ADC Administrators Meeting
Vancouver, BC
April 18, 2016

Neurology for the Non Neurologist

Steven T. DeKosky, MD, FACP, FAAN
Interim Executive Director, McKnight Brain Institute
Aerts/Cosper Professor of Alzheimer's Research
Professor of Neurology, Neuroscience, and Aging and Geriatrics Research
Assoc. Director, 1Florida Alzheimer's Disease Research Center
University of Florida College of Medicine

Disclosures

Consultant/Advisory Boards :

- Acumen Pharmaceuticals
- Biogen
- Cognition Therapeutics
- Roche

1 Florida ADRC

NIH National Institutes of Health
Turning Discovery Into Health

Todd Golde, MD, PhD, UF, Director

Ranjan Duara, MD, Mt. Sinai Med. Ctr., Miami Beach, Associate Director

Participating institutions in Florida

UNIVERSITY OF FLORIDA

FAU FLORIDA ATLANTIC UNIVERSITY

miami

FIU FLORIDA INTERNATIONAL UNIVERSITY

…true interdisciplinary collaborations

Overview

- Importance of the neurological examination
- Always do the exam in the same order:
  - Less likely to leave something out
  - Can go deeper into a particular part of the exam if necessary by findings or by complaint or symptom

- *"The history tells you what it is; the exam tells you where it is."*

1 Florida ADRC

Sequence of the Neurological Evaluation

- Chief Complaint (from patient *and* partner)
  - Especially if the complaint is cognitive
- History of the present illness:
  - How long has it been doing on?
  - Started suddenly or slow/insidious?
  - Stable now, recovering, or worsening?
- Medical history: other disorders; family history of diseases, especially similar symptoms; medications started around the time symptoms emerged

1Florida ADRC

Neurological Evaluation

- Review of systems: heart, lungs, GI, GU, etc.
- Social history: birthplace, languages, level of education, work history, smoking, alcohol, drug use, marriage, children, residential history
- Psychiatric History: depression or FH of depression; anxiety disorder, other

1Florida ADRC

Purpose of Neurological Exam

- Exam is an extension of the history to:
  - **Affirm** the presence of disease
  - **Confirm** anticipated features
  - **Localize** the disease process
  - Occasionally **provide a clue to etiology** (e.g. bruit, cardiac murmur, skin rash, etc.)

- It is part of a process of problem solving – the foundation for "thinking like a neurologist"

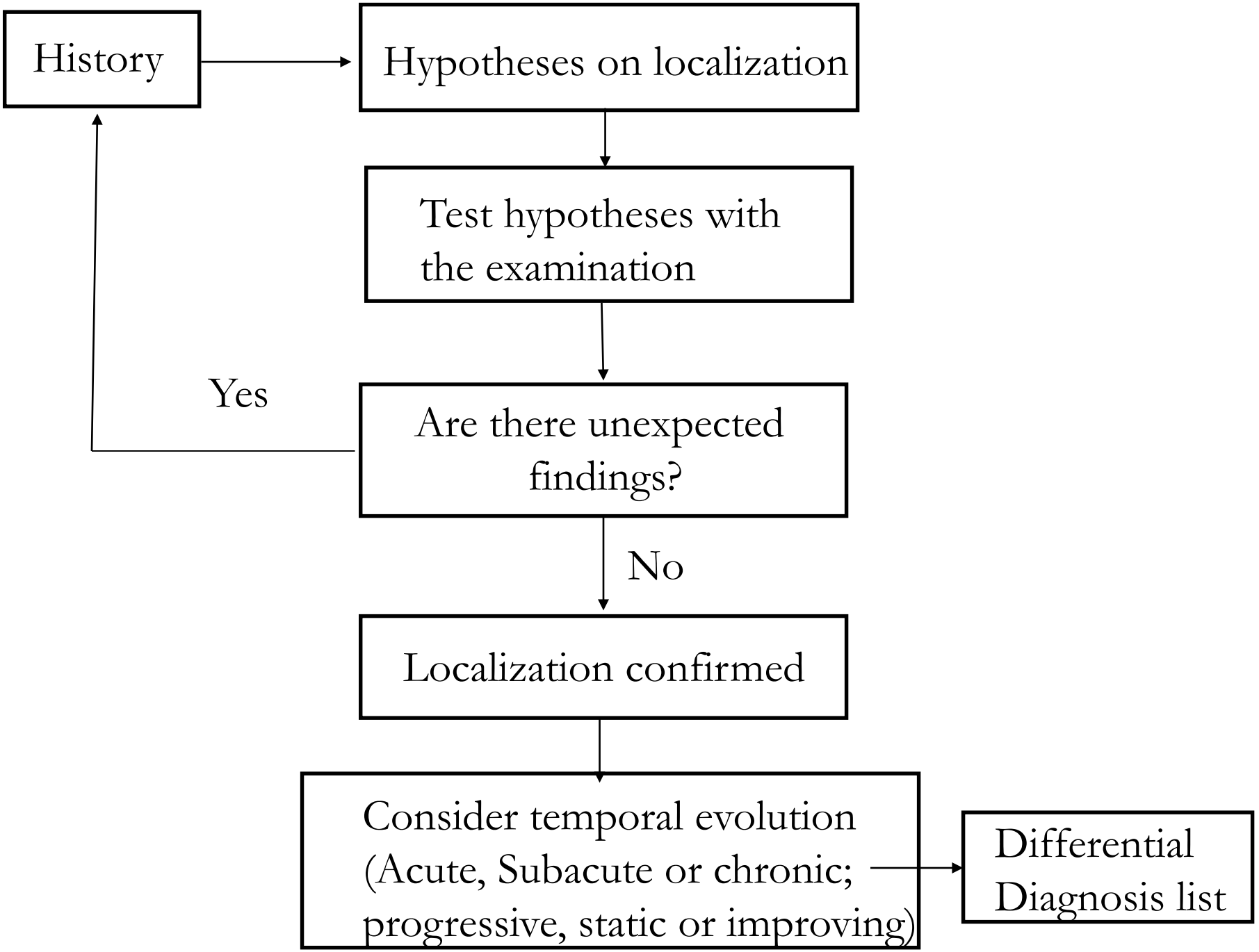
1Florida ADRC

Neurologic Exam

- At the end of the history you should already have a prioritized list of possible localizations
  - Formulate ideas during the interview

- The examination enables distinguishing among possibilities

1Florida ADRC


History
Hypotheses on localization
Test hypotheses with the examination
Are there unexpected findings?
Yes
No
Localization confirmed
Consider temporal evolution (Acute, Subacute or chronic; progressive, static or improving)
Differential Diagnosis list

Multiple causes of disease: VITAMIN C&D

V vascular

I infectious/inflammatory

T toxic or traumatic

A anoxia

M metabolic

I ictal (seizure)

N neoplasm

C congenital (genetic)

D degenerative, demyelinating

Now obviated by smartphone lists at the ready….

1Florida ADRC

Neurologic Examination

- Know how to expand upon each of the core examination categories:
  - **Mental status / Language**
  - **Cranial nerves**
  - **Sensory**
  - **Motor**
  - **Gait and Coordination**
  - **Reflexes**

1Florida ADRC

Formulating a case…

- Thinking like a neurologist
- Differential diagnosis and localization of lesion(s) while taking history and while doing examination
- Conclude with a differential diagnosis, localization of lesion, and studies to be done to confirm diagnosis (e.g, imaging, spinal tap)
- Therapeutic options if diagnosis confirmed
- Discussion with patient and family re diagnosis and prognosis (what does the future hold?)

1Florida ADRC

Mental Status Evaluation

- Orientation
- Attention
  - Forward/reverse digit span
  - Spell ‘world’ forward/backwards
- Fund of knowledge
  - Recent/past Presidents
  - Current events
- Memory
  - Encoding – list learning
  - Retrieval – list recall
- Language
  - Comprehension
  - Repetition
  - Fluency
  - Naming
  - Reading
  - Writing

1Florida ADRC

Mini-Mental State Exam

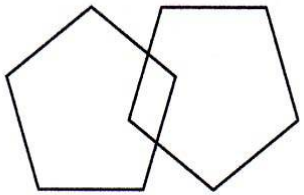
Folstein & Folstein

Folstein M, Folstein S, McHugh P. *Mini-Mental State. A practical method for grading the cognitive state of patients for the clinician.* J Psych Res 1975;12:189–198.

The Mini-Mental State Exam

Patient_____ Examiner _____ Date_____

Maximum	Score	
		Orientation
5	( )	What is the (year) (season) (date) (day) (month)?
5	( )	Where are we (state) (country) (town) (hospital) (floor)?
		Registration
3	( )	Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he/she learns all 3. Count trials and record. Trials _____
		Attention and Calculation
5	( )	Serial 7's. 1 point for each correct answer. Stop after 5 answers. Alternatively spell "world" backward.
		Recall
3	( )	Ask for the 3 objects repeated above. Give 1 point for each correct answer.
		Language
2	( )	Name a pencil and watch.
1	( )	Repeat the following "No ifs, ands, or buts"
3	( )	Follow a 3-stage command: "Take a paper in your hand, fold it in half, and put it on the floor."
1	( )	Read and obey the following: CLOSE YOUR EYES
1	( )	Write a sentence.
1	( )	Copy the design shown.

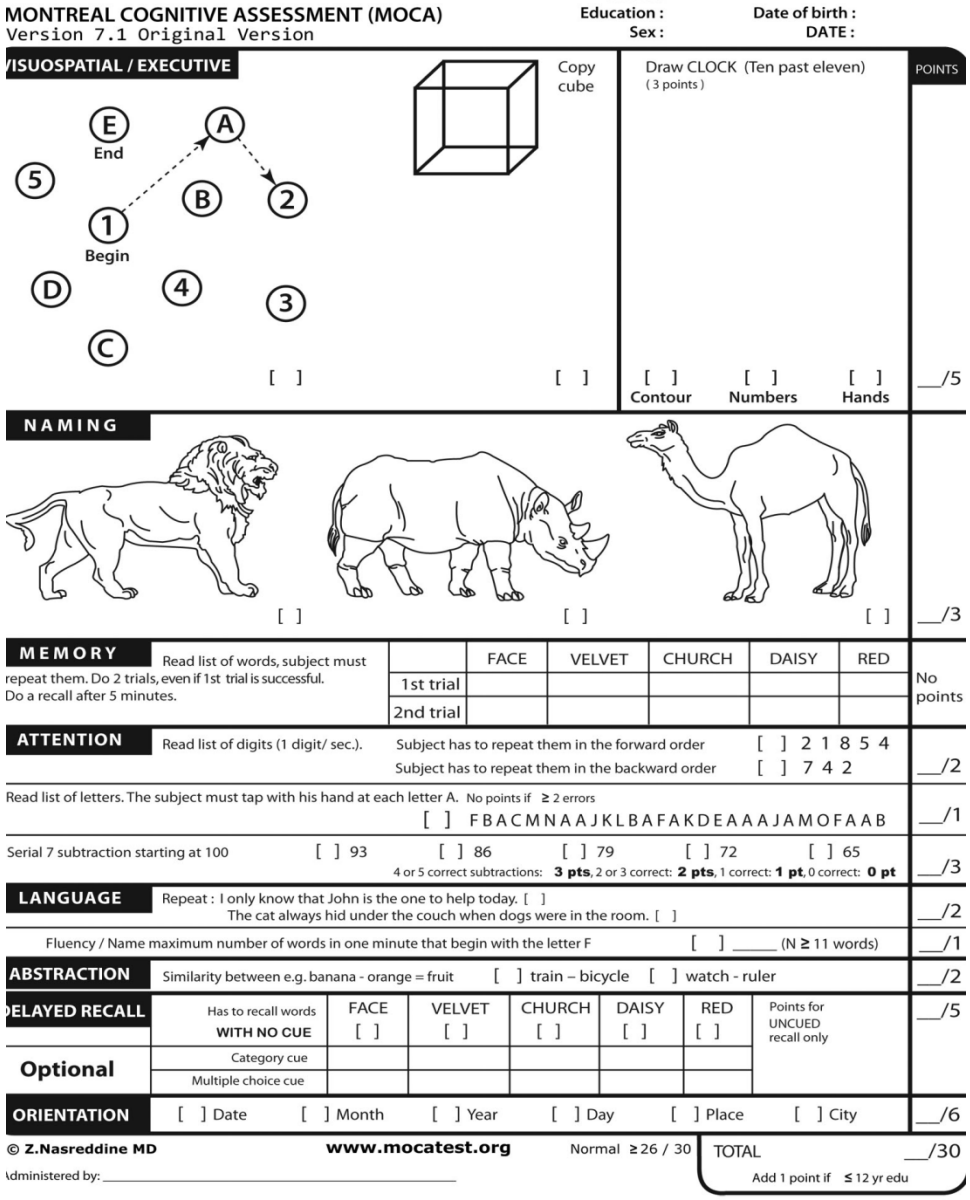


____ Total Score

ASSESS level of consciousness along a continuum _____

Alert Drowsy Stupor Coma

1 Florida ADRC



MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

Education :
Sex :

Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE

Copy cube

Draw CLOCK (Ten past eleven)
(3 points)

POINTS

E End
A
5
B
2
1 Begin
D
4
3
C

[ ] [ ] [ ] Contour [ ] Numbers [ ] Hands __/5

NAMING

[ ] [ ] [ ] __/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).
Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2 __/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B __/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt** __/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ] __/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words) __/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler __/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City __/6

© Z.Nasreddine MD www.mocatest.org Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

Montreal Cognitive Assessment (MoCA)

Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, Cummings JL, Chertkow H.
The Montreal Cognitive Assessment (MoCA): A Brief Screening Tool For Mild Cognitive Impairment.
Journal of the American Geriatrics Society 53:695-699, 2005

1 Florida ADRC

Applying these to Dementia…

Neurologic Findings that Alter Formulation of Alzheimer's Disease Diagnosis

- Age of onset below 55 without family history
- Focal weakness or sensory loss on one side or the other (structural lesion)
- Asymmetric reflexes (structural lesion)
- New onset of seizures (tumor, epilepsy, hemorrhage)
- Tremor or change in tone of limbs that suggests Parkinson's disease (PD? DLB?)
- Marked severity of language deficits and contralateral weakness or numbness (left hemisphere lesion)
- Findings on system exam suggesting other diagnoses: jaundice (hepatic encephalopathy), atrial fibrillation (emboli)
- Visual field deficits (structural lesion; emboli?)

1Florida ADRC

What is Alzheimer's Disease?

Alzheimer's disease is a progressive degenerative brain disease that slowly destroys memory and thinking skills

It is characterized by:

- Insidious onset, progressive loss of short-term memory, word finding deficits, reduced ability to plan, judge and organize (with a relative preservation of remote memory/social behavior)

- Progression to worsening of logical reasoning, language, loss of insight, behavioral symptoms, praxis, personal neglect, spatial orientation

- Severe stages show worsening of all cognitive processes, incontinence, myoclonus (involuntary jerk-like reactions) -> assistance in all Activities of Daily Living needed

Making the diagnosis of AD

- Evidence-based diagnostic guidelines
- No longer a diagnosis of exclusion!
- Indifference, denial, or lack of concern is common (confusion with ‘normal aging’)
- Anecdotes help make the diagnosis
- Biomarkers have diagnostic utility
- No longer true that you “don’t really know unless you get an autopsy”

Comorbidities: Aging doesn't come with just one disease…

Coexisting Condition	Percentage of People with Alzheimer's Disease and Other Dementias Who Also Had Coexisting Medical Condition
Coronary heart disease	30%
Diabetes	29%
Congestive heart failure	22%
Chronic kidney disease	17%
Chronic obstructive pulmonary disease	17%
Stroke	14%
Cancer	9%

Created from unpublished data from the National 20% Sample Medicare Fee-for-Service Beneficiaries for 2009.[107]

NINCDS/ADRDA Criteria for Probable Alzheimers Disease

- DEMENTIA established by clinical examination; confirmed by cognitive screening test (MMSE, Blessed)
- Deficits in TWO or MORE areas of cognition
- Progressive worsening of memory and other cognitive functions
- No disturbance of consciousness
- Onset between 40 and 90, most often after 65
- Absence of systemic disorders or other brain diseases that could account for the deficits and progression

McKhann et al. Neurology 1984;34:939-944

The 3 Stages of Alzheimer's Disease

- Preclinical: must have measureable changes in brain (MRI, PET), CSF, or blood before any cognitive symptoms present
- MCI Due to AD (Prodromal AD in IWG terminology)
  - Single domain, usually memory, impaired below expected for age and education
  - Measureable changes in brain (MRI, PET), CSF, or blood
- Dementia Due to AD
  - 2 domains impaired
  - Biomarkers show amyloid accumulation in brain
  - Biomarkers showing brain injury or degeneration

From McKhann et al., 2011

McKhann Criteria 25 Years Later

1984

Clinical diagnosis of Alzheimer's disease:

Report of the NINCDS-ADRDA Work Group* under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease

Guy McKhann, MD; David Drachman, MD; Marshall Folstein, MD; Robert Katzman, MD; Donald Price, MD; and Emanuel M. Stadlan, MD

ELSEVIER

Alzheimer's & Dementia 7 (2011) 263–269

Alzheimer's & Dementia

2011

The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease

Guy M. McKhann[a,b,*], David S. Knopman[c], Howard Chertkow[d,e], Bradley T. Hyman[f], Clifford R. Jack, Jr.[g], Claudia H. Kawas[h,i,j], William E. Klunk[k], Walter J. Koroshetz[l], Jennifer J. Manly[m,n,o], Richard Mayeux[m,n,o], Richard C. Mohs[p], John C. Morris[q], Martin N. Rossor[r], Philip Scheltens[s], Maria C. Carrillo[t], Bill Thies[t], Sandra Weintraub[u,v], Creighton H. Phelps[w]

AD as a Continuum:
New Research Diagnostic Criteria

Research Criteria Today, Operational in a Few Years?

The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for AD

May 2011 (Vol. 7 | No. 3 | Pages 263-269)

Guy M. McKhann, David S. Knopman, Howard Chertkow, Bradley T. Hyman, Clifford R. Jack, Claudia H. Kawas, William E. Klunk, Walter J. Koroshetz, Jennifer J. Manly, Richard Mayeux, Richard C. Mohs, John C. Morris, Martin N. Rossor, Philip Scheltens, Maria C. Carrillo, Bill Thies, Sandra Weintraub, Creighton H. Phelps

The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for AD

May 2011 (Vol. 7 | No. 3 | Pages 270-279)

Marilyn S. Albert, Steven T. DeKosky, Dennis Dickson, Bruno Dubois, Howard H. Feldman, Nick C. Fox, Anthony Gamst, David M. Holtzman, William J. Jagust, Ronald C. Petersen, Peter J. Snyder, Maria C. Carrillo, Bill Thies, Creighton H. Phelps

Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for AD

May 2011 (Vol. 7 | No. 3 | Pages 280-292)

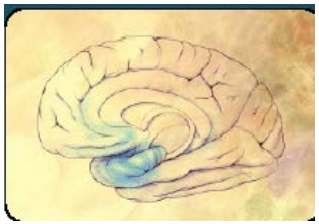
Reisa A. Sperling, Paul S. Aisen, Laurel A. Beckett, David A. Bennett, Suzanne Craft, Anne M. Fagan, Takeshi Iwatsubo, Clifford R. Jack, Jeffrey Kaye, Thomas J. Montine, Denise C. Park, Eric M. Reiman, Christopher C. Rowe, Eric Siemers, Yaakov Stern, Kristine Yaffe, Maria C. Carrillo, Bill Thies, Marcelle Morrison-Bogorad, Molly V. Wagster, Creighton H. Phelps

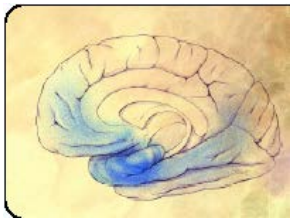
What has changed in the Criteria?

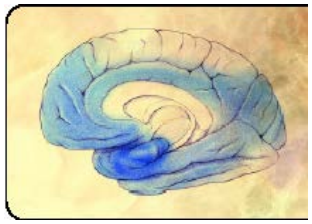
- 1984: based on clinical judgment
  - Input from patient, family, neuro exam, cognitive tests
- 2011: two notable changes
  - THREE stages of AD: preclinical, MCI, AD
  - Biomarkers included, notably in CSF and neuroimaging

Alzheimer's Disease:
A Continuum of Pathological & Clinical Progression

Intervention	Primary Prevention		Early Treatment	Treatment
Clinical State	Normal	"Pre-symptomatic" AD	Mild Cognitive Impairment	AD
Brain Pathologic State	No Disease No Symptoms	Early Brain Changes No Symptoms	AD Brain Changes Mild Symptoms	Mild, Moderate, or Severe Impairment







Disease Progression