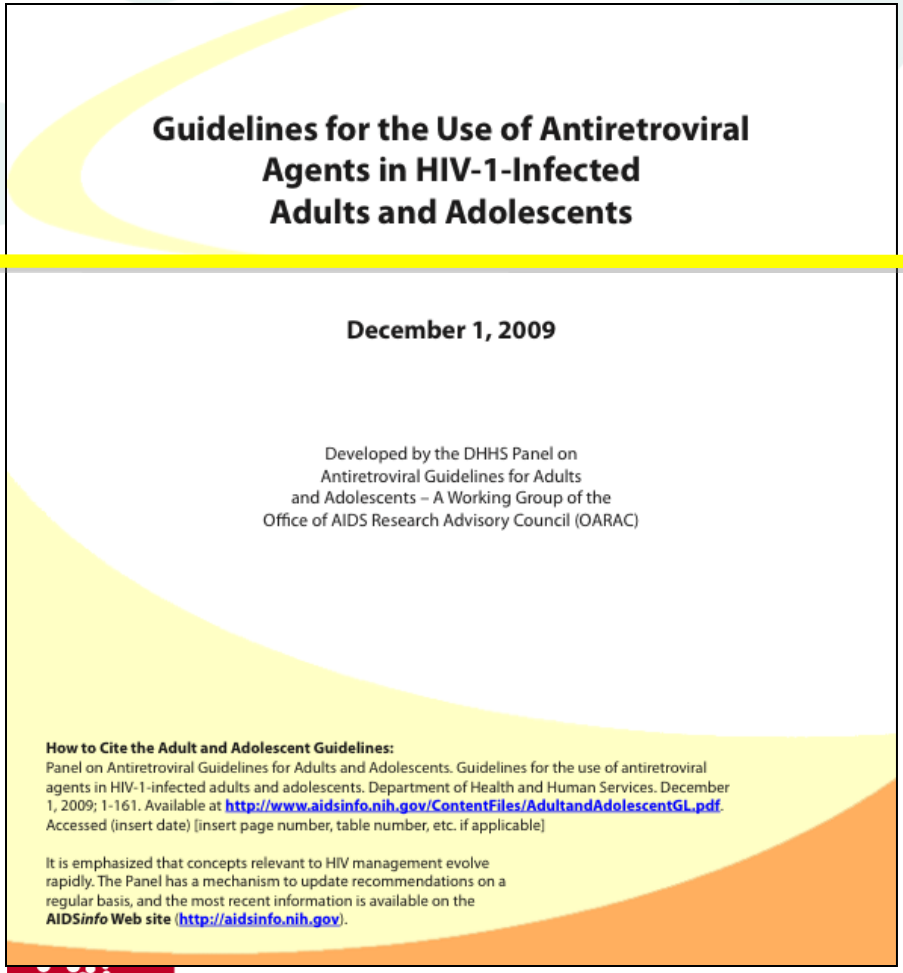
ARV Treatment Guidelines!



Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

December 1, 2009

Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

How to Cite the Adult and Adolescent Guidelines:
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. December 1, 2009; 1-161. Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed (insert date) [insert page number, table number, etc. if applicable]

It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the **AIDS*info* Web site** (http://aidsinfo.nih.gov).

Neurocognitive decline

Early in the HIV epidemic, HIV was identified in brain tissue *[57]* and assumed to be the cause of AIDS dementia complex *[58]*. The improvement of AIDS dementia complex symptoms with the use of antiretroviral therapy supported this assumption *[59-60]*. The CASCADE observational cohort reported a dramatic decline in the incidence of HIV-associated dementia from 6.49 per 1,000 person-years (before 1997) to 0.66 per 1,000 person-years (2003–2006), after the widespread use of potent antiretroviral therapy *[61]*. In this cohort, having a current CD4 count >350 cells/mm^3 was associated with the lowest risk of developing HIV-associated dementia. HIV infection has also been associated with a number of less severe neurologic complications, including changes in neuropsychological ability, speed of processing, and everyday functioning *[62]*. Such syndromes also were predicted by a lower pretherapy CD4 nadir and/or by CD4 count while on therapy *[63-64]*. Additional clinical data are needed to determine the relative roles of ongoing HIV replication and potential neurotoxicity of antiretroviral agents in the development of neurocognitive dysfunction. Whether early initiation of therapy will prevent HIV-associated neurocognitive dysfunction remains unclear. However, the neurological complications that may accompany uncontrolled HIV replication and CD4 depletion suggest a potential benefit of earlier initiation of antiretroviral therapy **(CIII)**.

64. Munoz-Moreno JA, Fumaz CR, Ferrer MJ, et al. Nadir CD4 cell count predicts neurocognitive impairment in HIV-infected patients. *AIDS Res Hum Retroviruses.* 2008;24(10):1301-1307.
65. The Collaboration of Observational HIV Epidemiological Research Europe (COHERE) study group. Response to combination antiretroviral therapy: variation by age. *AIDS.* 2008;22(12):1463-1473.
66. Nogueras M, Navarro G, Anton E, et al. Epidemiological and clinical features, response to HAART, and survival in HIV-infected patients diagnosed at the age of 50 or more. *BMC Infect Dis.* 2006;6:159.
67. Bosch RJ, Bennett K, Collier AC, et al. Pretreatment factors associated with 3-year (144-week) virologic and immunologic responses to potent antiretroviral therapy. *J Acquir Immune Defic Syndr.* 2007;44(3):268-277.

Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents (DHHS). December 2009:
http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf

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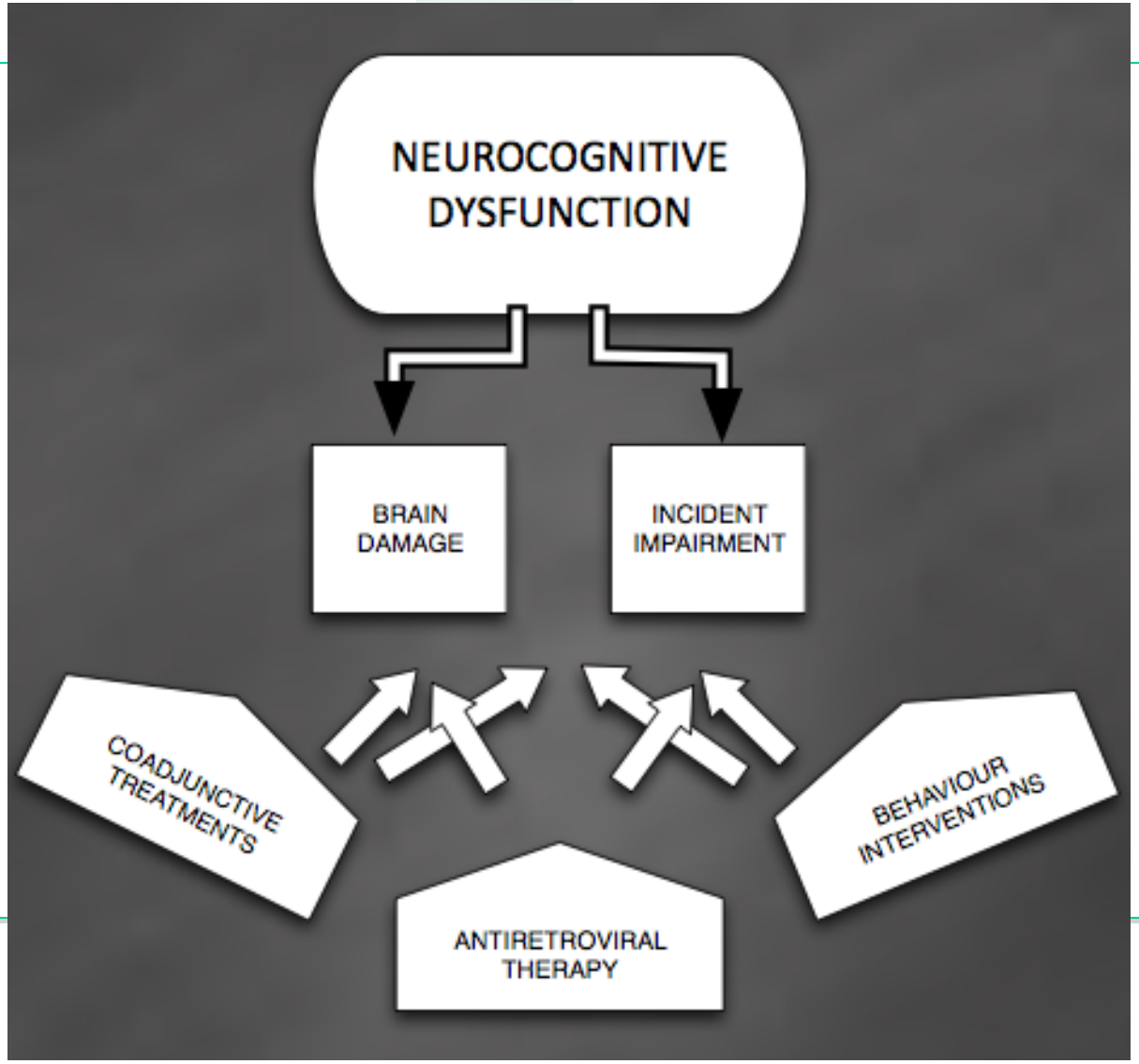
Therapeutical Approach



Which Tools?

Comprehensive Batteries of Neuropsychological Tests

Table 5. Ability domains recommended for HIV-related neuropsychological assessment and examples of most common neuropsychological tests

Ability Domain / Tests
Premorbid Intelligence
Wechsler Adult Intelligence Scale – Third Edition (WAIS-III) Vocabulary Test [16]
National Adult Reading Test (NART) Full IQ Scale (FIQS) [17]
Attention/Working Memory
California Computerized Assessment Package (CalCAP) [18]
Paced Auditory Serial Addition Task (PASAT) [19]
WAIS-III Digits Test [16]
WAIS-III Letter-Numbers Test [16]
Continuous Performance Tests - Second Edition (CPT-II) [20]
Information Processing Speed
Trail Making Tests (TMT) - Part A [21]
Symbol Digit Modalities Test (SDMT) [22]
CalCAP [18]
Motor Function
Grooved Pegboard Test (GPT) [23]
Electronic Tapping Test (ETT) [24]
Learning/Memory
California Verbal Learning Test - Second Edition (CVLT-II) [25]
Rey Auditory Verbal Learning Test [26]
Wechsler Memory Scale - Revised (WMS-R) [27]
Visual Memory
Rey Complex Figure Test [28]
Modified Visual Reproduction Test [29]
WMS-R [27]
Visuoconstruction
Rey Complex Figure Test [28]
WAIS-III Block Design Test [16]
Executive Functions
Stroop Test [30]
TMT - Part B [21]
Wisconsin Card Sorting Test (WCST) [31]
Category Test [21]
Verbal Fluency
Controllled Oral Word Association (COWAT) [32]
Animals Test [33]
Boston Naming Test [34]
Emotional Status (Depression, Anxiety)
Beck Depression Inventory - Second Edition (BDI-II) [35]
State-Trait Anxiety Inventory (STAI) [36]
Hamilton Depression Scale (HDS) [37]
Hospital Anxiety Depression Scale (HADS) [38]
Depression Anxiety Stress Scale (DASS) [39]

NEUROCOGNITIVE AND MOTOR DISORDERS IN HIV INFECTION. ASSESSMENT AND INTERVENTIONS

Jose A. Muñoz-Moreno•
Lluita contra la SIDA Foundation - HIV Unit, Germans Trias i Pujol University Hospital, Ctra. de Canyet, S/N 08916, Badalona, Barcelona, Catalonia, Spain.

Muñoz-Moreno JA, in Research Focus on Cognitive Disorders, NY, 2007

Neurocognitive Areas and Tests

PROCESSING INFORMATION SPEED: → - TMT-A: Trail Making Test - Part A

MOTOR FUNCTION: → - GPT: Grooved Pegboard Test

VERBAL MEMORY: → - CVLT-II: California Verbal Learning Test - II

LEARNING: → - TMT-B: Trail Making Test - Part B

EXECUTIVE FUNCTIONS: → - WCST: Wisconsin Card Sorting Test

EXECUTIVE FUNCTIONS: → - Stroop's Test

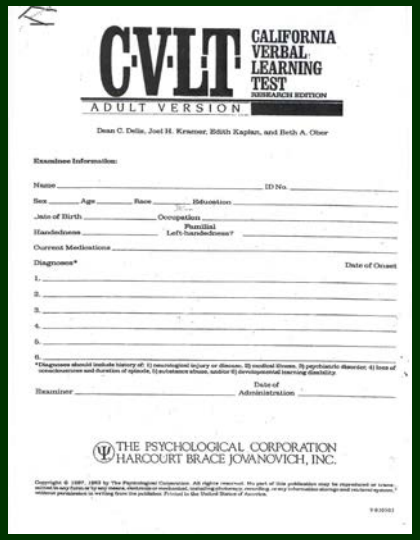
Motor Function

Grooved Pegboard Test

Matthews, 1964

Verbal Memory and Learning

California Verbal Learning Test - II



CALIFORNIA VERBAL LEARNING TEST
ADULT VERSION
RESEARCH EDITION

Dean C. Delis, Joel H. Kramer, Edith Kaplan, and Beth A. Ober

Examinee Information:

Name _____ ID No. _____

Sex _____ Age _____ Race _____ Education _____

Date of Birth _____ Occupation _____

Handedness _____ Familial Left-handedness? _____

Current Medications _____

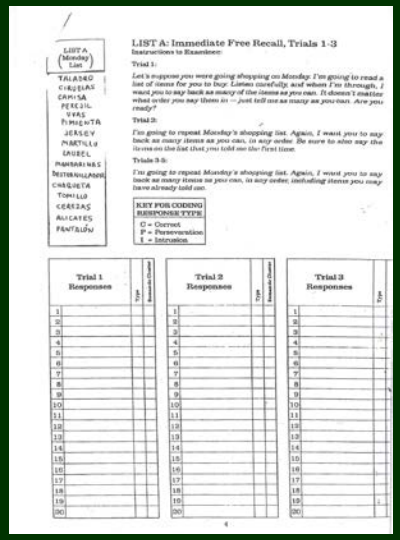
Diagnoses* _____ Date of Onset

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____

*Diagnoses should include history of: 1) neurological injury or disease, 2) medical illness, 3) psychiatric disorder, 4) loss of consciousness and duration of episode, 5) substance abuse, and/or 6) developmental learning disability.

Examiner _____ Date of Administration _____

THE PSYCHOLOGICAL CORPORATION
HARCOURT BRACE JOVANOVICH, INC.



LIST A (Monday) List

TALADRO
CAMISA
PERCHA
VIAS
PIMIENTA
JERSEY
MARTILLO
LAUREL
MANDARINA
DESTORNILLADOR
CHAQUETA
TOMILLO
CEREZAS
ALICATES
PANTALÓN

LIST A: Immediate Free Recall, Trials 1-3

Instructions to Examiner:

Trial 1:

Let's suppose you were going shopping on Monday. I'm going to read a list of items for you to buy. Listen carefully, and when I'm through, I want you to say back as many of the items as you can. It doesn't matter what order you say them in — just tell me as many as you can. Are you ready?

Trial 2:

I'm going to repeat Monday's shopping list. Again, I want you to say back as many items as you can, in any order. Be sure to also say the items on the list that you told me the first time.

Trials 3-5:

I'm going to repeat Monday's shopping list. Again, I want you to say back as many items as you can, in any order, including items you may have already told me.

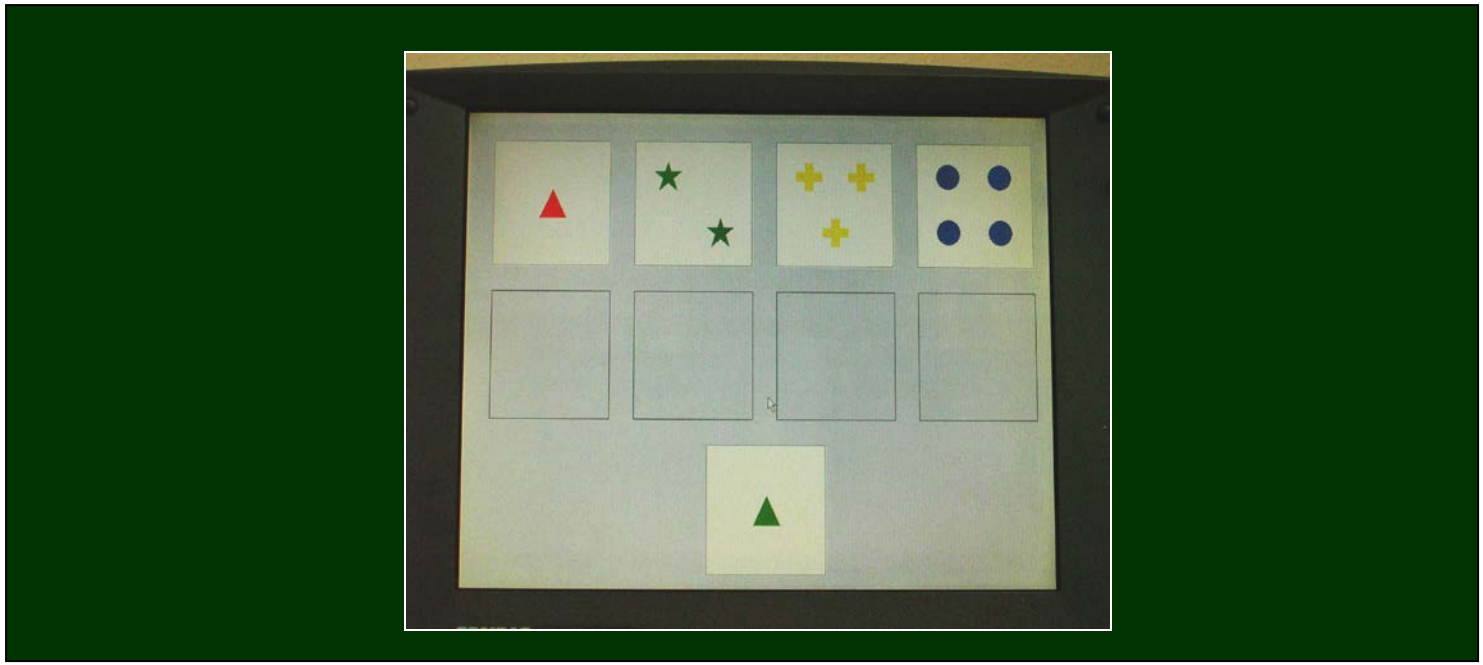
KEY FOR CODING RESPONSE TYPE
C = Correct
P = Perseveration
I = Intrusion

	Trial 1 Responses	Type	Intrusion (Order)	Trial 2 Responses	Type	Intrusion (Order)	Trial 3 Responses	Type
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
13								
14								
15								
16								
17								
18								
19								
20								

Delis, 2000

Executive Functioning

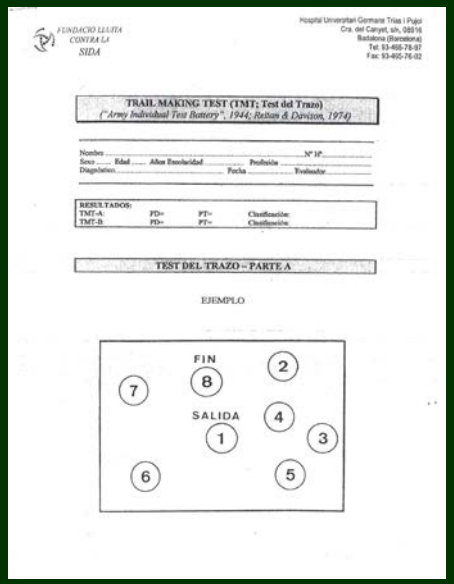
Wisconsin Card Sorting Test (WCST)



Kongs, 1993

Information Processing Speed

Trail Making Test - Part A (TMT-A)



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Crta. del Canyet, s/n, 08916
Badalona (Barcelona)
Tel. 93-465-78-97
Fax: 93-465-76-02

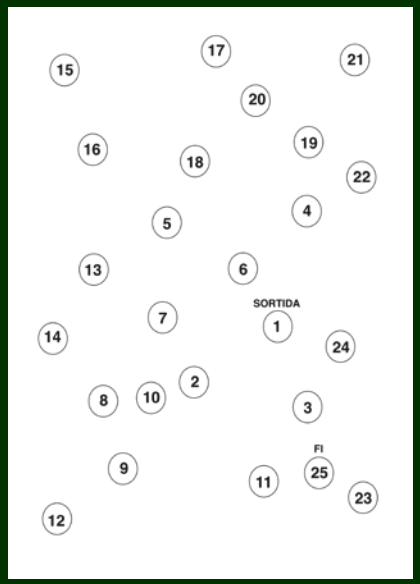
TRAIL MAKING TEST (TMT; Test del Trazo)
("Army Individual Test Battery", 1944; Reitan & Davison, 1974)

Nombre ..... Nº H° .....
Sexo ..... Edad ..... Años Escolaridad ..... Profesión .....
Diagnóstico ..... Fecha ..... Evaluador .....

RESULTADOS:
TMT-A: PD= PT= Clasificación:
TMT-B: PD= PT= Clasificación:

TEST DEL TRAZO – PARTE A

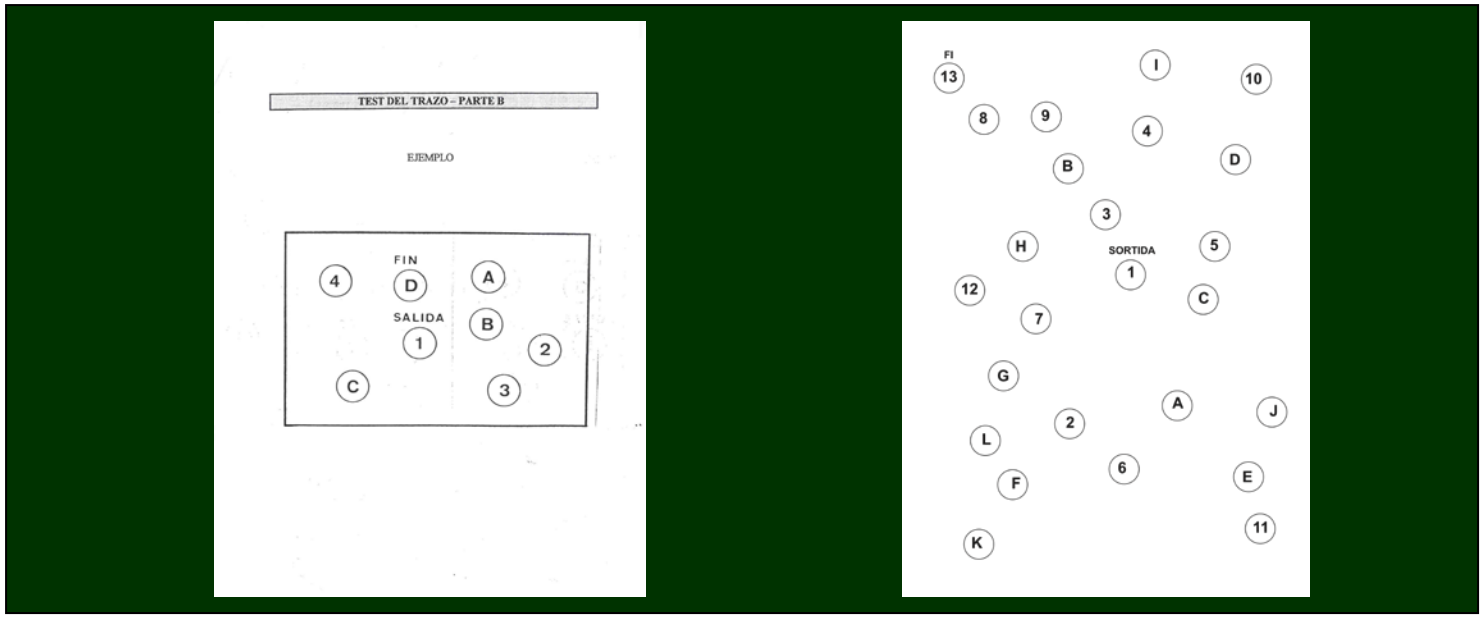
EJEMPLO



Reitan, 1974

Executive Functioning

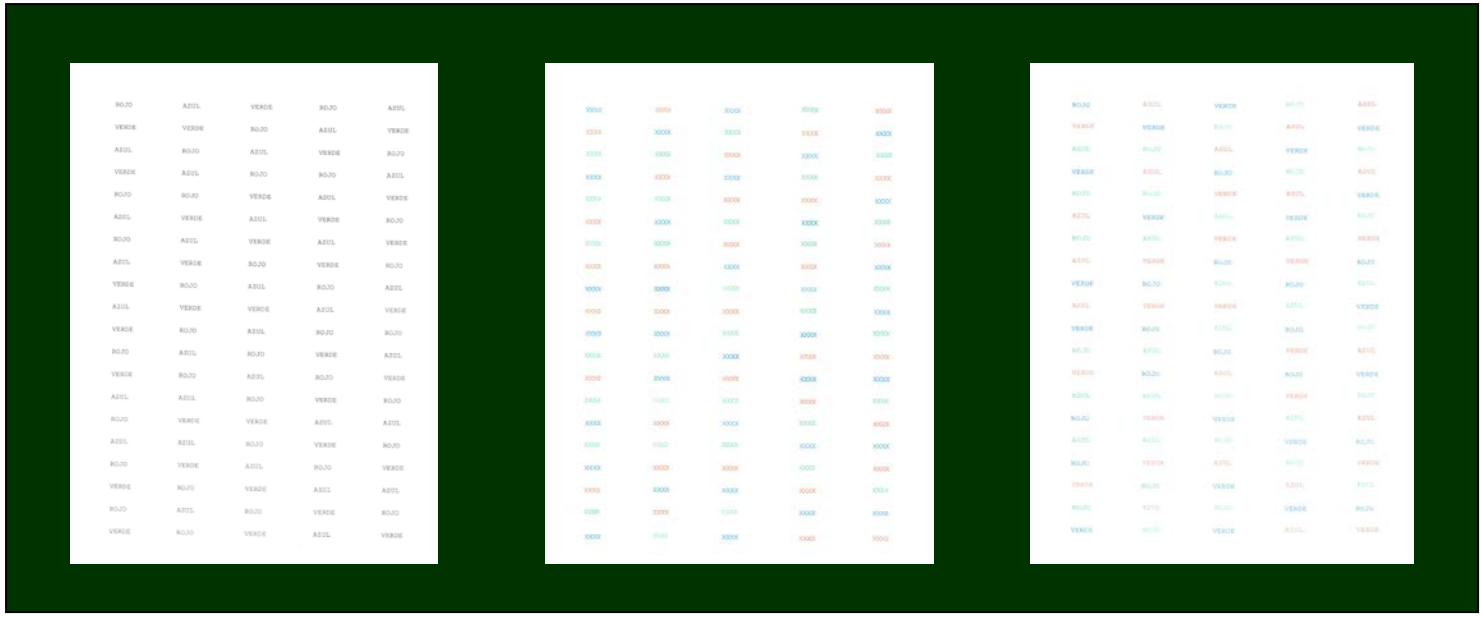
Trail Making Test - Part B (TMT-B)



Reitan, 1974

Executive Functioning

Stroop's Test



Golden, 1978

Requirements for Comprehensive NC Testing

- Recommendations by Frascati Group,
in
Antinori et al, Neurology, 2007:

1) Assessment of 7 recommended areas

2) Evaluation and control of demographic, clinical and emotional variables

3) Exclusion of conditions associated with NCI, currently or in past (confouding comorbidities!)

Confounding Factors

Neurology, 2007:

Table 1. Criteria for clinical diagnosis of central nervous system disorders in HIV-infected adults and adolescents

Table 2. HAND Criteria

Table 3. Examples of Tests

Table 4. Guidelines for classifying confounds to HIV-associated neurocognitive disorders

Confounding Factors

"Evidence of another etiology, including active CNS opportunistic infection or malignancy, psychiatric disorders (e.g., depressive disorder), active alcohol or substance use, or acute or chronic substance withdrawal, must be sought from history, physical and psychiatric examination, and appropriate laboratory and radiologic investigation (e.g., lumbar puncture, neuroimaging). If another potential etiology (e.g., major depression) is present, it is not the cause of the above cognitive, motor, or behavioral symptoms and signs."

Mainly:

- Drug abuse
- CNS opportunistic infections
- Psychatric or emotional disorders

Depression and Anxiety Symptoms

- Hospital Anxiety and Depression Scale (HADS):

Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983; 67: 361-370.

- Beck Depression Inventory (BDI):

Beck AT, Rush AJ, Shaw BF, and Emery G: *Cognitive Therapy of Depression*. Guilford Press, New York, 1979.

- State-Trait Anxiety Inventory (STAI):

Spielberger CD, Gorsuch RL, and Lushene RE: *Manual for the State-Trait Anxiety Inventory*. Consulting Psychologists Press, Palo Alto, CA, 1970.

Depression Symptoms

Hospital Anxiety and Depression Scale (HADS)

1. Me siento tenso o "nervioso"
- O Todos los días
- O Muchas veces
- O A veces
- O Nunca

2. Todavía disfruto con lo que antes me gustaba
- O Como siempre
- O No lo bastante
- O Sólo un poco
- O Nada

3. Tengo una sensación de miedo, como si algo horrible me fuera a suceder
- O Definitivamente, y es muy fuerte
- O Sí, pero no es muy fuerte
- O Un poco, pero no me preocupa
- O Nada

4. Puedo reírme y ver el lado divertido de las cosas
- O Al igual que siempre lo hice
- O No tanto ahora
- O Casi nunca
- O Nunca

5. Tengo mi mente llena de preocupaciones
- O La mayoría de las veces
- O Con bastante frecuencia
- O A veces, aunque no muy a menudo
- O Sólo en ocasiones

- 14 items
- 2 scales
- 1 total scale

Golden, 1978

Depression Symptoms

Beck Depression Inventory (BDI)

1	☐	a	No me siento triste
	☐	b	Me siento triste
	☐	c	Siempre me siento triste, no puedo evitarlo
	☐	d	Me siento tan triste o infeliz que no puedo soportarlo
2	☐	a	No me siento especialmente desanimado ante el futuro
	☐	b	Me siento desanimado ante el futuro
	☐	c	No hay nada que me haga ilusión
	☐	d	Veo el futuro sin esperanza y creo que las cosas no pueden mejorar
3	☐	a	No me siento fracasado
	☐	b	Me siento más fracasado que la mayoría de la gente
	☐	c	Cuando recuerdo mi pasado no veo más que fracasos
	☐	d	Creo que soy un fracaso total como persona
4	☐	a	Disfruto de las cosas igual que siempre
	☐	b	No disfruto de las cosas como antes
	☐	c	Nada me produce verdadera satisfacción
	☐	d	Estoy insatisfecho o aburrido de todo
5	☐	a	No me siento especialmente culpable
	☐	b	Me siento culpable con frecuencia
	☐	c	Me siento culpable la mayor parte del tiempo
	☐	d	Me siento culpable todo el tiempo

- 21 items
- 1 scale
- 2 sub-scales

Golden, 1978

Anxiety Symptoms

State-Trait Anxiety Inventory (STAI)

		Casi nunca	A veces	A menudo	Casi siempre
1.	Me siento bien	1	2	3	4
2.	Me siento nervioso/a e inquieto/a	1	2	3	4
3.	Me siento satisfecho/a conmigo mismo/a	1	2	3	4
4.	Me gustaría poder ser tan feliz como otros parecen serlo	1	2	3	4
5.	Me siento un fracaso	1	2	3	4
6.	Me siento descansado/a	1	2	3	4
7.	Soy una persona tranquila, serena y sosegada	1	2	3	4
8.	Veo que las dificultades se amontonan y no puedo superarlas	1	2	3	4
9.	Me preocupo demasiado por cosas sin importancia	1	2	3	4
10.	Soy feliz	1	2	3	4
11.	Tengo pensamientos que me perturban	1	2	3	4
12.	Me falta confianza en mí mismo/a	1	2	3	4

- 20 items

- 1 scale

Golden, 1978

Why Neurocognitive Testing??

PROS:

- Strongly recommended
- Large experience in clinical neuropsychology
- Experience in HIV infection
- Different areas potentially assessed
- Variable tools

CONS:

- Availability / feasibility
- Duration of evaluations

Neuropsychological Testing

PROS:

- Strongly recommended
- Large experience in clinical neuropsychology
- Experience in HIV infection
- Different areas potentially assessed
- Variable tools

CONS:

- Availability / feasibility
- Duration of evaluations

Recommendations

- National Institute of Mental Health, 1990
- American Tasks Force, 1991
- UNAIDS, 1997
- Antinori, 2007
- Significant number of reviews and studies recommending

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

Janssen RS, Cornblath DR, Epstein LG, Foa RP, McArthur JC, Price RW, *et al*. **Nomenclature and research case definitions for neurological manifestations of human immunodeficiency virus type-1 (HIV-1) infection. Report of a Working Group of the American Academy of Neurology AIDS Task Force.** *Neurology* 1991; **41**:778–785.

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

Updated research nosology for HIV-associated neurocognitive disorders

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Neuropsychological Testing

PROS:

- Strongly recommended
- Large experience in clinical neuropsychology
- Experience in HIV infection
- Different areas potentially assessed
- Variable tools

CONS:

- Availability / feasibility
- Duration of evaluations

Clinical Neuropsychology

In multiple diseases regardless of HIV infection!

Pattern of neurocognitive alteration in...:

Multiple Sclerosis
Schizophrenia
Aging
Alzheimer's Disease
Parkinson's Disease
ETC, ETC...

Neuropsychological Testing

PROS:

- Strongly recommended
- Large experience in clinical neuropsychology
- Experience in HIV infection
- Different areas potentially assessed
- Variable tools

CONS:

- Availability / feasibility
- Duration of evaluations

HIV Infection

PubMed:

Early publications: 1985-1987 (Grant et al, 1987)

"Evidence for early central nervous system involvement in the acquired immunodeficiency syndrome (AIDS) and other human immunodeficiency virus (HIV) infections. Studies with neuropsychologic testing and magnetic resonance imaging".

Currently: Neurocognitive + HIV: 357 studies / 75 reviews

Neuropsychological + HIV: 1014 studies / 129 reviews

Cognitive + HIV: 1934 studies / 357 reviews

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Neuropsychological Testing

PROS:

- Strongly recommended
- Large experience in clinical neuropsychology
- Experience in HIV infection
- Different areas potentially assessed
- Variable tools

CONS:

- Availability / feasibility
- Duration of evaluations

HIV-Associated Neurocognitive Profile

- Fronto-subcortical pattern, with altered areas well defined:

Attention / Working Memory
Information Processing Speed
Learning
Verbal Memory

Executive Functioning
Verbal Fluency
Motor Function

- Maybe currently is this changing??

Cortical hypothesis:

Brew, 2004
Valcour, 2006

Neuropsychological Testing

PROS:

- Strongly recommended
- Large experience in clinical neuropsychology
- Experience in HIV infection
- Different areas potentially assessed
- Variable tools

CONS:

- Availability / feasibility
- Duration of evaluations

HAND Diagnosis: HIV-Associated Neurocognitive Disorders

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
K. Goodkin, MD, PhD
M. Gisslen, MD, PhD
I. Grant, MD
R.K. Heaton, PhD
J. Joseph, PhD
K. Marder, MD, MPH
C.M. Marra, MD
J.C. McArthur, MBBS, MPH
M. Nunn, PhD
R.W. Price, MD
L. Pulliam, PhD
K.R. Robertson, PhD
N. Sacktor, MD
V. Valcour, MD
V.E. Wojna, MD

Antinori et al, Neurology, 2007

Diagnosis Establishment

	No Prior Cause	*No Delirium*	*Acquired Impairment in ≥ 2 Functions*	*Daily Functioning Inerference / NC Complaint*
1. Asymptomatic NC Impairment (ANI)	☑	☑	☑	No
2. Mild NC Disorder (MND)	☑	☑	☑	Mild
3. HIV-Associated Dementia (HAD)	☑	☑	Marked	Marked

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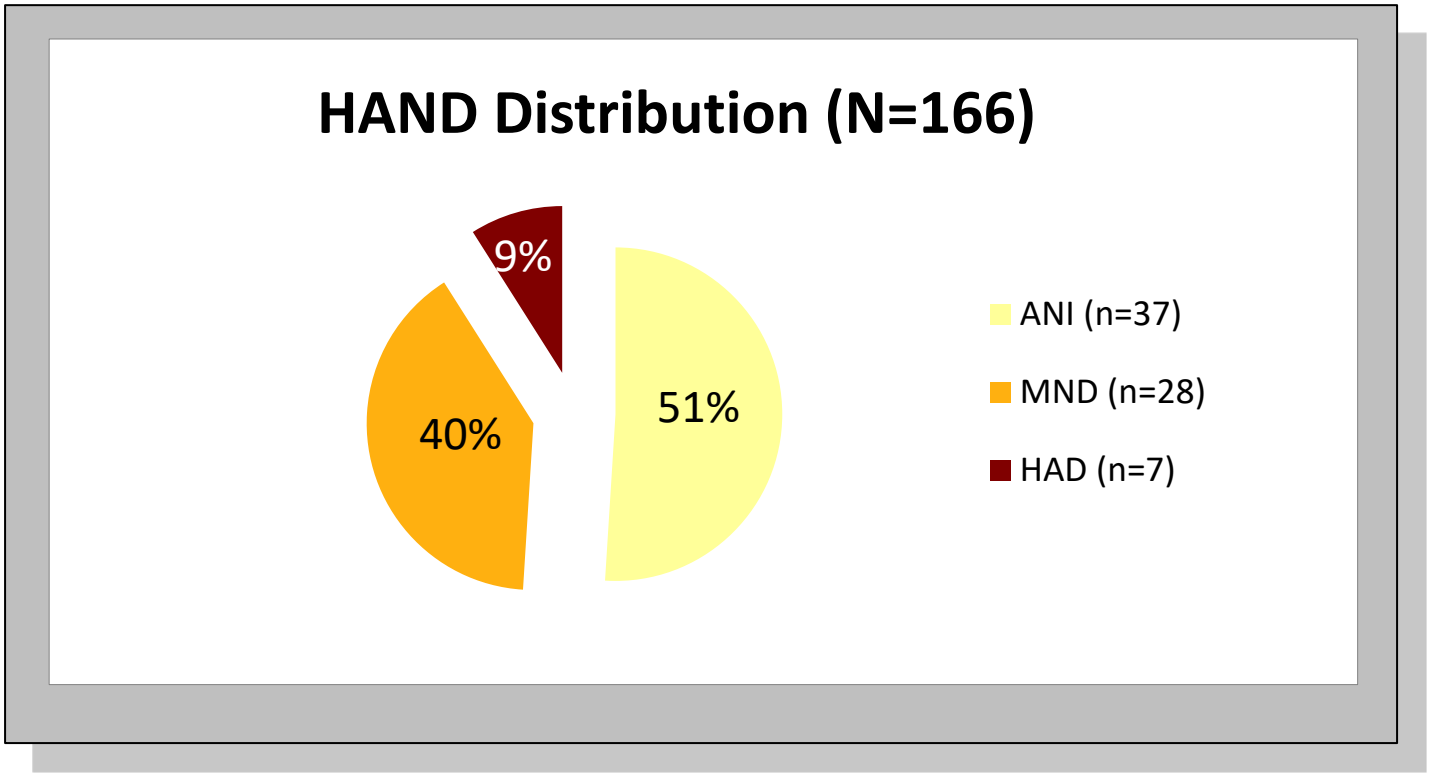
HAND Distribution



Muñoz-Moreno et al, 10th International Symposium on Neurovirology, Milan, 2010

Neuropsychological Testing

PROS:

- Strongly recommended
- Large experience in clinical neuropsychology
- Experience in HIV infection
- Different areas potentially assessed
- Variable tools

CONS:

- Availability / feasibility
- Duration of evaluations

Availability and Feasibility

MAIN LIMITATIONS:

- Need of a trained neuropsychologist
- Expertise and skills are relevant aspects in the application
- Multiple and variable instructions / correction processes
- Manipulative tools
- Duration of assessments (*next section*)

Neuropsychological Testing

PROS:

- Strongly recommended
- Large experience in clinical neuropsychology
- Experience in HIV infection
- Different areas potentially assessed
- Variable tools

CONS:

- Availability / feasibility
- Duration of evaluations

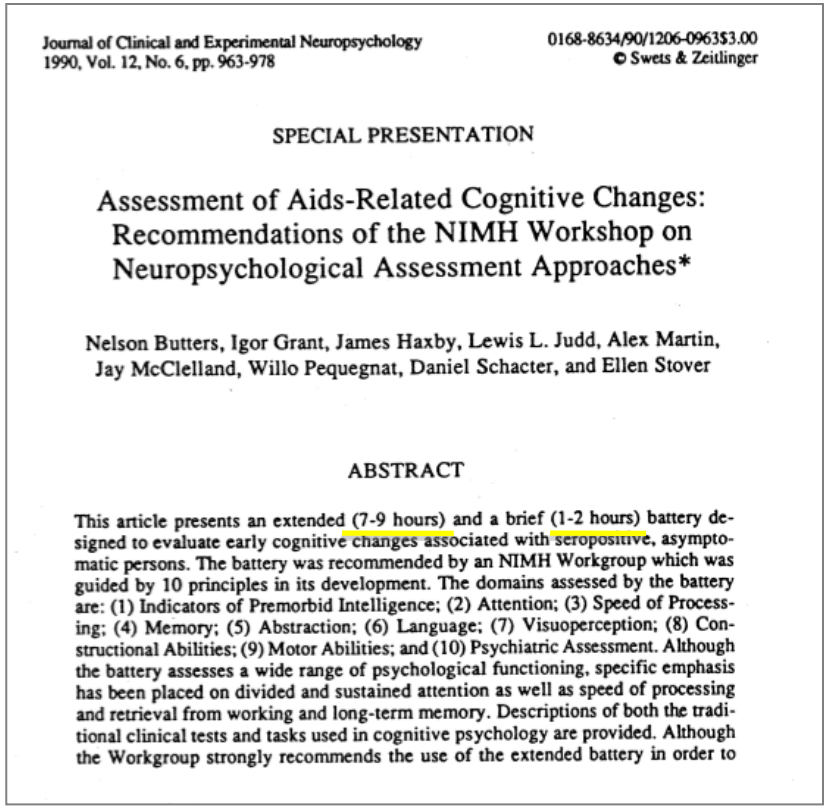
Multiple Tools

NIMH, 1990: 2 recommendations

Extended: 7-9 hours of duration
Brief: 1-2 hours of duration

Nowadays...

Extended: 2-3 hours of duration
☞ Relevant need of screening tools!



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

0168-8634/90/1206-0963$3.00

SPECIAL PRESENTATION

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

Nelson Butters, Igor Grant, James Haxby, Lewis L. Judd, Alex Martin, Jay McClelland, Willo Pequegnat, Daniel Schacter, and Ellen Stover

ABSTRACT

This article presents an extended (7-9 hours) and a brief (1-2 hours) battery designed to evaluate early cognitive changes associated with seropositive, asymptomatic persons. The battery was recommended by an NIMH Workgroup which was guided by 10 principles in its development. The domains assessed by the battery are: (1) Indicators of Premorbid Intelligence; (2) Attention; (3) Speed of Processing; (4) Memory; (5) Abstraction; (6) Language; (7) Visuoperception; (8) Constructional Abilities; (9) Motor Abilities; and (10) Psychiatric Assessment. Although the battery assesses a wide range of psychological functioning, specific emphasis has been placed on divided and sustained attention as well as speed of processing and retrieval from working and long-term memory. Descriptions of both the traditional clinical tests and tasks used in cognitive psychology are provided. Although the Workgroup strongly recommends the use of the extended battery in order to

What Do We Know About Screening Tools?

Test	*Reference*	Duration	Pros	Cons
HIV Dementia Scale (HDS)	*Power et al, JAIDS, 1995**	10-15 min	- Instructions - Quantitative score	- Validated for dementia - Low sensitivity
HNRC Screening	*Carey et al, Clin Neuropsychol, 2004 **	10-15 min	- Duration	- Feasibility (pegboard) - Scarce information
CogState	*Cysique et al,* J Int Neuropsychol Soc , *2006 **	10-15 min	- Instructions - Statistical validation	- Feasibility? - Economical cost?
Brief Neurocognitive Screen	*Robertson et al, AIDS, 2007 **	10 min	- Duration - Feasibility (in paper)	- Scarce information
NEU Questionnaire	*Muñoz-Moreno et al (in development) **	25-30 min	- Instructions - Feasibility (in paper) - Statistical validation	- *Duration?* - *Statistical sensitivity?*

What Do We Know About Screening Tools?

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CogState	*Cysique et al,* J Int Neuropsychol Soc , *2006 **	10-15 min	- Instructions - Statistical validation	- Feasibility? - Economical cost?
Brief Neurocognitive Screen	*Robertson et al, AIDS, 2007 **	10 min	- Duration - Feasibility (in paper)	- Scarce information
NEU Questionnaire	*Muñoz-Moreno et al (in development) **	25-30 min	- Instructions - Feasibility (in paper) - Statistical validation	*- Duration?* *- Statistical sensitivity?*

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Brief Quantitative Instrument in Development

- NEU Instrument (Muñoz-Moreno, et al):

- Brief (25-30 minutes)
- Assessing 7 areas
- Not only a screening tool: quantitative outcomes (adapted to HAND diagnosis)
- Printable
- Easy instructions and correction

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PRESENTACIÓN:

A continuación le presentamos el **Test NEU**, un instrumento que evalúa el funcionamiento neurocognitivo de personas infectadas con el VIH. Está compuesto por diferentes pruebas, las cuales evalúan 7 funciones neurocognitivas.
Por favor, siga atentamente las instrucciones que se detallan a continuación hasta llegar al final del documento.

DATOS DEL PACIENTE:

INICIALES:	FECHA:
ID:	

DATOS DEL EVALUADOR:

NOMBRE:	CARGO:
CENTRO:	

1. PRUEBA DE MEMORIA Y APRENDIZAJE:

1º. Ensayo 1: *"A continuación le leeré unas palabras. Cuando acabe me gustaría que me repitiera tantas palabras como le sea posible, teniendo en cuenta que el orden no importa".*

2º. Antes de los ensayos 2, 3, 4 y 5: *"Ahora le volveré a repetir las mismas palabras. Por favor, cuando acabe dígame tantas como le sea posible, teniendo en cuenta que ha de volver a decirme todas las que pueda, a pesar de que las haya dicho antes, y sin importar el orden".*

LISTA A	ENSAYO1	ENSAYO2	ENSAYO3	ENSAYO4	ENSAYO5	
CAMIÓN						
ESPINACA						
JIRAFA						
ESTANTERÍA						
CEBOLLA						
MOTO						
CAMA						
CEBRA						
TREN						
SILLA						
APIO						
VACA						
ESCRITORIO						
BANCO						
ARDILLA						
COL						TOTAL
CORRECTAS						
Perseveraciones						
Intrusiones						

3º. *"Ahora le leeré una lista de palabras totalmente diferente. Cuando acabe debería decirme todas aquellas palabras que pueda sin tener en cuenta el orden".*

LISTA B	ENSAYO 1
VIOLÍN	
PEPINO	
ELEFANTE	
ARMARIO	
NABO	
GUITARRA	
SÓTANO	
OVEJA	
CLARINETE	
GARAJE	
MAÍZ	
CONEJO	
PATIO	
SAXOFÓN	
TIGRE	
RÁBANO	
CORRECTAS	

4º. *Ahora se trata de hacer lo mismo que acaba de hacer, diciendo el color de la tinta, sin tener en cuenta lo que está escrito, lo más rápidamente que pueda".* **45 segundos.**

ROJO	AZUL	VERDE	ROJO	AZUL
VERDE	VERDE	ROJO	AZUL	VERDE
AZUL	ROJO	AZUL	VERDE	ROJO
VERDE	AZUL	ROJO	ROJO	AZUL
ROJO	ROJO	VERDE	AZUL	VERDE
AZUL	VERDE	AZUL	VERDE	ROJO
ROJO	AZUL	VERDE	AZUL	VERDE
AZUL	VERDE	ROJO	VERDE	ROJO
VERDE	ROJO	AZUL	ROJO	AZUL
AZUL	VERDE	VERDE	AZUL	VERDE
VERDE	ROJO	AZUL	ROJO	ROJO
ROJO	AZUL	ROJO	VERDE	AZUL
VERDE	ROJO	AZUL	ROJO	VERDE
AZUL	AZUL	ROJO	VERDE	ROJO
ROJO	VERDE	VERDE	AZUL	AZUL
AZUL	AZUL	ROJO	VERDE	ROJO
ROJO	VERDE	AZUL	ROJO	VERDE
VERDE	ROJO	VERDE	AZUL	AZUL
ROJO	AZUL	ROJO	VERDE	ROJO
VERDE	ROJO	VERDE	AZUL	VERDE

2. PRUEBA DE ATENCIÓN Y MEMORIA DE TRABAJO:

1º. *"Ahora le leeré una secuencia de números. Cuando acabe, por favor, ¿me la podría repetir?"*

			ORDEN DIRECTO Intento/Elemento	Punt. Intento		Punt. Elemento		
SPAN	2	1	1-7	0	1	0	1	2
		2	6-3	0	1			
	3	1	5-8-2	0	1	0	1	2
		2	6-9-4	0	1			
	4	1	6-4-3-9	0	1	0	1	2
		2	7-2-8-6	0	1			
	5	1	4-2-7-3-1	0	1	0	1	2
		2	7-5-8-3-6	0	1			
	6	1	6-1-9-7-4-3	0	1	0	1	2
		2	3-9-2-4-8-7	0	1			
	7	1	5-9-1-7-4-2-8	0	1	0	1	2
		2	4-1-7-9-3-8-6	0	1			
	8	1	5-8-1-9-2-6-4-7	0	1	0	1	2
		2	3-8-2-9-5-1-7-4	0	1			
	9	1	2-7-5-8-6-2-5-8-4	0	1	0	1	2
		2	7-1-3-9-4-2-5-6-8	0	1			

TOTAL:

2º. *" Ahora volveré a leerle secuencias de números. Cuando acabe me las debería repetir, pero en orden inverso (comenzando por el final hasta llegar al principio)".*

			ORDEN INVERSO Intento/Elemento	Punt. Intento		Punt. Elemento		
SPAN	2	1	2-4	0	1	0	1	2
		2	5-7	0	1			
	3	1	6-2-9	0	1	0	1	2
		2	4-1-5	0	1			
	4	1	3-2-7-9	0	1	0	1	2
		2	4-9-6-8	0	1			
	5	1	1-5-2-8-6	0	1	0	1	2
		2	6-1-8-4-3	0	1			
	6	1	5-3-9-4-1-8	0	1	0	1	2
		2	7-2-4-8-5-6	0	1			
	7	1	8-1-2-9-3-6-5	0	1	0	1	2
		2	4-7-3-9-1-2-8	0	1			
	8	1	9-4-3-7-6-2-5-8	0	1	0	1	2
		2	7-2-8-1-9-6-5-3	0	1			

TOTAL:

3º. *"Ahora debajo puede ver un conjunto de números. Su tarea consiste en unirlos con una línea lo más rápidamente posible, teniendo en cuenta que no puede levantar el lápiz del papel".*

EJEMPLO:

PRUEBA:

6. PRUEBA DE FLUENCIA VERBAL:

1º. *"Ahora le voy a decir una letra y usted deberá decir todas aquellas palabras que se le ocurran que empiecen con esa misma letra. En este caso NO podrá decir nombres propios (por ejemplo, nombres de personas o ciudades), ni tampoco derivados (aumentativos, diminutivos, ...)".*
1 minuto por letra.

F: _____

A: _____

S: _____

2º. *"Ahora deberá decirme todos los animales que se le ocurran. Hasta que yo le diga basta".*
1 minuto.

ANIMALES: _____

¡Muchas gracias por su colaboración!

Which Patients and When Monitoring?

Characteristics of Patients: Which Predictors?

According to biomarkers?

According to clinical factors?

According to demographic variables?

According to emotional variables?

According to subjective complaints?

Clinical Factors

☞ High number of clinical factors are associated

Some of most representative:

☞ **AIDS**

☞ **CD4 Nadir**

☞ **Time with HIV**

☞ **Interruptions of ART**

☞ **Coinfection with HCV**

☞ **Virological Failure (in Plasma)**

☞ **<u>CSF Viral Load</u> ***

: Considering availability of lumbar puncture in clinical practice!

New Potential Risk Factors

Tozzi et al, Journal of Neurovirology, 2005

To assess prevalence and risk factors for human immunodeficiency virus (HIV)-related neurocognitive impairment (NCI), the authors performed a 7-year survey in the period 1996 to 2002. A total of 432 patients were examined. HIV-related NCI was diagnosed in 238 patients (55.1%), meeting the HIV dementia (HIV-D) criteria in 45 (10.4%). The prevalence of both NCI and HIV-D did not change significantly during the study period. Compared with patients without NCI, patients with NCI were older (40.4 versus 38.2 years; $P = .003$), had a higher prevalence of positive HCV serology (61.1% versus 38.9%; $P = .003$), and a lower nadir CD4 cell count (156 versus 222 cells/μl; $P < .001$). Compared with patients seen during 1996 to 1999, patients with NCI seen during 2000 to 2002 were older (40.7 versus 38.8 years; $P = .004$), had a less advanced disease stage (previous acquired immunodeficiency syndrome [AIDS] 28.8% versus 65.7%; $P < .001$) and a higher nadir CD4 count (174 versus 132 cells/μl; $P = .026$). This study showed an unchanged prevalence of both HIV-related NCI and HIV-D in the period 1996 to 2002. The authors found evidences for new additional potential risk factors for HIV-related NCI (older age, lower nadir CD4 count, positive hepatitis C virus [HCV] serology), and for a change of risk factors for NCI in the late highly active antiretroviral therapy (HAART) era (older age, less advanced disease, higher nadir CD4 count). *Journal of NeuroVirology* (2005) **11**, 265–273.

Demographic Factors

Well identified:

- ☞ **Older Age**
- ☞ **Education Level (*Cognitive Reserve!*)**
- ☞ **Employment!**

Self-Reported NC Complaints

FIGURE 1.

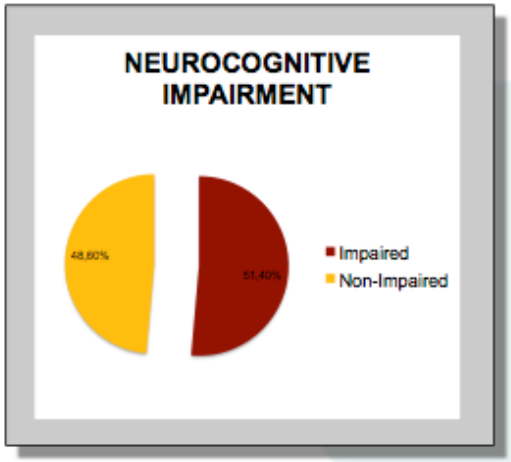
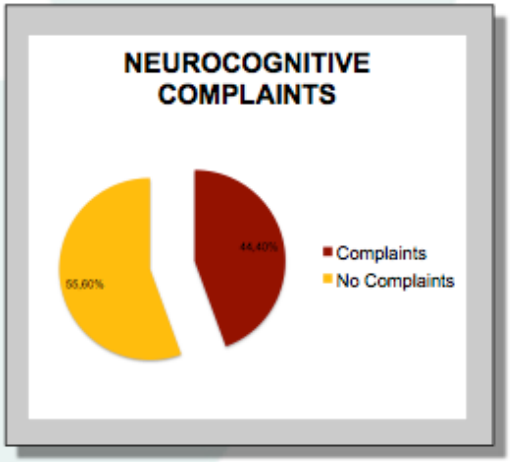


FIGURE 2.



Muñoz-Moreno et al, INS, Helsinki, 2009

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Self-Reported NC Complaints

3 patients' patterns according to presence or not of NC complaints:

☞ 1) NC Complaint + Neurocognitive Impairment

☞ 2) NC Complaint + No Neurocognitive Impairment

☞ 3) No NC Complaint + Neurocognitive Impairment!

Self-Reported NC Complaints

FIGURE 4.

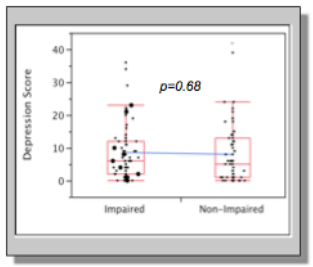


FIGURE 5.

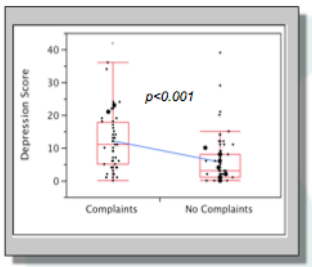


FIGURE 6.

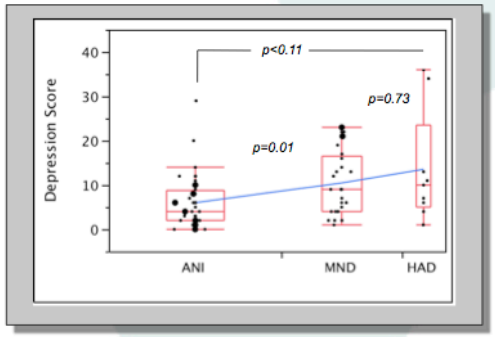
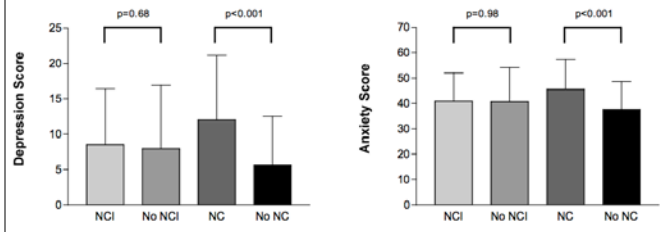


Table 1. Depression and anxiety scores according to the presence of neurocognitive impairment and neurocognitive complaints.



NCI, Neurocognitive Impairment; NCC, Neurocognitive Complaints.

Unpublished Data

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And When Monitoring?

A screening algorithm for HIV-associated neurocognitive disorders

LA Cysique,[1] JM Murray,[2,3] M Dunbar,[2] V Jeyakumar[2] and BJ Brew[4]

Results

The final algorithm utilized age, current CD4 cell count, past central nervous system HIV-related diseases and current treatment duration and required approximately 3 min to complete, with a good overall prediction accuracy of 78% (against the gold standard; NP-impairment status derived from standard NP testing) and a good specificity of 70%.

Conclusion

This noncognitive-based algorithm should prove useful to identify HIV-infected patients with advanced disease at high risk of HAND who require more formal assessment. We propose staged guidelines, using the algorithm, for improved HAND therapeutic management. Future larger, international studies are planned to test the predictive effect of nadir CD4 cell count, hepatitis C virus infection, gender, ethnicity and HIV viral clade. We recommend the use of this first version for HIV-infected Caucasian men with advanced disease.

$$\begin{aligned}\text{NP impairment:}\quad & 0.351 \times \text{age} - 0.005 \times \text{CD4} - 0.681 \\ & \times \log_{10}\text{HIV RNA} - 0.225 \\ & \times \text{HIV duration} + 3.356 \\ & \times \text{CNS disease} - 0.098 \\ & \times \text{CART duration} - 9.8748 \geq 0.\end{aligned}$$

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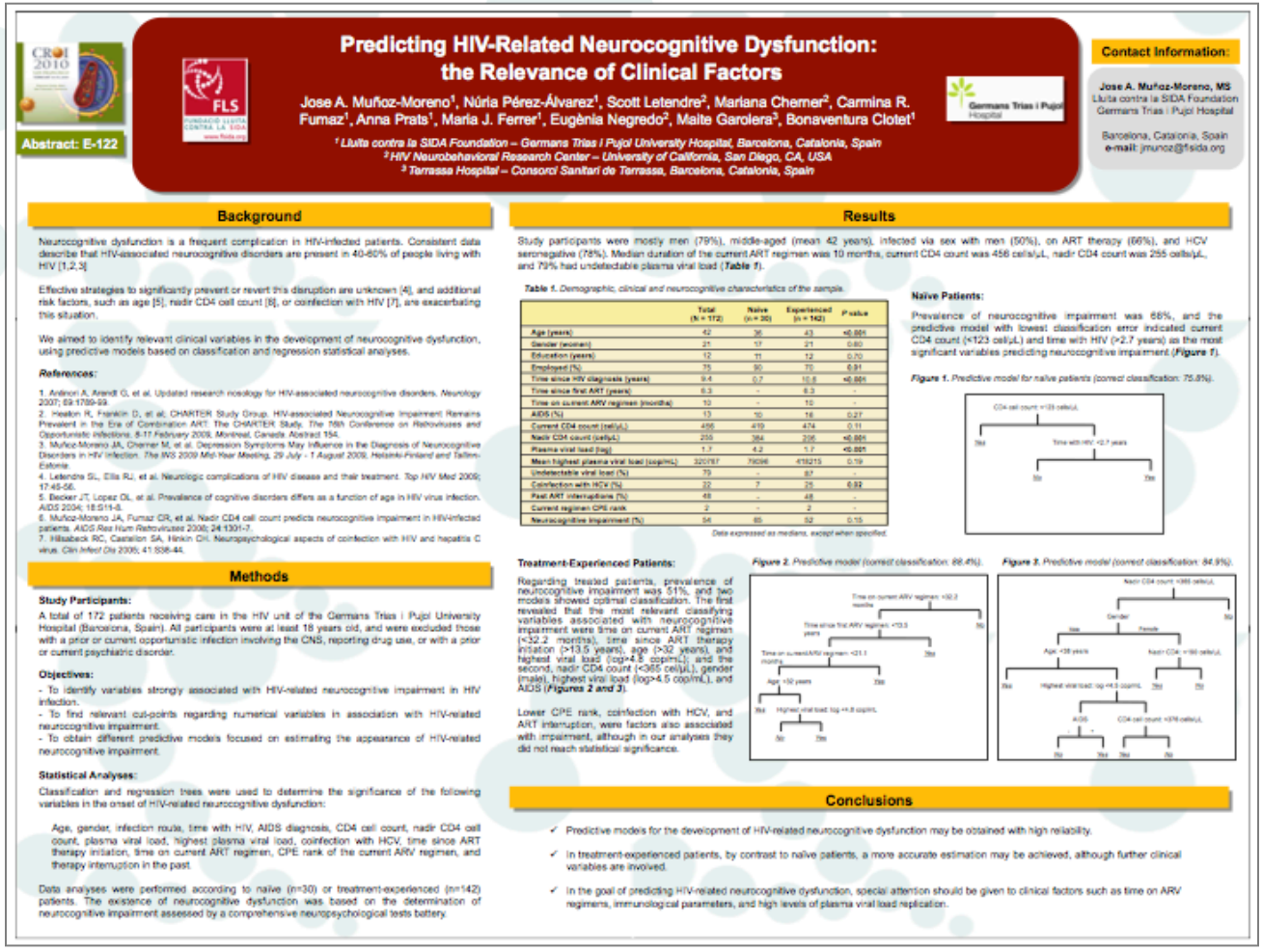
Similar Findings



Predicting HIV-Related Neurocognitive Dysfunction: the Relevance of Clinical Factors

Jose A. Muñoz-Moreno[1], Núria Pérez-Álvarez[1], Scott Letendre[2], Mariana Cherner[2], Carmina R. Fumaz[1], Anna Prats[1], María J. Ferrer[1], Eugènia Negredo[3], Maite Garolera[3], Bonaventura Clotet[1]

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[2] HIV Neurobehavioral Research Center – University of California, San Diego, CA, USA
[3] Terrassa Hospital – Consorci Sanitari de Terrassa, Barcelona, Catalonia, Spain

Abstract: E-122

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Barcelona, Catalonia, Spain
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Background

Neurocognitive dysfunction is a frequent complication in HIV-infected patients. Consistent data describe that HIV-associated neurocognitive disorders are present in 40-60% of people living with HIV [1,2,3].

Effective strategies to significantly prevent or revert this disruption are unknown [4], and additional risk factors, such as age [5], nadir CD4 cell count [6], or coinfection with HIV [7], are exacerbating this situation.

We aimed to identify relevant clinical variables in the development of neurocognitive dysfunction, using predictive models based on classification and regression statistical analyses.

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4. Letendre SL, Ellis RJ, et al. Neurologic complications of HIV disease and their treatment. *Top HIV Med* 2009; 17:45-56.
5. Becker JT, Lopez OL, et al. Prevalence of cognitive disorders differs as a function of age in HIV virus infection. *AIDS* 2004; 18:511-8.
6. Muñoz-Moreno JA, Fumaz CR, et al. Nadir CD4 cell count predicts neurocognitive impairment in HIV-infected patients. *AIDS Res Hum Retroviruses* 2008; 24:1301-7.
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Methods

Study Participants:

A total of 172 patients receiving care in the HIV unit of the Germans Trias i Pujol University Hospital (Barcelona, Spain). All participants were at least 18 years old, and were excluded those with a prior or current opportunistic infection involving the CNS, reporting drug use, or with a prior or current psychiatric disorder.

Objectives:

- To identify variables strongly associated with HIV-related neurocognitive impairment in HIV infection.
- To find relevant cut-points regarding numerical variables in association with HIV-related neurocognitive impairment.
- To obtain different predictive models focused on estimating the appearance of HIV-related neurocognitive impairment.

Statistical Analyses:

Classification and regression trees were used to determine the significance of the following variables in the onset of HIV-related neurocognitive dysfunction:

Age, gender, infection route, time with HIV, AIDS diagnosis, CD4 cell count, nadir CD4 cell count, plasma viral load, highest plasma viral load, coinfection with HCV, time since ART therapy initiation, time on current ART regimen, CPE rank of the current ARV regimen, and therapy interruption in the past.

Data analyses were performed according to naïve (n=30) or treatment-experienced (n=142) patients. The existence of neurocognitive dysfunction was based on the determination of neurocognitive impairment assessed by a comprehensive neuropsychological tests battery.

Results

Study participants were mostly men (79%), middle-aged (mean 42 years), infected via sex with men (50%), on ART therapy (66%), and HCV seronegative (78%). Median duration of the current ART regimen was 10 months, current CD4 count was 456 cells/µL, nadir CD4 count was 255 cells/µL, and 79% had undetectable plasma viral load (**Table 1**).

Table 1. *Demographic, clinical and neurocognitive characteristics of the sample.*

	Total (N = 172)	Naïve (n = 30)	Experienced (n = 142)	P value
Age (years)	42	36	43	<0.001
Gender (women)	21	17	21	0.60
Education (years)	12	11	12	0.70
Employed (%)	75	90	70	0.01
Time since HIV diagnosis (years)	9.4	0.7	10.8	<0.001
Time since first ART (years)	6.3	-	6.3	-
Time on current ARV regimen (months)	10	-	10	-
AIDS (%)	13	10	16	0.27
Current CD4 count (cell/µL)	456	419	474	0.11
Nadir CD4 count (cell/µL)	255	364	206	<0.001
Plasma viral load (log)	1.7	4.2	1.7	<0.001
Mean highest plasma viral load (cop/mL)	320787	76096	418213	0.19
Undetectable viral load (%)	79	-	87	-
Coinfection with HCV (%)	22	7	25	0.02
Past ART interruptions (%)	48	-	48	-
Current regimen CPE rank	2	-	2	-
Neurocognitive impairment (%)	54	65	52	0.15

Data expressed as medians, except when specified.

Naïve Patients:

Prevalence of neurocognitive impairment was 65%, and the predictive model with lowest classification error indicated current CD4 count (<123 cell/µL) and time with HIV (>2.7 years) as the most significant variables predicting neurocognitive impairment (**Figure 1**).

Figure 1. *Predictive model for naïve patients (correct classification: 75.8%).*

Treatment-Experienced Patients:

Regarding treated patients, prevalence of neurocognitive impairment was 51%, and two models showed optimal classification. The first revealed that the most relevant classifying variables associated with neurocognitive impairment were time on current ART regimen (<32.2 months), time since ART therapy initiation (>13.5 years), age (>32 years), and highest viral load (log>4.8 cop/mL); and the second, nadir CD4 count (<365 cel/µL), gender (male), highest viral load (log>4.5 cop/mL), and AIDS (**Figures 2 and 3**).

Lower CPE rank, coinfection with HCV, and ART interruption, were factors also associated with impairment, although in our analyses they did not reach statistical significance.

Figure 2. *Predictive model (correct classification: 68.4%).*

Figure 3. *Predictive model (correct classification: 84.9%).*

Conclusions

- ✓ Predictive models for the development of HIV-related neurocognitive dysfunction may be obtained with high reliability.
- ✓ In treatment-experienced patients, by contrast to naïve patients, a more accurate estimation may be achieved, although further clinical variables are involved.
- ✓ In the goal of predicting HIV-related neurocognitive dysfunction, special attention should be given to clinical factors such as time on ARV regimens, immunological parameters, and high levels of plasma viral load replication.

Muñoz-Moreno et al, CROI, 2010

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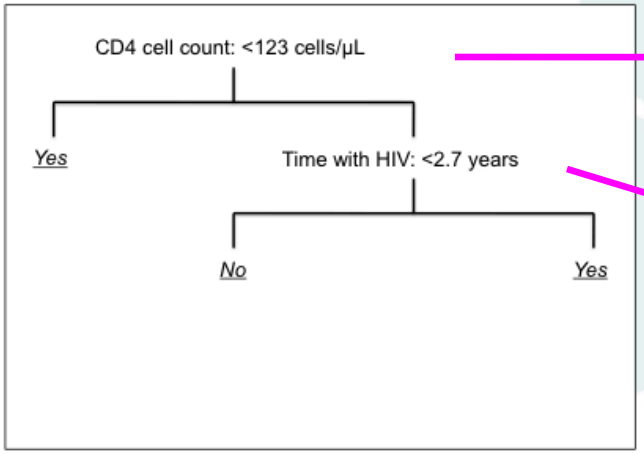
Clinical Factors As Predictors

Figure 1. *Predictive model for naïve patients (correct classification: 75.8%).*



- Current CD4 cell count (<123 cells/µL)

- Time with HIV (>2.7 years)

**: 75.8% of correct classification*

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Clinical Factors As Predictors

Figure 2. *Predictive model (correct classification: 88.4%).*

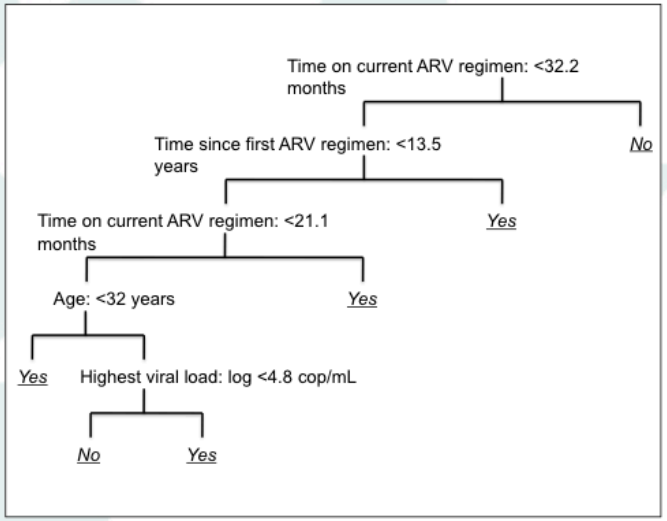
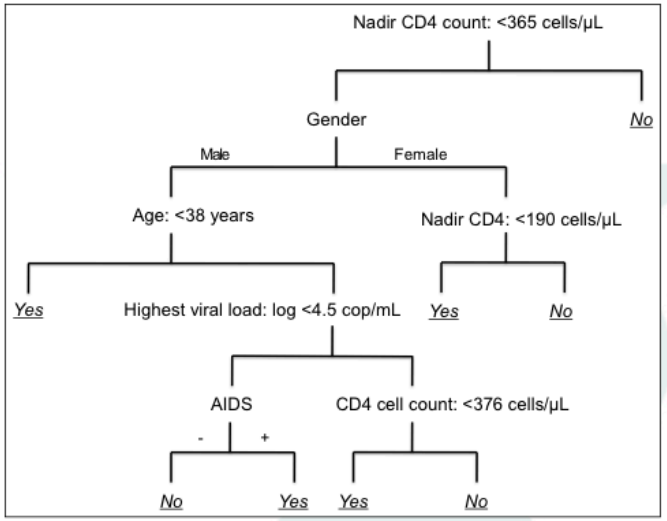


Figure 3. *Predictive model (correct classification: 84.9%).*



- Nadir CD4 cell count (
<365 cells/µL)

- Time on current regimen
(>32.2 months)

- Highest viral load
(>4.5 cop/mL)

**: 88.4% and 84.9%*
of correct classification

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Algorithm Proposed - Cysique

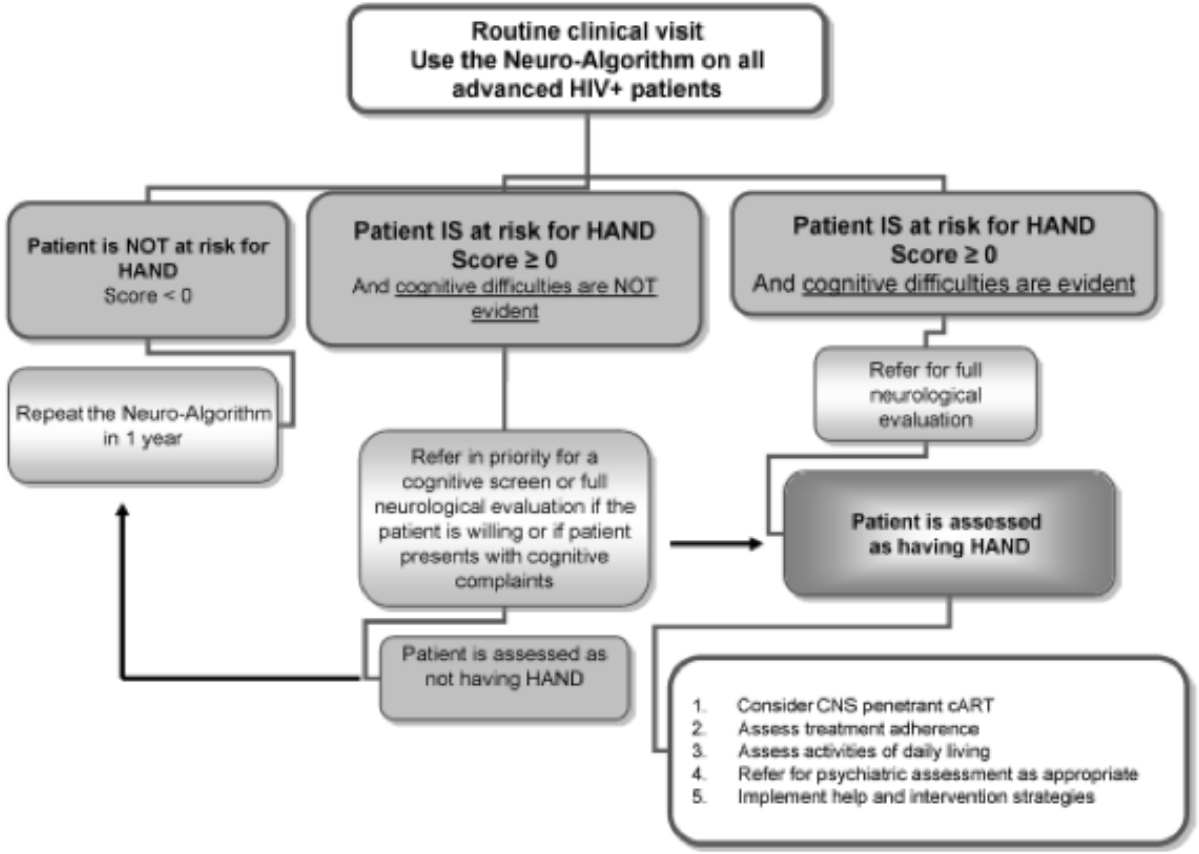
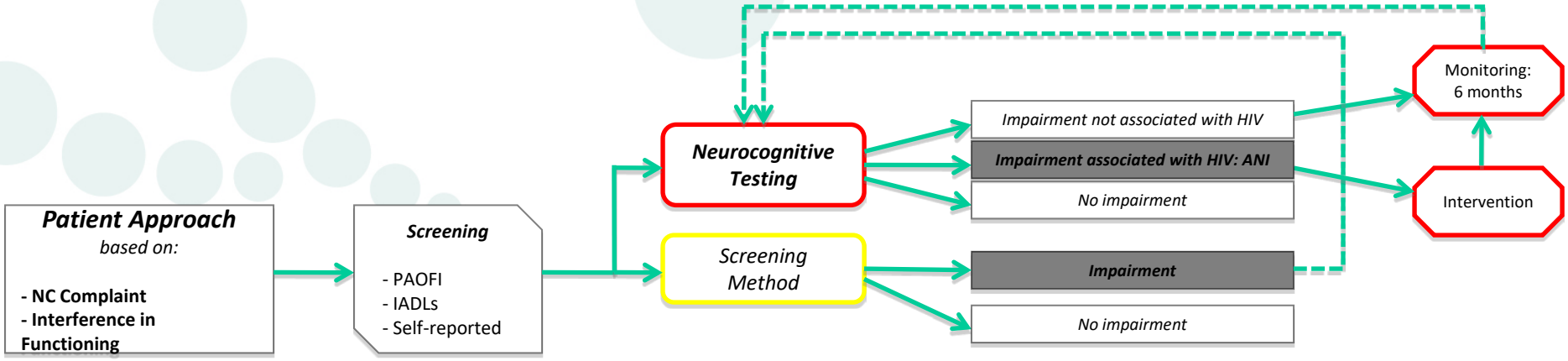


Fig. 1 Suggested algorithmic approach for the detection of cognitive impairment in HIV-infected individuals.


Patient Approach
based on:
- NC Complaint
- Interference in Functioning
Screening
- PAOFI
- IADLs
- Self-reported
Neurocognitive Testing
Screening Method
Impairment not associated with HIV
Impairment associated with HIV: ANI
No impairment
Impairment
No impairment
Monitoring: 6 months
Intervention

Clinician Approach

based on clinical suspicion according to:

- Clinical Risk Factors, particularly:

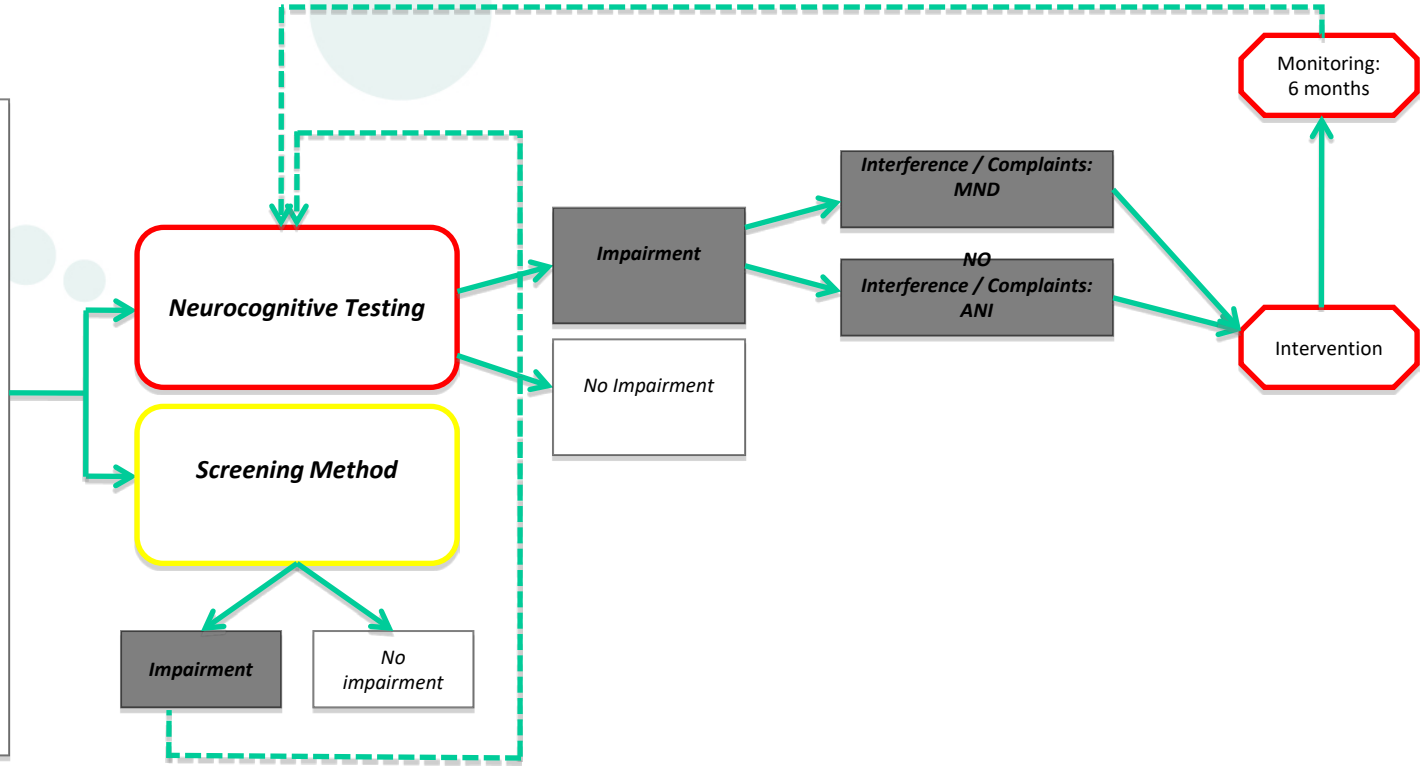
AIDS
CD4 Nadir
Time with HIV
Interruptions of ART
Coinfection with HCV
Virological Failure

*In case of Lumbar Puncture availability:

CSF Viral Load*

- Additional Risk Factors:

Aging
Education
Others



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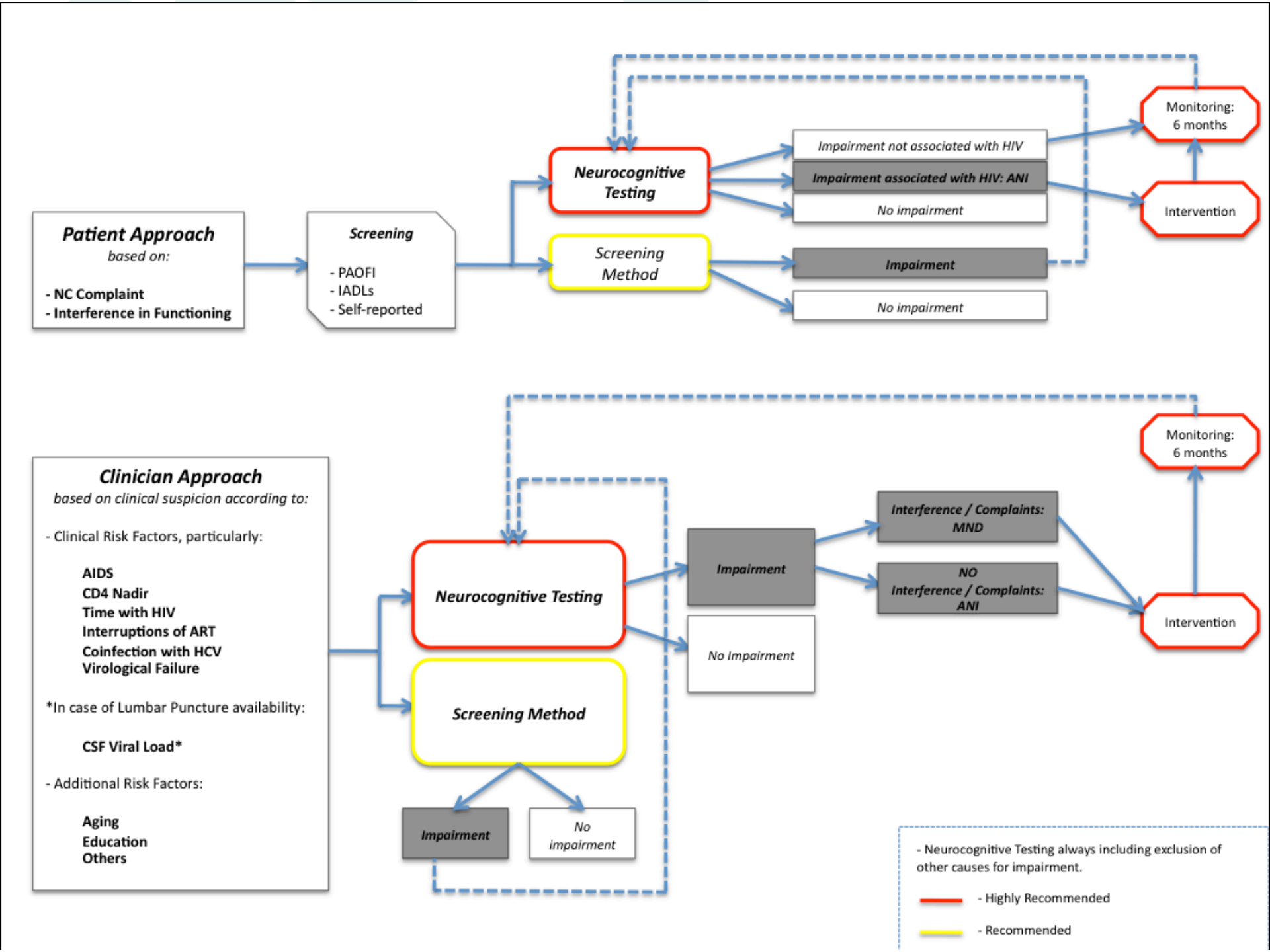
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Clinician Approach
based on clinical suspicion according to:
- Clinical Risk Factors, particularly:
AIDS
CD4 Nadir
Time with HIV
Interruptions of ART
Coinfection with HCV
Virological Failure
*In case of Lumbar Puncture availability:
CSF Viral Load*
- Additional Risk Factors:
Aging
Education
Others
Neurocognitive Testing
Screening Method
Impairment
No Impairment
Impairment
No impairment
Interference / Complaints: MND
NO Interference / Complaints: ANI
Monitoring: 6 months
Intervention
- Neurocognitive Testing always including exclusion of other causes for impairment.
- Highly Recommended
- Recommended

Announcement of Training in Neuropsychological Skills (Barcelona, Spain, July 2011)

Workshop on

Neuropsychological and Neuropsychiatric

Aspects in HIV Infection

- - -

July 7th - 8th, 2011

- Location: Germans Trias i Pujol University Hospital (Barcelona, Spain)
- Duration: 2 days (15 hours)
- Programme: Particularly focused on CNS disturbances and HAND

A: ***Preliminary Concepts and Clinical Relevance***

B: ***Interventions and Clinical Management***

- - -

C: ***Neurocognitive Testing***

(Practical Approach)

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Many Thanks!

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