3rd Symposium on Psychiatry and HIV

- - -

Barcelona, May 7th 2010

Developing Skills on Neuropsychological Screening in Clinical Practice:

Which Tools, Which Patients and When Monitoring

Jose A. Muñoz-Moreno

- - -

Lluita contra la SIDA Foundation

Germans Trias i Pujol University Hospital

- - -

Barcelona, Catalonia, Spain

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Which Tools?

Which Patients?

When Monitoring?

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Which Tools?

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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

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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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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.

Neuropsychological Testing

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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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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

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Neuropsychological Testing

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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*)

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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

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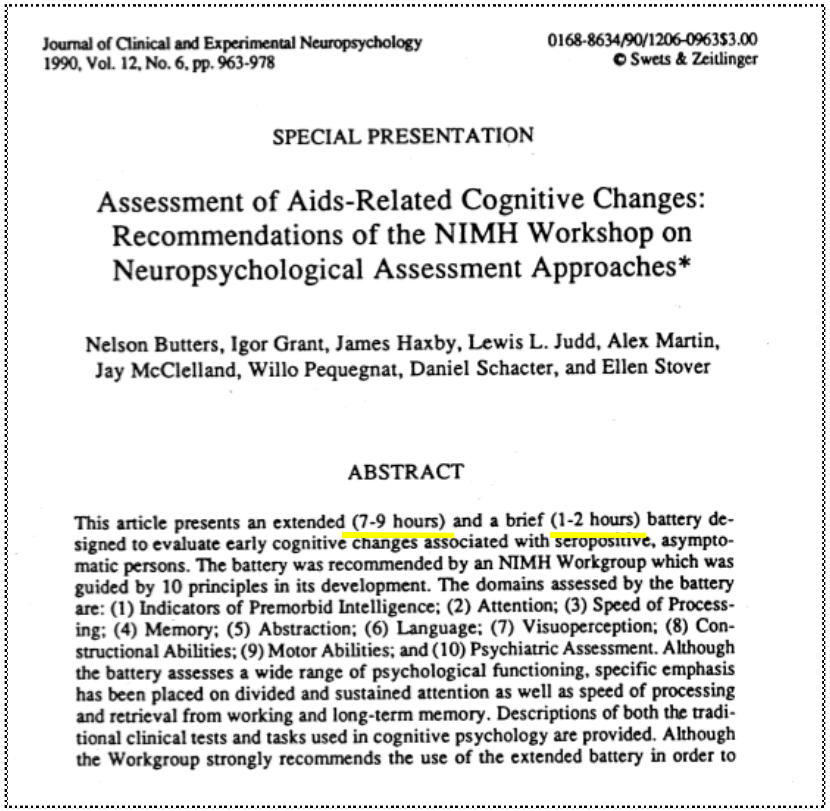
Multiple Tools

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

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What Do We Know About Screening Tools?

1) HIV Dementia Scale (HDS)

2) HNRC (Carey, 2004): 2 combinations of Cognitive Measures

3) Brief Z Scores: NPZ4, NPZ9, NPZ16, ...

4) Computerized Time Reaction Tests

5) CogState (Cysique, 2006)

6) Algorithm (Cysique, 2010)

7) NEU (Muñoz-Moreno, 2010): Brief Instrument in Development

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HIV Dementia Scale

1) **HIV Dementia Scale (HDS)**:

- Brief (10-15 minutes)
- Easy instructions (5 items)
- Well validated (USA and Uganda)

But...

- Specific for dementia
- Sensitivity with clinical manifestations

JAIDS, 2003: Clifford A. Smith, Wilfred G. van Gorp, Elizabeth R. Ryan, Stephen J. Ferrando, Judith Rabkin

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HNRC (Carey, 2004)

Initial Validation of a Screening Battery for the Detection of HIV-Associated Cognitive Impairment

Catherine L. Carey[1,2], Steven Paul Woods[1,3], Julie D. Rippeth[1,3], Raul Gonzalez[1,2], David J. Moore[1,2], Thomas D. Marcotte[1,2,3], Igor Grant[1,2,3], Robert K. Heaton[1,2,3], and the HNRC Group

ABSTRACT

This study sought to develop and validate a screening battery for detecting HIV-related neuropsychological (NP) impairment. Six NP measures representing the ability areas most likely affected by HIV infection were paired in 14 combinations and their diagnostic accuracy rates compared. The measures were selected from a larger NP battery administered to 190 HIV-seropositive (HIV+) participants. Screening battery performance was classified as NP impaired if demographically corrected *T*-scores fell below 40 on both tests, or below 35 on one test. Using blind clinical ratings of NP test results from the larger battery as the "gold standard" for global NP status (impaired or unimpaired), we found that several test combinations demonstrated adequate diagnostic accuracy in detecting NP impairment. The most sensitive test combinations were the Hopkins Verbal Learning Test – Revised (HVLT–R; Total Recall) and the Grooved Pegboard Test nondominant hand (PND) pair and the HVLT–R and WAIS-III Digit Symbol (DS) subtest pair (sensitivity = 78% and 75%, respectively). Both test combinations (HVLT–R/PND, HVLT–R/DS) were more accurate than the HIV Dementia Scale (HDS) in classifying HIV+ participants as NP impaired or unimpaired. Results suggest that demographically corrected *T*-scores from pairs of common NP measures may serve as valid screening instruments to identify subjects with HIV-related neurocognitive impairment who could benefit from more extensive NP examination.

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Reduced Z Scores

3) Used in different AIDS Clinical Trial Group (ACTG) studies - **NPZ4**:

- Brief (20-25 minutes)
- Standardized
- Used in longitudinal studies

But...

- Assessing 3 areas
- Learning / training effect??

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Computerized Tools

4) **Computerized vs Traditional Batteries**:

- ☞ They do not measure exactly the same
- ☞ Both are adequate for neurocognitive testing
- ☞ Traditional batteries continue as appropiate

González et al, JINS, 2003

Computerized reaction time battery *versus* a traditional neuropsychological battery: Detecting HIV-related impairments

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CogState

5**) CogState** (Cysique, 2006):

- Computerized
- Assessing 3 areas
- 10-15 minutes

The assessment of cognitive function in advanced HIV-1 infection and AIDS dementia complex using a new computerised cognitive test battery

Lucette A.J. Cysique [a,*], Paul Maruff [b,c], David Darby [c,d], Bruce J. Brew [e]

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New Screening Algorithm (Cysique, 2010)

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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Brief Quantitative Instrument in Development

7) **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					
BARCO					
ARDILLA					
COL					TOTAL
CORRECTAS					
Perseveraciones					
Intrusiones					

3º. *"Ahora le leeré una lista de palabras totalmente diferente. Cuando acabe deberá 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, cree 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 deberá 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!

Other Tools?

Neurophysiology and neuroimaging:

1) Research setting: economical cost, variable feasibility in clinical practice, ...

2) Lower number of published studies, although increasing!

3) Expectation in future, because of probable advances...

However, relevant to exclude other causes:
for differential diagnosis

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PRACTICE PART:

Neurocognitive Testing

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Requirements for Comprehensive NC Testing

- Assessment of the 7 recommended areas

- Evaluation and control of demographic, clinical and emotional variables

- Exclusion of other conditions not associated with NCI currently or in past (possible confounds to HIV-associated neurocognitive disorders)

  CNS-related pathology
  Drug use
  Psychiatric conditions
  ...

- To follow the diagnosis classification proposed by:

Antinori et al, 2007 in Neurology

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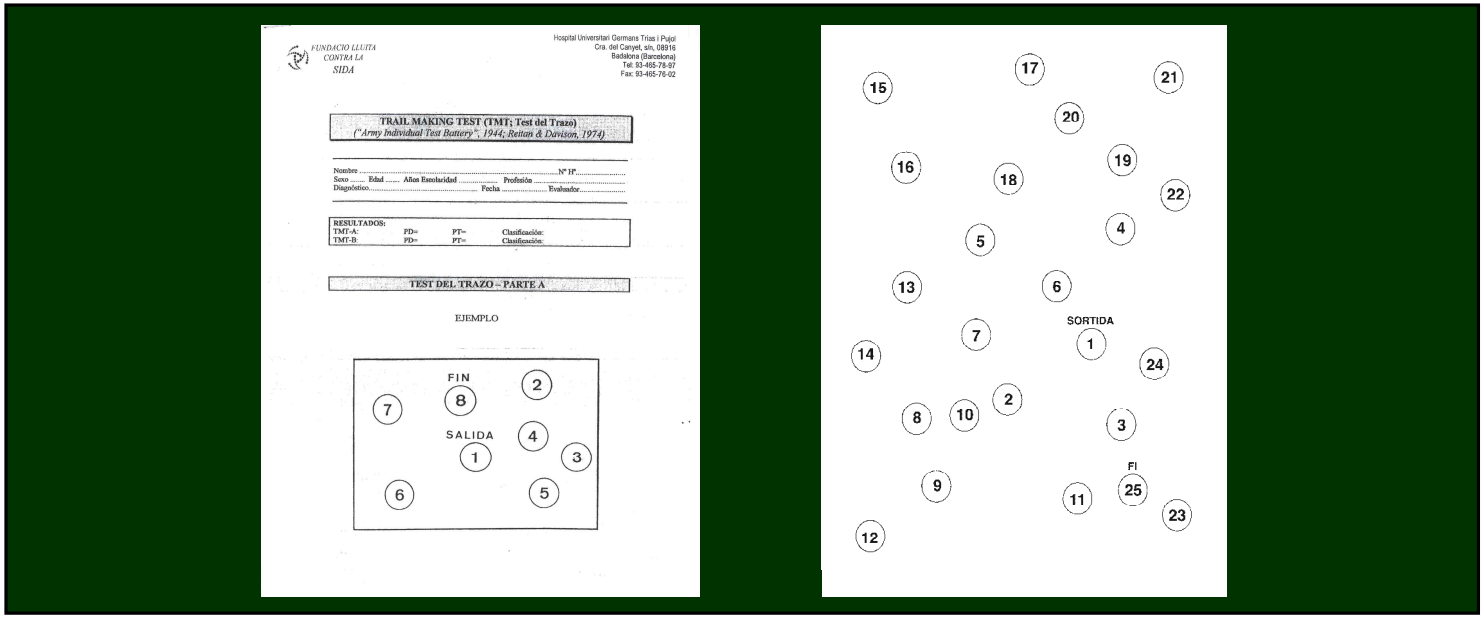
Neuropsychological Tests

INFORMATION PROCESSING 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
	- Stroop's Test

Information Processing Speed

Trail Making Test - Part A (TMT-A)



Reitan, 1974

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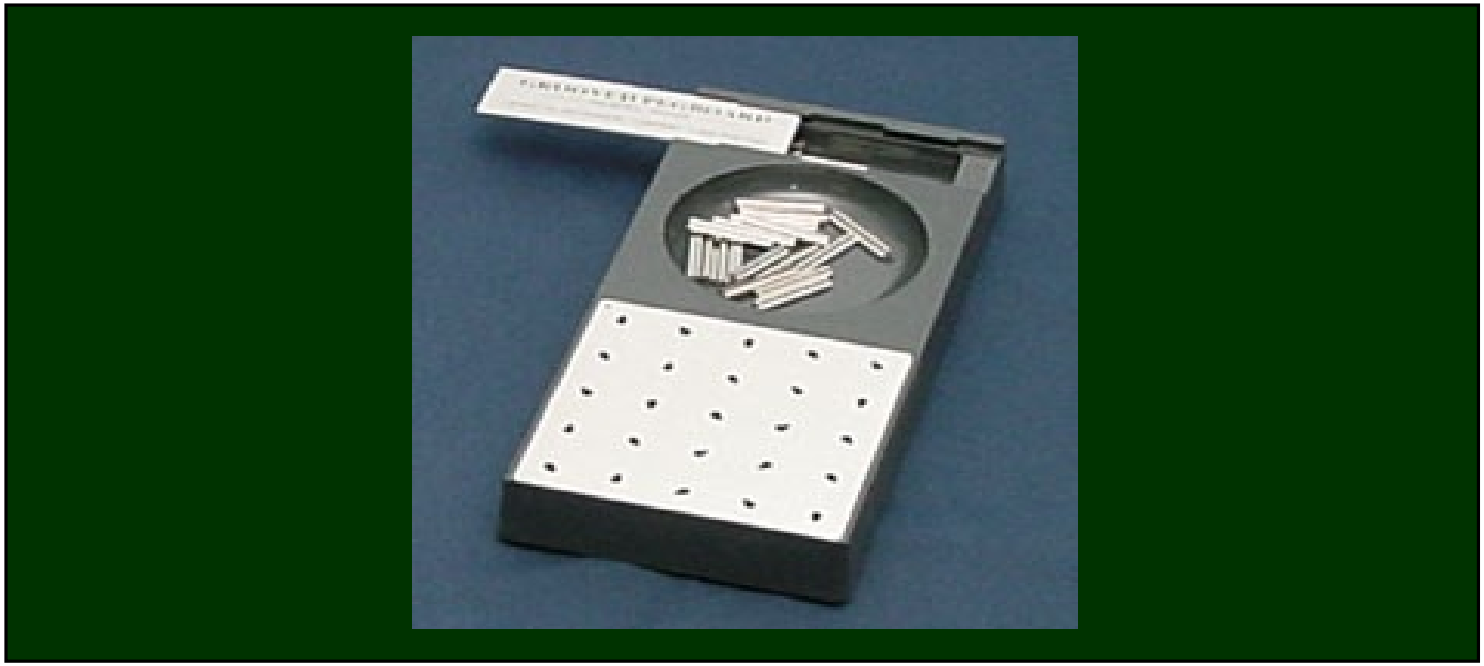
Motor Function

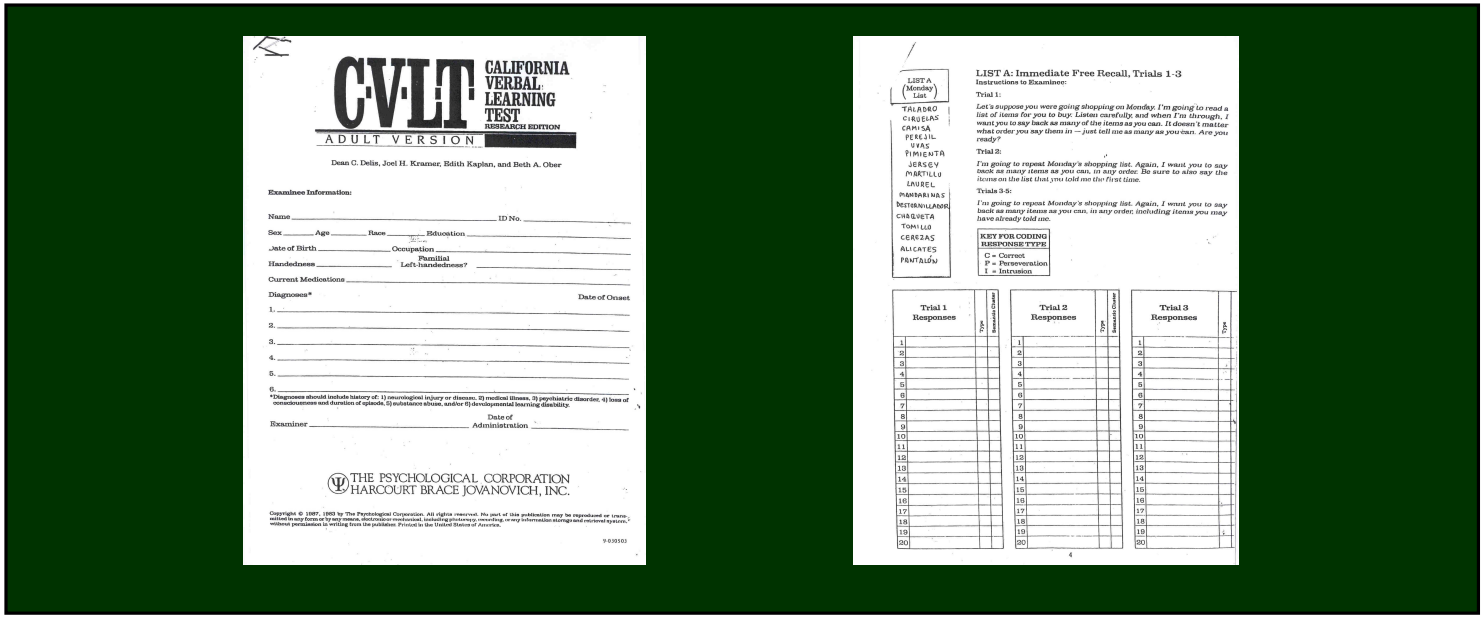
Grooved Pegboard Test



Matthews, 1964

Verbal Memory and Learning

California Verbal Learning Test - II



CVLT 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.

9 035103

LIST A (Monday) List
TALADRO
CIRUELAS
CAMISA
PEREJIL
VIAS
PIMIENTA
JERSEY
MARTILLO
LAUREL
MANDARINAS
MOTOCICLADOR
CHAQUETA
TOMILLO
CEREZAS
ALICATES
PANTALÓN

LIST A: Immediate Free Recall, Trials 1-3

Instructions to Examinee:

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	Semantic Cluster	Trial 2 Responses	Type	Semantic Cluster	Trial 3 Responses	Type
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
13								
14								
15								
16								
17								
18								
19								
20								

4

Delis, 2000

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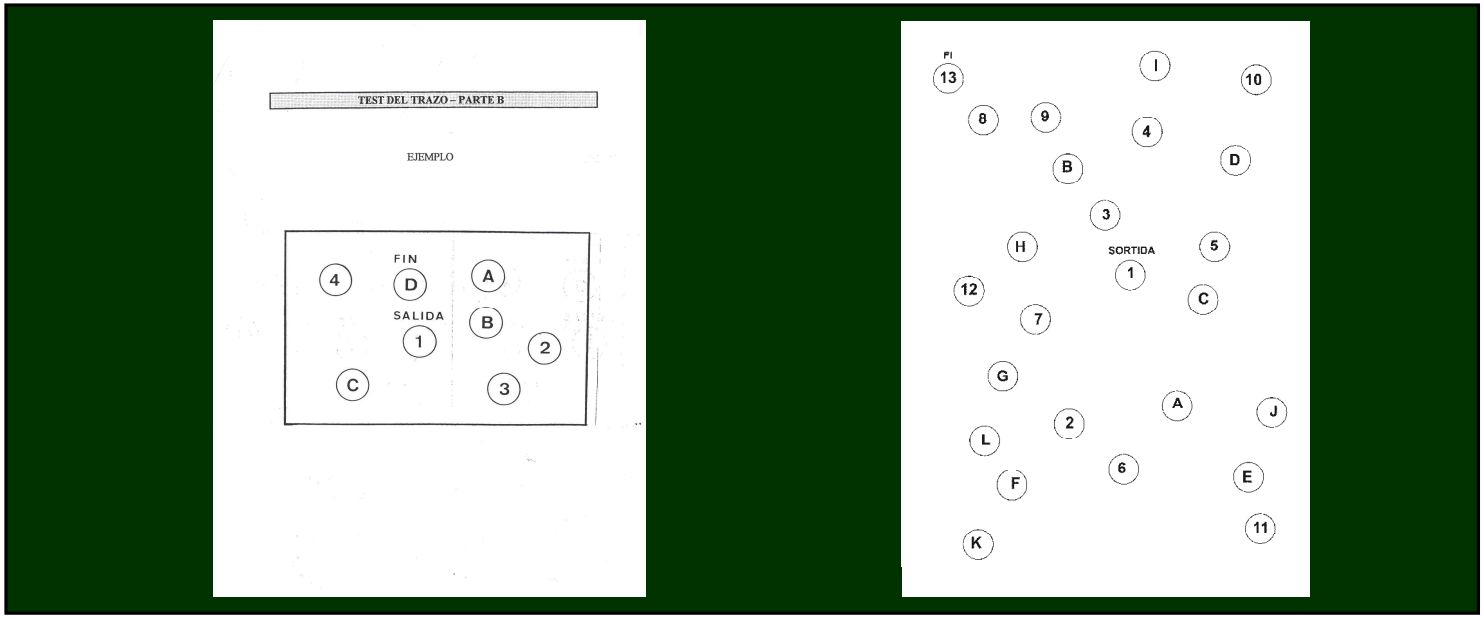
Executive Functioning

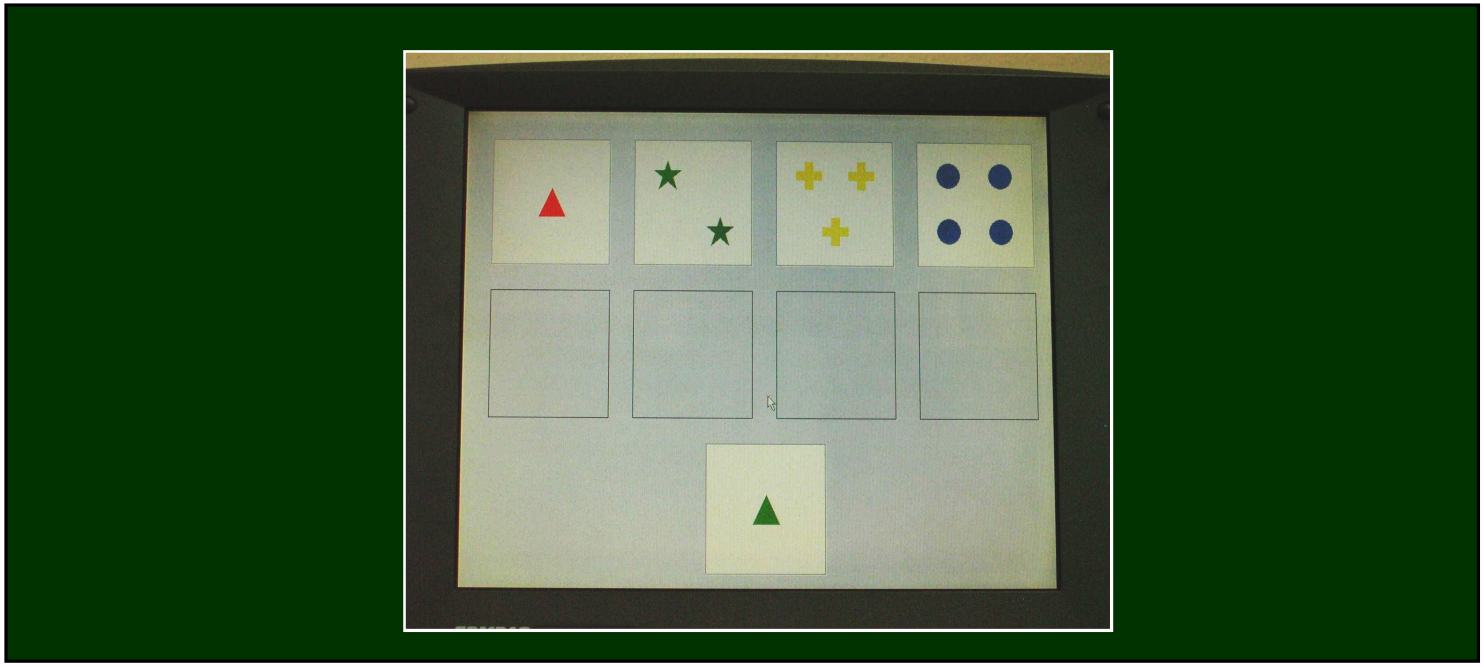
Trail Making Test - Part B (TMT-B)



Reitan, 1974

Executive Functioning

Wisconsin Card Sorting Test (WCST)



Kongs, 1993

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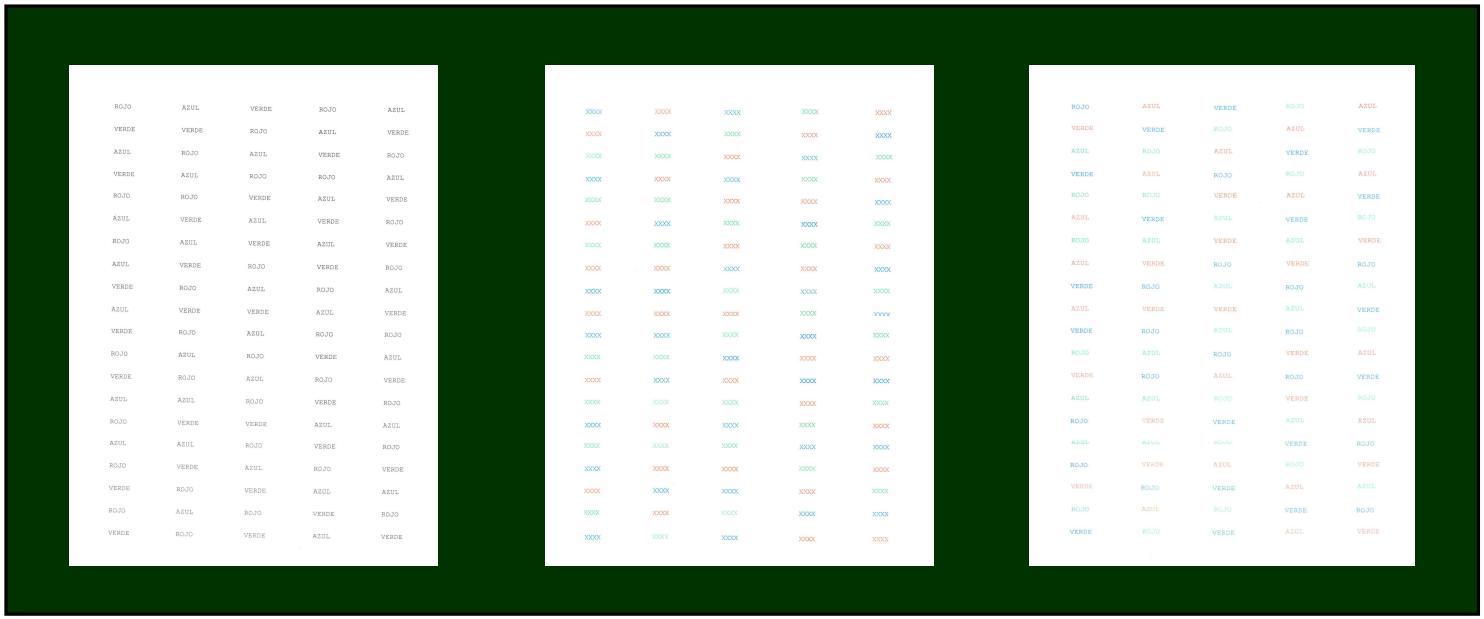
Executive Functioning

Stroop's Test



Golden, 1978

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

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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

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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.

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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

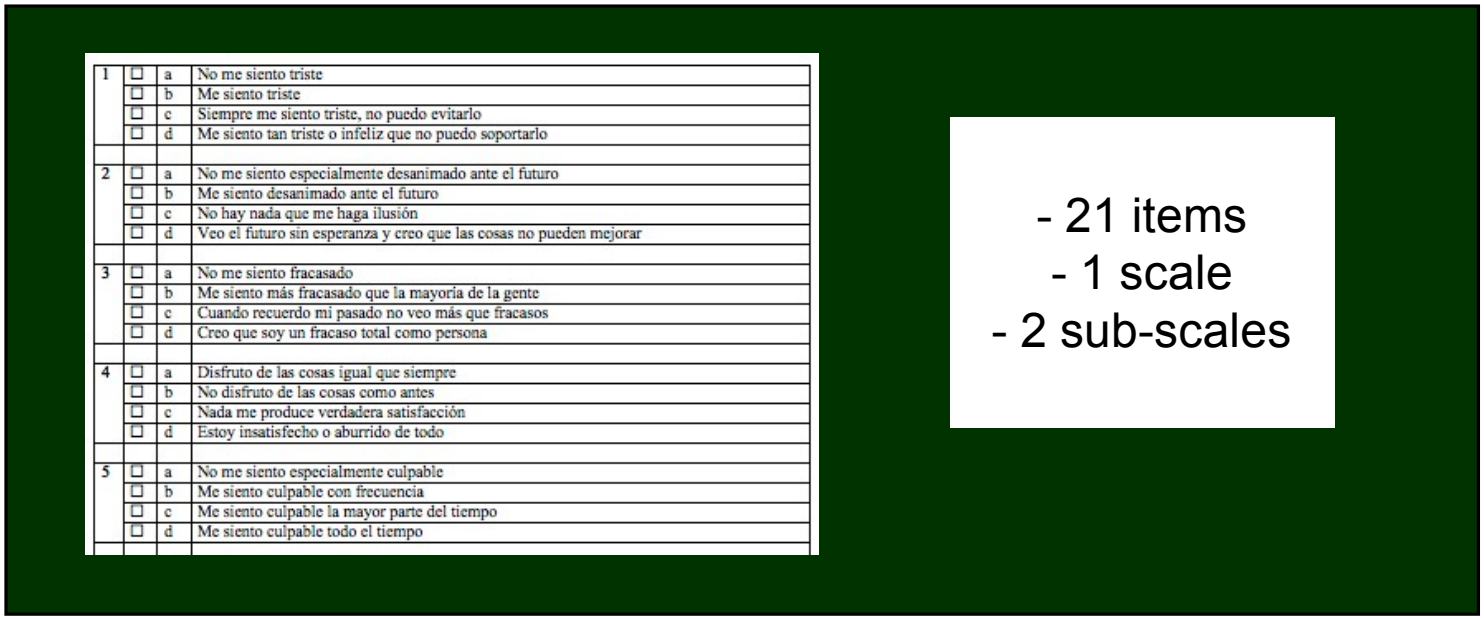
4. Puedo reírme y ver el lado divertido de las cosas
- O Al igual que siempre lo hice
- O No tanto ahora
- O Casi nunca
- O Nunca

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

Golden, 1978

Depression Symptoms

Beck Depression Inventory (BDI)



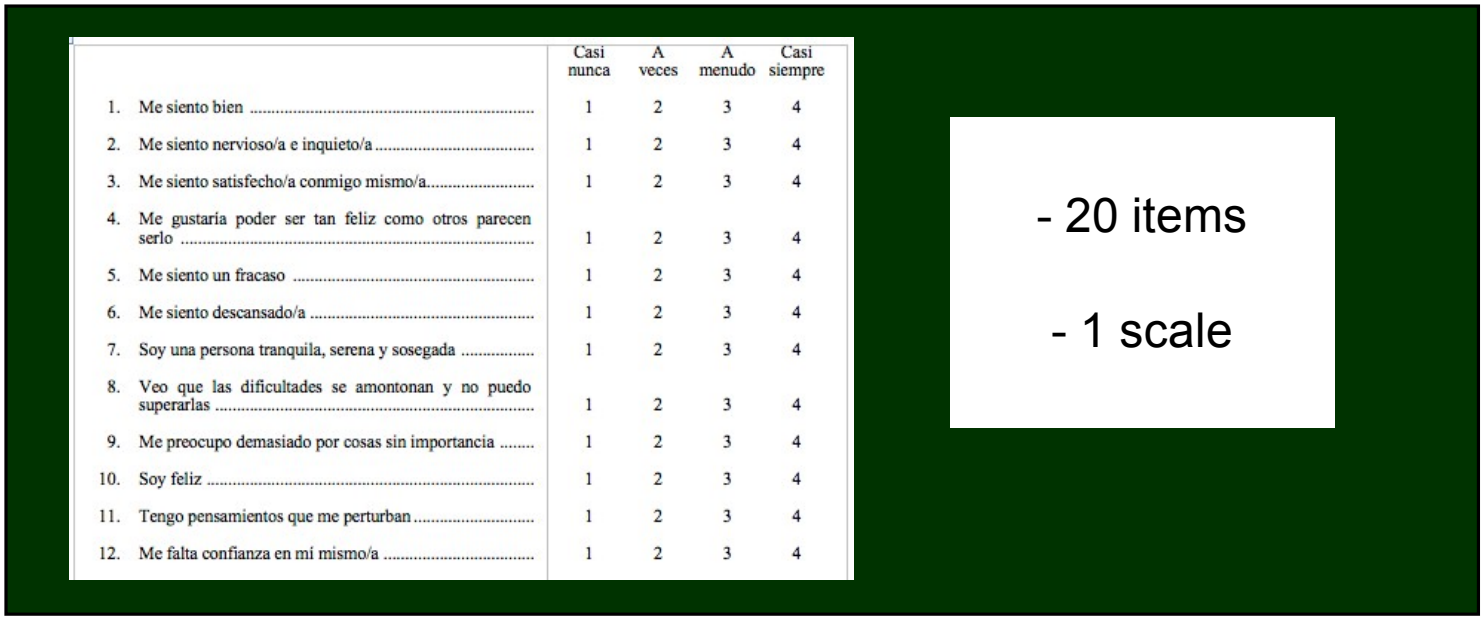
1	☐	a	No me siento triste
	☐	b	Me siento triste
	☐	c	Siempre me siento triste, no puedo evitarlo
	☐	d	Me siento tan triste o infeliz que no puedo soportarlo
2	☐	a	No me siento especialmente desanimado ante el futuro
	☐	b	Me siento desanimado ante el futuro
	☐	c	No hay nada que me haga ilusión
	☐	d	Veo 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

Which Patients?

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Characteristics of Patients: Which Predictors?

According to biomarkers?

According to clinical factors?

According to demographic variables?

According to emotional variables?

According to subjective complaints?

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Characteristics of Patients: Which Predictors?

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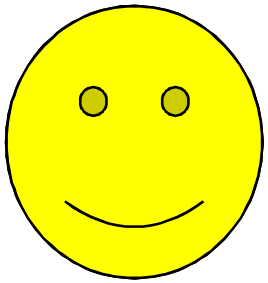
Biomarkers

Dr. Letendre and Dr. Antinori



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Characteristics of Patients: Which Predictors?

According to biomarkers?

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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> *

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: 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.

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Nadir CD4 Cell Count

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]

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

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)	

Ellis, CROI, 2010

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And Interruptions of ART?

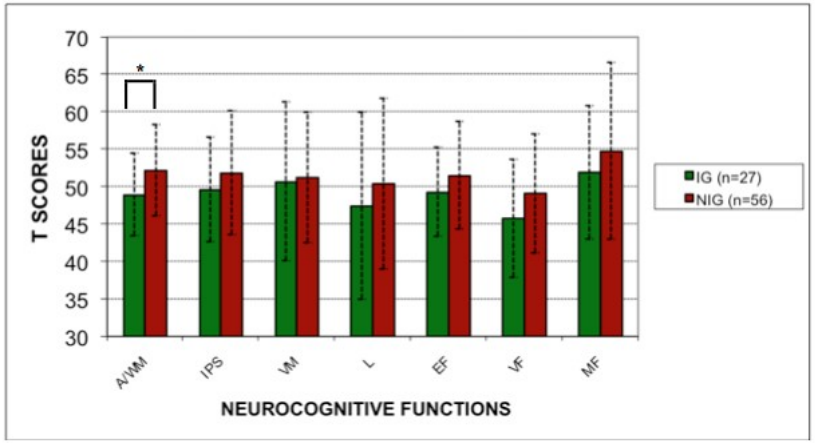
Journal of NeuroVirology, 00: 1–11, 2010
© 2010 Journal of NeuroVirology
ISSN 1355-0284 print/ 1538-2443 online
DOI: 10.3109/13550281003767710

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.

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Characteristics of Patients: Which Predictors?

According to biomarkers?

According to clinical factors?

According to demographic variables?

According to emotional variables?

According to subjective complaints?

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Demographic Factors

Well identified:

- ☛ **Age**
- ☛ **Alcohol and Drug Use**
- ☛ **Education**

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Characteristics of Patients: Which Predictors?

According to biomarkers?

According to clinical factors?

According to demographic variables?

According to emotional variables?

According to subjective complaints?

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Emotional Status

☞ Both **Depression** and **Anxiety** symptoms related to self-reported NC complaints

☞ Neurocognitive impairment and depression different independent mechanisms

☞ Wide evidence about the need of including both constructs in assessments!

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Characteristics of Patients: Which Predictors?

According to biomarkers?

According to clinical factors?

According to demographic variables?

According to emotional variables?

According to subjective complaints?

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Self-reported NC Complaints

FIGURE 1.

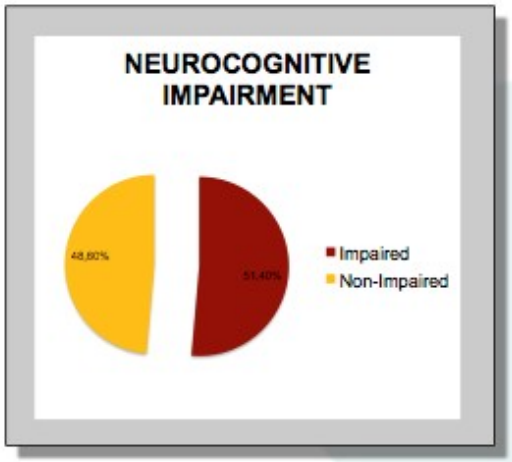
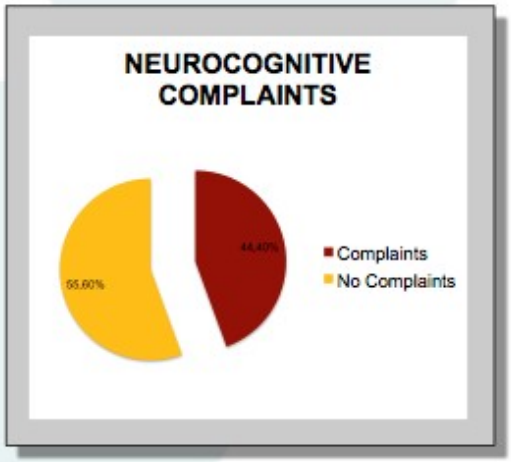


FIGURE 2.



Muñoz-Moreno et al, INS, Helsinki, 2009

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Self-reported 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!!

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Self-reported NC Complaints

FIGURE 4.

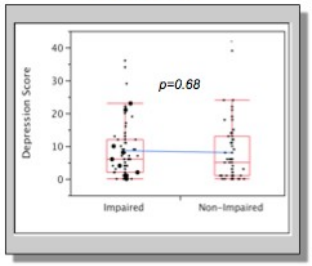


FIGURE 5.

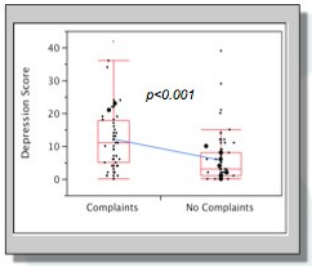


FIGURE 6.

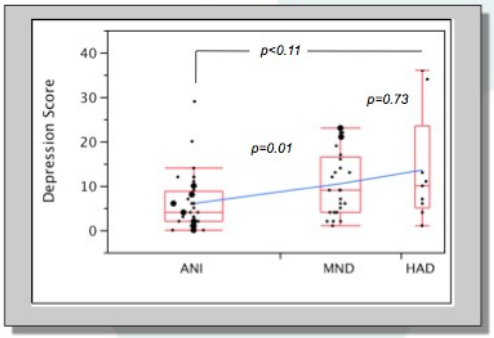
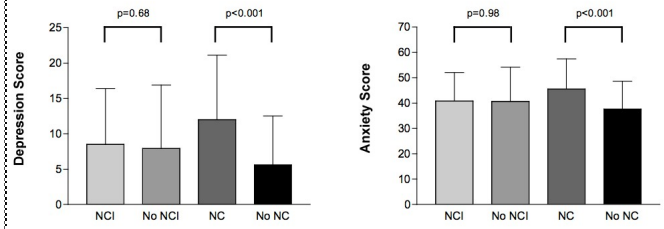


Table 1. Depression and anxiety scores according to the presence of neurocognitive impairment and neurocognitive complaints.



NCI, Neurocognitive Impairment; NCC, Neurocognitive Complaints.

Unpublished Data

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Self-reported Complaints

3 strategies:

1) To assess different scales of complaints:

PAOFI Questionnaire
An adapted NC Complaints Questionnaire

2) To assess daily functioning:

IADLs Questionnaire

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When Monitoring?

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Algorithm Proposed - Cysique

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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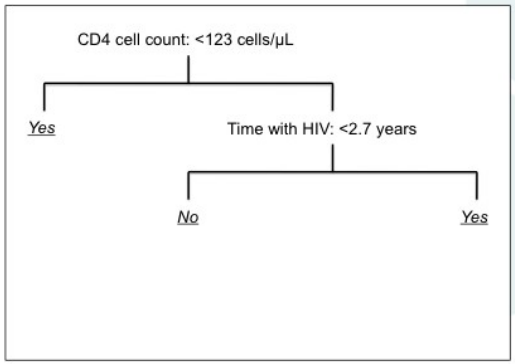
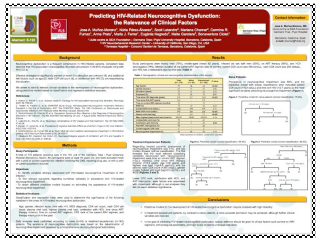
Similar Findings

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





Muñoz-Moreno et al, CROI, 2010

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

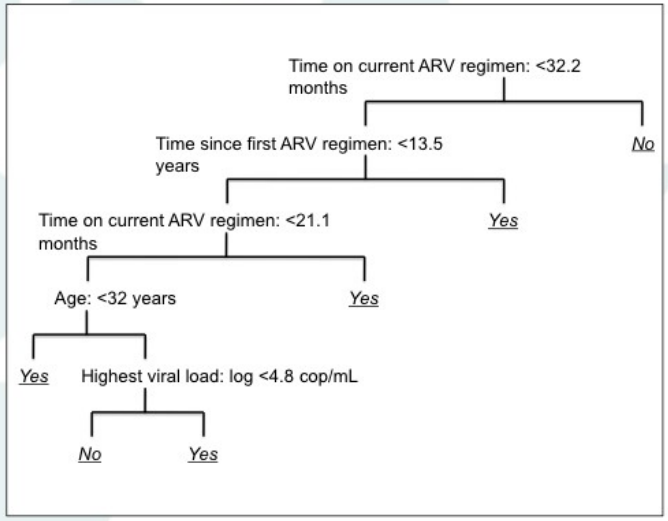
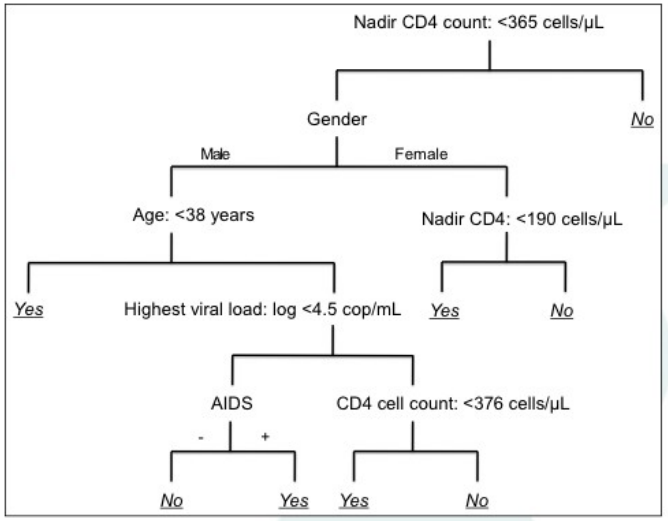


Figure 3. *Predictive model (correct classification: 84.9%).*



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Algorithm Proposed - Cysique

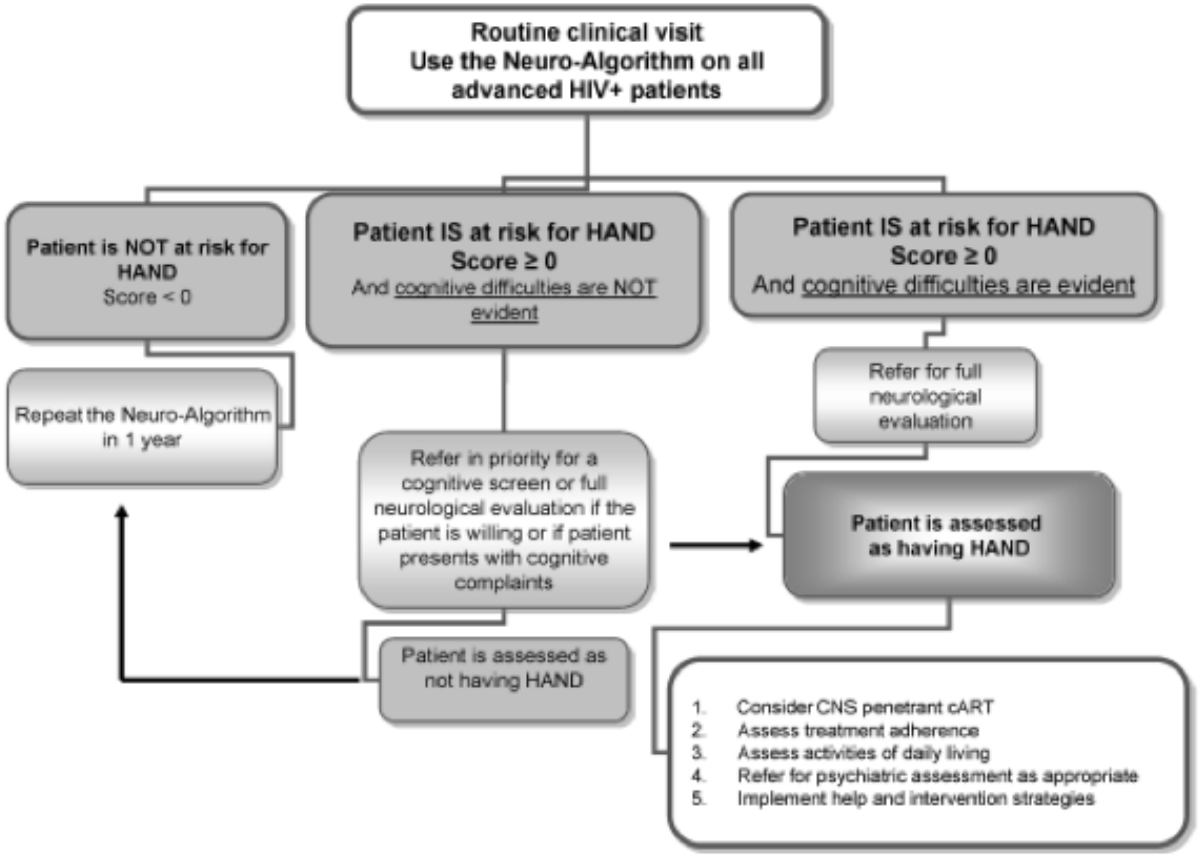

Fig. 1 Suggested algorithmic approach for the detection of cognitive impairment in HIV-infected individuals.

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Algorithm Proposed

2 prior aspects...

- Applicable regardless of ART status: both in ART-naïve or experienced patients

- Based only on assessment and monitoring, not interventions (!)

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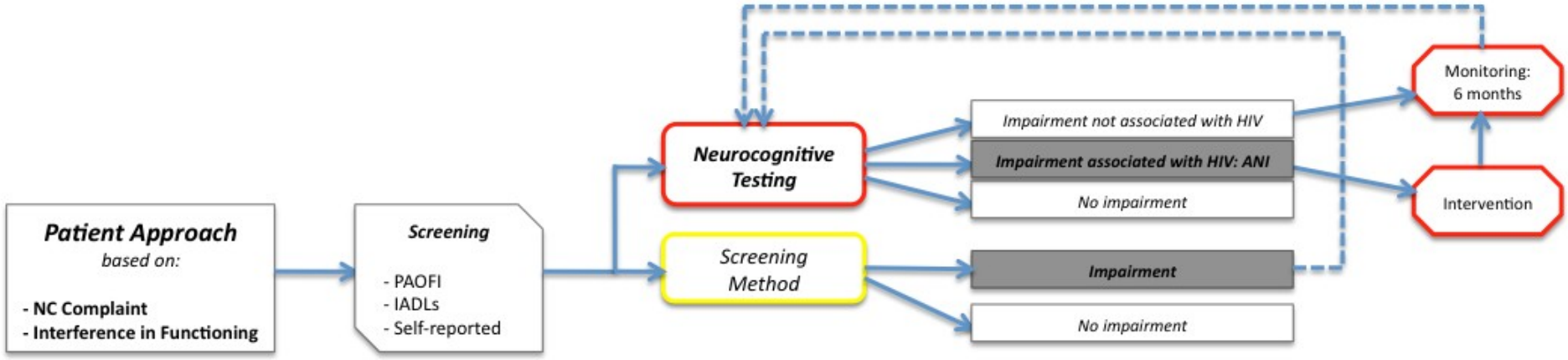
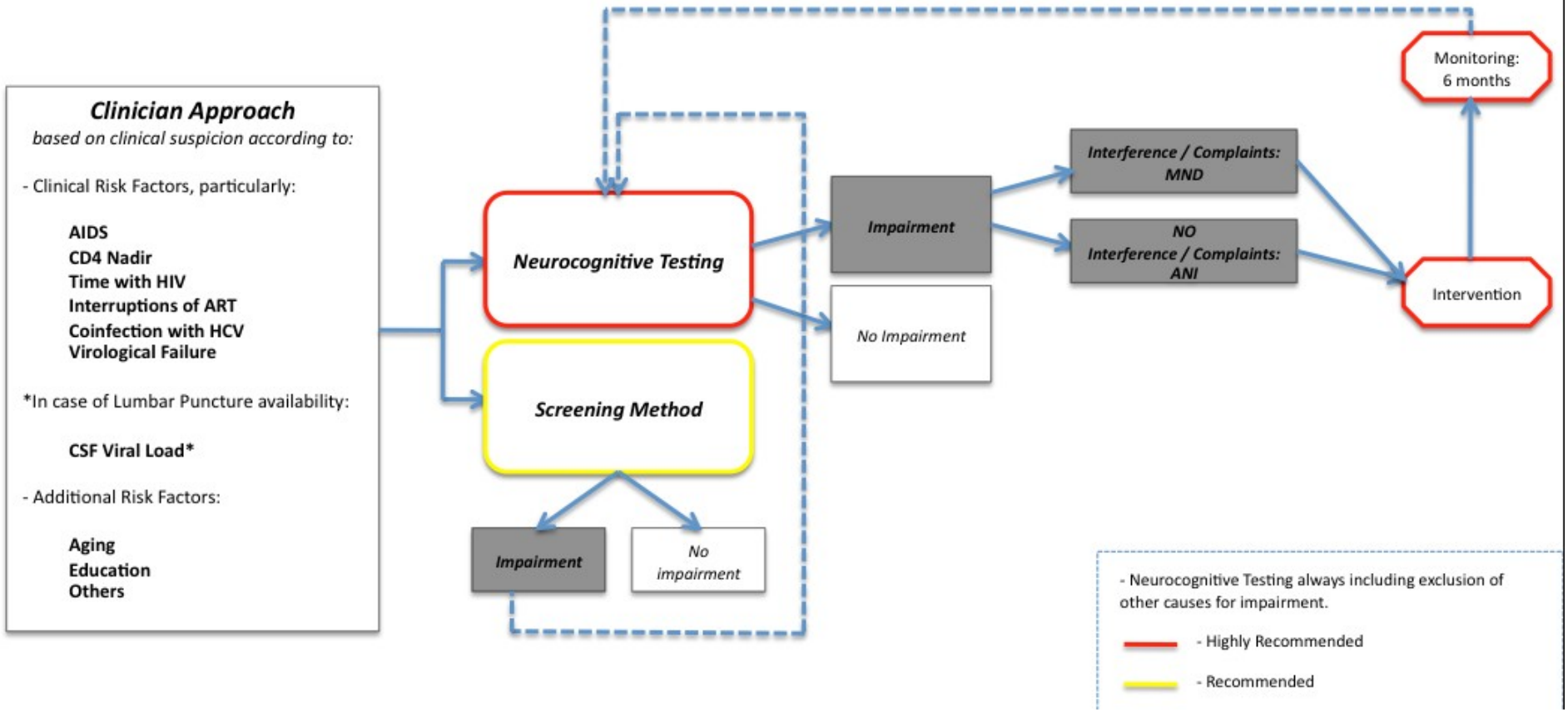
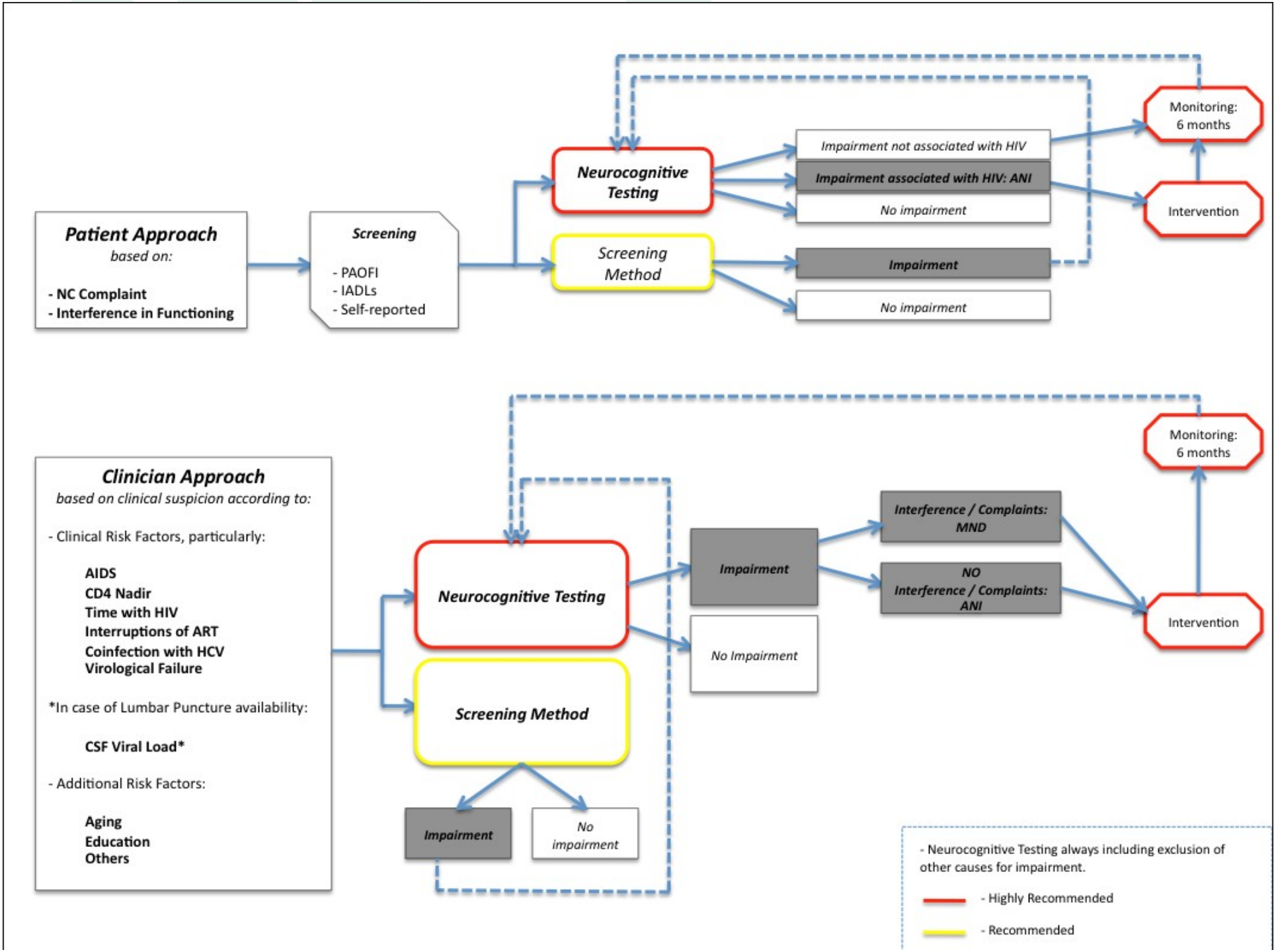


- Neurocognitive Testing always including exclusion of other causes for impairment.

- Highly Recommended

- Recommended


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


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
Neurocognitive Testing
Screening Method
Impairment
No Impairment
Interference / Complaints: MND
NO Interference / Complaints: ANI
Impairment
No impairment
Monitoring: 6 months
Intervention
- Neurocognitive Testing always including exclusion of other causes for impairment.
- Highly Recommended
- Recommended

Training in Neuropsychological Skills

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Training in Neurocognitive and Neuropsychiatric Aspects in HIV Infection

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- Duration: 2 days / 15 hours
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B: Interventions and Clinical Management

C: Use of Neuropsychological Tests

- Contact E-mail: info.fls.germanstrias@gencat.cat

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Many Thanks!

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