





Ancillary Tests in Cognitive Impairment

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Learning Objectives

At the end of this lecture, participants should be able:

To understand the <u>concept of cognition and</u> <u>classification of neurocognitive disorders</u>

To understand principles of assessment of cognitive function, particularly instruments relevant to SSA

To highlight ancillary tests in cognitive impairment

Cognition

- The mental processes of:
- ✓ acquisition, organization, storage and retrieval of knowledge
- thinking, understanding, and engaging with self and the environment

Importance of Cognition

"Cogito ego sum"

Rene Descates

"I think, therefore, I am"

Essentials of cognitive ability

Alert mind / awareness of self in contact with the environment Being able to think and reason

Cognitive Domains





Brain Networks



Bigler ED. 2016. Systems Neuroscience;10:35

Neurocognitive Disorders

Group of diseases characterized by <u>decline/impairment in one</u> or more cognitive domains

Diagnosis can be clinically overt or may be asymptomatic

May be combined with loss of independence/ loss of capacity to do activities of daily living

The most severe form is <u>Dementia</u>

Cognitive Profile



ADL normal, Cognitive decline

Severe cog. deficits Impaired ADL Need for supervision

Trajectory of Cognition



Function

Time

Mild Cognitive Impairment

- Transitional state between normal aging and dementia
- Cognitive deficits present but functioning preserved
- Inherently 'unstable condition' at both extremes
- Divided into amnestic and non-amnestic types
- Amnestic type at greater risk of developing AD



Petersen RC, Continuum 2004 10:9-28





Clinical syndrome characterized by cognitive decline in one or more domain(s)[memory, language, judgment etc.], sufficiently severe to cause impairment in social or occupational functioning, in the conscious and alert state.

Approach to the patient with dementia

History:

- Try and speak to the patient and also a relative
- Ask about:
 - » Symptoms at onset
 - » Pattern and speed of evolution
 - » Impact on work/family life/ Family history
 - » Risk factors (e.g. vascular, alcohol)
 - » Past medical history
 - » Treatment history

Approach to the patient with dementia

- Determine dominant cognitive features and stage of disease
- Determine pattern of progression
- Exclude treatable causes (trauma, infection, drugs, metabolic diseases etc)
- Examine for focal signs
- Examine for movement disorders
- Investigate and initiate treatment

Cognitive deficits in dementia

- Memory problems typical of Alzheimer's disease
- Disturbed language functions (aphasia) FTD, AD
- Problems with recognition of objects previously perceived (agnosia)
- Impaired reasoning, judgment, slow mental processing (Executive function impairment) – VCI, HAND

Pattern of presentation of some dementia syndromes



ICD-10 Dementia criteria

- **G1- Decline in memory** (first, inability to learn new information then loss of previously learned information)
- This should be supported by cognitive testing and interview of a reliable informant
- AND
- Decline in other cognitive areas such as judgement and thinking and planning and organising (must be decline from previous level of functioning NB learning disability)
- G2 no clouding of consciousness (i.e. no delirium)
- **G3 Decline** in social functioning, motivation or emotional control (apathy, coarsening of social behaviour, irritability) Essentially evidence of a change in functional ability
- G4 Present for at least 6 months
- Mild/Moderate/Severe
- With additional symptoms (behavioural and psychological symptoms of dementia (depression, delusions, psychosis) Up to 90% have these

DSM-V Major Neurocognitive Disorder (Dementia)

- 1. Evidence of significant cognitive decline from a previous level of performance in <u>one or more</u> cognitive domains such as <u>complex attention</u>, <u>executive</u> <u>function</u>, <u>learning</u>, <u>memory</u>, <u>language</u>, <u>perceptual-motor or social cognition</u>
- Evidence should consist of history of significant decline (from patient, reliable informant or clinician)

AND

- Impairment in cognitive performance from standardised neuropsychological testing (or another assessment if this is not available
- 2. The cognitive deficits interfere with independence in everyday (functional) activities (at a minimum, assistance with complex activities of daily living such as paying bills)
- 3. Not occurring only in delirium and not better explained by another mental disorder
- Specify subtype (see criteria for subtypes of dementia)

Differences with DSM-V criteria

- NCD acquired, rather than developmental disorders -represent decline. Due to underlying brain pathology.
- 'Dementia' typically refers to degenerative diseases in older people, whereas NCD expands category to diseases in younger people.
- Allows for one area of deficit only (i.e. amnestic syndrome, cognitive impairment post head injury) except in Alzheimers disease
- For degenerative dementias, use consensus guidelines for dementia subtype in addition to DSM-V.

NOT dementia

- **DELIRIUM**: an acute confusional state (causes include infection, malignancy, etc.)
- **PSYCHIATRIC PROBLEMS ("pseudodementia"):** e.g. depression, anxiety. Relatively abrupt onset often with identifiable trigger. Should not progress



Delirium: definition

A complex disorder typically of acute onset and fluctuating course which manifests as

- attention deficit or disturbance of awareness

- impaired cognition that may involve any or all of the following domains: memory, orientation, visuospatial and executive functions

- sleep wake cycle disturbance

. Psychomotor disturbances (hypo- or hyperactivity and mixed forms with unpredictable shifts from one to the other

Perceptual disturbances

- of enough severity to have a negative impact on the individual

Delirium: "off the track"

'Acute confusional state'

Major Causes of Delirium (HIDE)

- Hypoxia
- Infections
- Drugs
- Electrolyte disturbances

Delirium vs. Cognitive impairment/Dementia

Feature	Delirium	Dementia
Onset	Acute	Gradual (insidious)
Duration	Hours- weeks	Months-years
Course	Fluctuating	Progressive deterioration
Consequences	Impaired	Motor skills
Perceptual disturbance	Common	Occurs late stage
Sleep-wake cycle	Disrupted	Usually normal (except late stages)
Prognosis	Potentially reversible	Irreversible
Primary effects	Attention	Memory (Working / amestic)
Medical Emergency	Yes	Νο

Figure 1. Factors Contributing to Changes in Neurotransmitters, Leading to Delirium



How to diagnose delirium without investigations?

Single Question in Delirium (SQiD): 'Do you think [name of patient] has been more confused lately? Sensitivity and specificity of 80% (95% CI 28.3-99.49%) and 71% (41.90-91.61%) respectively compared to CAM





Sands MB et al, Palliat Med 2010; 24:561-5

Cognitive Function Assessment

Neuropsychometric Assessment

 Cognitive function tests have been used and developed over several years

 Neuropsychometric batteries may contain several components to test different cognitive abilities, e.g.
 CANTAB, CAMCOG, ADAS-Cog etc.

• The Mini-Mental State Examination (MMSE)- widely used. Montreal Cognitive Assessment (MoCA) test.

• Value of informant questionnaires eg IQCODE

Neuropsychological Test Criteria: General considerations

- Quality of the standardization sample
- Psychometric qualities
- Portability
- Brevity
- Cost
- Ease of use
- Domain specificity (for 1-hour battery)
- Availability of multiple forms
- International or cross-cultural capability
- The lack of ceiling and floor effects

Mini-Mental State Examination

- MMSE is a short test which measures general cognitive status including short-term memory (Folstein, et al, 1975)
- MMSE includes tests for orientation (e.g. year, season, etc.), registration, attention and calculation, recall, and language
- MMSE is a 30 points score test. Mildly cognitively impaired subjects can have scores 26 to 21



Montreal Cognitive Assessment (MoCA)





•MoCA also includes tests for orientation (e.g. year, season, etc.), registration, attention and calculation, recall, and language biased towards **Executive Dysfunction**

 MoCA a 30 points score test.
 Mildly cognitively impaired subjects can have scores 26 to 21



VCI and Cognitive Function after Stroke



American Heart Stroke Association

MoCA, ACE-R, and MMSE Versus the National Institute of Neurological Disorders and Stroke–Canadian Stroke Network Vascular Cognitive Impairment Harmonization Standards Neuropsychological Battery After TIA and Stroke Sarah T. Pendlebury, Jose Mariz, Linda Bull, Ziyah Mehta and Peter M. Rothwell

Stroke. 2012;43:464-469; originally published online December 8, 2011; doi: 10.1161/STROKEAHA.111.633586 Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231 Copyright © 2011 American Heart Association, Inc. All rights reserved. Print ISSN: 0039-2499. Online ISSN: 1524-4628

MoCA = Montreal Cognitive Assessment (30 point test)

ACE-R= Addenbrooke's Cognitive Examination– Revised (100 point test)

MoCA and ACE-R had good sensitivity and specificity for MCI defined using the **NINDS-CSN** Battery (Hachinski et al, 2006) 1 year after TIA and stroke but MMSE showed a ceiling effect

CogFAST – Nigeria: Vascular Neuropsychological Battery

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Cognitivo Domoin	Test
Cognitive Domain	Test
Executive Function	Category (Animal) Fluency Test
/Activation	
	Phonemic (Letter) Fluency Test
	Verbal Reasoning (Similarities Test)
	Ideational Fluency Test
Language/	Boston Naming Test (2nd version)
Lexical Retrieval	
Memory/ Learning	Word List Test (Learning, Recall,
	Recognition)
	Delayed Recall of Stick Design
Visuospatial/	Stick Design Test
Visuoconstruction	Modified Tokens Test
	(IU Token Test)
General Cognitive	Community Screening Instrument
Functioning	for Dementia (CSID
	Minimental State Examination
	(MMSE)

- Based on the 60 min VCI
 Harmonization Standards –
 Neuropsychological Protocol
 proposed by the NINDS –
 CSN (Hachinski et al, 2006).
- Multiple test items assessing each cognitive domain were selected in consonance with the recommendations of the Harmonization standards
- Utility of tests in previous cognitive evaluations in environment of study population

Refs: Folstein, 1995; Hall et al, 1993; 2000; Gureje et al., 1995; Blessed et al, 1991; Unverzagt et al., 1999; Ballard et al, 2002; Baiyewu et al., 2005; Akinyemi et al., 2008

The Vascular Neuropsychological Battery

CAMCOG – Executive Function/Activation

- i Category (Animal) Fluency Test
- ii. Phonemic (Letter) Fluency Test
- iii. Verbal Reasoning (Similarities Test)
- iv. Ideational Fluency Test
- v. Visual Reasoning Test

Language/Lexical Retrieval

• Boston Naming Test (2nd version)

□ Memory/ Learning

- Word List Test (Learning, Recall, Recognition)
- Delayed Recall of Stick Design

□ Visuospatial/Visuoconstruction

- Stick Design Test
- Modified Tokens Test

Computerized test items (Choice Reaction Time)



ROC Curve

Diagonal segments are produced by ties.

AUC: 081 - 0.88

Hachinski et al, Stroke. 2006;37:2220-2241 Akinyemi et al, J Neurol Sci. 2014 ;346(1-2):241-9.

Screening tools for dementia designed for use in SSA?

• MMSE is still the most widely used test – but almost useless in those with low education

Test	Questions	Sensitivity	AUROC
CSI-D	30 + 30	92	0.9191 (90–92)
TEST OF SENEGAL	39		0.967

- CSI-D validated in
 >2000 older people
 in LMICs (but only
 20 from SSA)
- False positive rate still 25% in low edu.
- Both tests take over 30-40 min to complete – too long for screening

The IDEA six-item cognitive screen

- Developed for low-literacy settings in sub-Saharan Africa
- Takes 5-10 minutes to administer
- Validated for dementia screening in community and geriatric OPD (Tanzania)
- Validated for major cognitive impairment (dementia or delirium) in older inpatients (Tanzania, Nigeria and Zambia)

The IDEA study brief screening test

- 6 item screening test
- Designed for non specialists and low literacy population
- Designed to cover all lobes of the brain
- Most discriminating questions from CSI-D (used in Hai dementia prevalence study)
- CERAD 10 word list learning
- Baiyewu matchstick test

	First attempt	Second attempt	Third attempt
Siagi			
Mkono			
Barua			
Mfalme			
Tikiti			
Nyasi			
Kona			
Jiwe			
Kitabu			
Fimbo			

Paddick et al. BMC Geriatr. 2015; 15: 53.

IDEA Screening tool -2

I will tell you the name of something and I want you to describe what it is. What is a bridge? (correct answer: something that goes across a river, canyon or road)	0 if incorrect 2 if correct	Score:/2
I want you to name as many different animals as you can in one minute.	Number of animals named: 0 for 0-3 animals named 1 for 4-7 animals named 2 for 8 or more animals	Score:/2
Who is the chief/head/leader of this village?	0 if incorrect 1 if correct	Score:/1
What day of the week is it?	0 if incorrect 2 if correct	Score:/2
Can you tell me any of the words you learned earlier?	1 one word 2 two words 3 three words 4 four words 5 5 or more words	Score: /5

Paddick et al. BMC Geriatr. 2015; 15: 53.

IDEA screening tool - 3



Paddick et al. BMC Geriatr. 2015; 15: 53.

IDEA Study Screening Tools

Matchsticks (Orientation) Test (Baiyewu et al 2003)

Subject asked to make the design shown above using four matchsticks. He/She is shown once and then they have **to** copy exactly

Score 1 for each part of the design that is performed correctly



Comparison with other cognitive screening tools commonly used in high income countries

TEST	Sensitivity	Specificity	Area under ROC
MMSE – specialist clinic (meta-analysis 34 studies)	79.8	81.3	
MMSE - mixed hospital (meta- analysis)	71.1	96.6	
RUDAS	89	98	0.95
Addenbrookes (meta-analysis 5 studies	96.7	77.4	
Six-item screener (for ER)	63	81	0.77
IDEA inpatients Tanzania	90.9	87.5	0.917
IDEA outpatients Tanzania > 8	84.6	89.1	0.919
IDEA inpatients Nigeria	100	96.3	0.990

Instrumental Activities of Daily Living in highincome countries

Instrumental Activities of Daily Living (IADL)

Instructions: Circle the scoring point for the statement that most closely corresponds to the patient's current functional ability for each task. The examiner should complete the scale based on information about the patient from the patient him-/herself, informants (such as the patient's family member or other caregiver), and recent records

Score

A. Ability to use telephone	<u>Score</u>	<u>E. Laundry</u>	Score
 Operates telephone on own initiative; 	1	1. Does personal laundry completely	1
looks up and dials numbers, etc.		Launders small items; rinses stockings, etc.	1
Dials a few well-known numbers	1	All laundry must be done by others	0
Answers telephone but does not dial	1		
Does not use telephone at all	0	F. Mode of transportation	
		 Travels independently on public 	1
B. Shopping		transportation or drives own car	
 Takes care of all shopping needs 	1	Arranges own travel via taxi, but does not	1
independently		otherwise use public transportation	
Shops independently for small purchases	0	Travels on public transportation when	1
Needs to be accompanied on any		assisted or accompanied by another	
shopping trip	0	Travel limited to taxi or automobile with	0
Completely unable to shop	0	assistance of another	
		5. Does not travel at all	0
C. Food preparation			
 Plans, prepares, and serves adequate 	1	G. Responsibility for own medications	
meals independently		 Is responsible for taking medication in 	1
Prepares adequate meals if supplied with	0	correct dosages at correct time	
ingredients		Takes responsibility if medication is	0
Heats and serves prepared meals, or	0	prepared in advance in separate dosages	
prepares meals but does not maintain		Is not capable of dispensing own medicatio	n O
adequate diet	-		
Needs to have meals prepared and served	0	H. Ability to handle finances	
D. Haveakaaning		 Manages financial matters independently 	1
D. Housekeeping		(budgets, writes checks, pays rent and bills,	
1. Maintains house alone or with occasional	1	goes to bank), collects and keeps track of	
assistance (e.g., "heavy work domestic help")		income	
2. Performs light daily tasks such as	1	2. Manages day-to-day purchases, but needs	1
dishwashing, bed making		help with banking, major purchases, etc.	
3. Performs light dally tasks but cannot		3. Incapable of handling money	U
A Needs help with all home maintenance tasks	. 1	(Lawton & Brody	1969)
 Neeus neip with all nome maintenance tasks Dees net participate in any bausekeeping 	, , , , , , , , , , , , , , , , , , ,	(Lawon a brody	,
tacke	5		

Scoring: The patient receives a score of 1 for each item labeled A - H if his or her competence is rated at some minimal level or higher. Add the total points circled for A - H. The total score may range from 0 - 8. A lower score indicates a higher level of dependence.

Sources:

- Cromwell DA, Eagar K, Poulos RG. The performance of instrumental activities of daily living scale in screening for cognitive . impairment in elderly community residents. J Clin Epidemiol. 2003;56(2):131-137.
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- Polisher Research Institute. Instrumental Activities of Daily Living Scale (IADL). Available at: http://www.abramsoncenter.org/PRI/documents/IADL.pdf. Accessed February 15, 2005.

Instrumental Activities of daily living (IADL) Scale

- 1. **Wanatoa Historia**/They give histories of the family, their life, past events
- 2. Wana suluhisha/They settle conflicts
- 3. **Wanasaidia shughuli ndogo ndog**o/They assist in small works in the home
- 4. Wanatoa ushauri/They give advice
- 5. **Wanadumisha na kufundisha mila/unyago**/They teach traditions of society
- 6. **Ni walinzi wa nyumban**i/They watch over the house when others are out.
- 7. Wanatunza wajukuu/they look after the grandchildren
- 8. **Wanatoa ushawishi**/Persuasion, or changing people's ideas for the better.
- 9. Wanasaidia katika maswala mazito kama sherehe/They preside over feasts and ceremonies
- 10. Wanapangia watu majukumu/Delegation of responsibilities to others.
- 11. Wanasimamia haki/They ensure fairness.

Results of combined screening, Hai Dementia screening programme

Assessment	Auroc
IDEA 6 item screen, used alone	0.846 (0.776-0.915)
IADL –SSA scale, used alone	0.896 (0.842-0.951)
IDEA 6 item screen and IADL-SSA used together	0.937 (0.896-0.979)

Conclusions

- The IDEA brief dementia screening tool performed well in hospital inpatient, outpatient and community settings
- This screening test should prove useful in screening for dementia in SSA
- Performance in the community was improved by addition of a functional assessment tool
- Further testing in of this system of dementia screening in other lowresource and community settings is required

Ancillary Investigations

Goals of Ancillary Tests in Neurocognitive Disorders

- To:
- Detect potentially reversible causes of cognitive impairment and dementia
- Detect co-morbidities that impact on outcomes
- Demonstrate in vivo degree of pathology in dementia subtypes.
- Map changes in brain structure and function

Investigations

- Brain Imaging Studies
- Full Blood Count
- Folate/Vitamin B12
- Thyroid Stimulating Hormone
- Blood Glucose
- Renal and Liver Function Tests
- Serological tests for Syphilis, Borelia VDRL
- HIV Serology
- CSF for Biomarkers and to exclude infections
- Electroencephalography

Blood Tests

- Folate
- Vitamin B12
- Thyroid Stimulating Hormone
- Calcium
- Glucose
- Full Blood Count
- Renal and Liver Function Tests
- Serological tests for Syphilis, Borelia VDRL
- HIV Serology

CSF analysis

- Indicated when vasculitis, inflammatory, haematological and demyelinating diseases are suspected
- Elevation of 14-3-3 protein +/- neuron specific enolase reflecting acute neuronal loss suggests CJD
- Elevated total tau or phospho-tau with decreased beta-amyloid 42 (Aβ42) suggest AD [sensitivity 86%; specificity 90%]
- CSF neurofilament light (nFL) protein in TBI and VCI

Neuroimaging

- <u>Structural Imaging</u>:
- MRI better than CT in demonstrating structural lesions and monitoring changes over time
- Hippocampal atrophy
- Vascular lesions including microbleeds, WMH, infarcts
- Diffusion Tensor Imaging disconnection syndromes
- Functional imaging fMRI, PET, SPECT
- To detect and measure cerebral blood flow, metabolic levels, receptor binding and pathological depositions

Figure 1



MRI Study in Older Nigerian Stroke Survivors

Medial temporal lobe atrophy (MTLA) was independently associated with VCI/VaD in PS survivors at 12 months

MTLA correlated significantly with cognitive performance and white matter hyperintensities (WMHs) on T2W MRI Akinyemi et al. BMC Res Notes (2015) 8:625 DOI 10.1186/s13104-015-1552-7



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RESEARCH ARTICLE

Medial temporal lobe atrophy, white matter hyperintensities and cognitive impairment among Nigerian African stroke survivors

Rufus O. Akinyemi^{1,2}, Michael Firbank², Godwin I. Ogbole³, Louise M. Allan², Mayowa O. Owolabi⁴, Joshua O. Akinyemi⁵, Bolutife P. Yusuf³, Oluremi Ogunseyinde³, Adesola Ogunniyi^{4†} and Raj N. Kalaria^{2*†}



**MTLA vs WMH score showed positive correlation (r =0.461, p = 0.002) supporting a vascular basis for MTLA.



Akinyemi et al, BMC Res Notes. 2015 ;8:625

	Normal vs vCIND		,	vCIND vs PSD		Normal vs (vCIND + PSD)			
Variable	OR	95%CI	*p value	OR	95%CI	p value	OR	95%CI	*p value
MTLA rating	2.02	1.05 - 3.87	0.035				2.25	1.16 - 4.35	0.016
Log_TBV							0.01	0- 1996.50	0.260

Functional Imaging: PET and SPECT Tracers

Tracer	Target
[99mTc] ethylcysteinatedimer	Cerebral blood flow
[18F] 2-fluoro-2-deoxy-D- glucose	Cerebral glucose metabolism
[123I] iodobenzamide	Dopamine D2/D3 receptor
[11C] Pittsburg compound B	Amyloid – beta plaques
[18F]Flortaucipir (AV1451)	Neurofibrillary tangles

Brain Amyloid Imaging



Rowe et al. J Nucl Med 2011; 52:1733-1740

PET Imaging of Tau Deposits





Okamura et al. Clin and Transl Neuroimaging. 2018; 6(4); 305-16

FDG PET Imaging Metabolic Patterns in Different Dementia Phenotypes



Heiss et al. BMC Medicine. 2016;14:174

Take Home Points

• Evaluation of subjects with cognitive and dementia requires formal cognitive testing

Useful cognitive tools exist in SSA

 Ancillary tests are useful in detecting reversible dementias, co-morbidities and evaluating pathological deposits and metabolic activities.

