Mild Cognitive Impairment

James Y Lin, DO, MHSA
Program Director, LIGHT (GWEP)
VP Senior Services & Adult Living
Medical Director, LECOM Senior Living Center
Director, LECOM Institute for Successful Aging

LIGHT
LAKE ERIE INTEGRATED GERIATRIC HEALTH TEAM

LECOM HEALTH

Objectives

2

- Understand the risks for and causes of cognitive impairment
- Incorporate screening evaluation of patients at risk
- Plan treatment strategies to minimize the personal, social and financial impacts

Cognitive Continuum

Normal

Mild Cognitive Impairment

Dementia

LIGHT

LECOM HEALTH

Spectrum of cognitive changes

4

Asymptomatic

↓

Normal Cognitive Aging

↓

Subjective Cognitive Aging

↓

Mild Neurocognitive Disorder

↓

Major Neurocognitive Disorder

LIGHT

LECOM HEALTH

Cognitive functions that are vulnerable to the effects of aging

5

Processing Speed

General control processes "executive functions" *

Working Memory *

Inhibitory Control

Long Term Memory

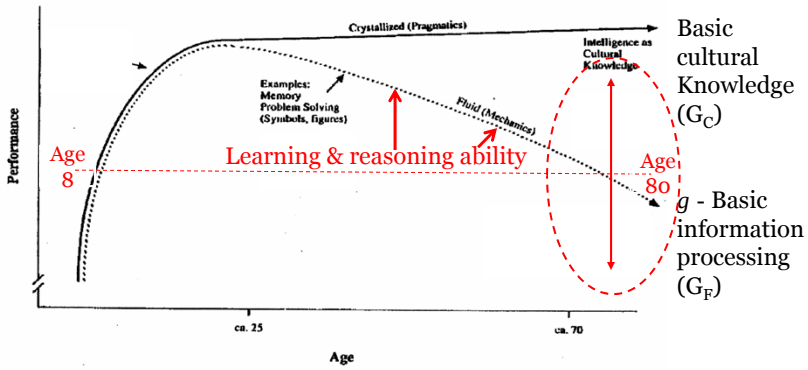
Sensory Perception

LIGHT

LECOM HEALTH

Normal age-related cognitive decline

6



Basic cultural Knowledge (G_C)

g - Basic information processing (G_F)

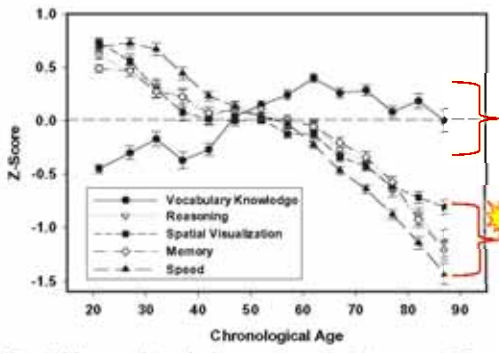
LIGHT

LECOM HEALTH

Age-related cognitive decline

Normal age-related cognitive decline

A finer-grained look



"Crystallized" intelligence [past learning]

- Breadth/depth of general knowledge (e.g., language)
- Accrued over lifetime based on fluid intelligence, education, interests

"Fluid" intelligence [on-the-spot learning & reasoning]

- Aptness in processing information (e.g., learning, reasoning, abstract thinking, problem solving)
- Includes executive function, working memory
- Reflects overall integrity of brain (speed, connectedness, etc.)

***This is the norm, but individuals vary a lot around the norm!**

Source: Figure 1 in Salthouse, T. A. (2009). Selective review of cognitive aging, *J of Int Neuropsych Soc, 16*, 754-760.

LIGHT

LECOM HEALTH

Mild neurocognitive disorder

8

- Cognitive decline abnormal for age and education but does not interfere with function and activities
- "At risk" state to develop a degenerative dementia
- When memory loss predominates, termed Amnestic MCI. This has ~15% per year of conversion to AD.

LIGHT

LECOM HEALTH

Mild neurocognitive disorder

9

- Significant, but less severe cognitive deficit
- Need to develop compensatory behaviors that limit the impact of cognitive decline
- May need more accommodation to maintain day-to-day function
- Interference with daily activities may not be noticeable but higher-level cognition is likely affected

Adapted from the American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders: **DSM-5**. Washington, D.C: American Psychiatric Association.

LECOM HEALTH

What Is Dementia?

10

- Impairment in intellectual function affecting more than one cognitive domains
- Interferes with social or occupational function
- Decline from a previous level
- Not explained by delirium or major psychiatric disease

LIGHT

LECOM HEALTH

Major Neurocognitive Disorder (aka Dementia)

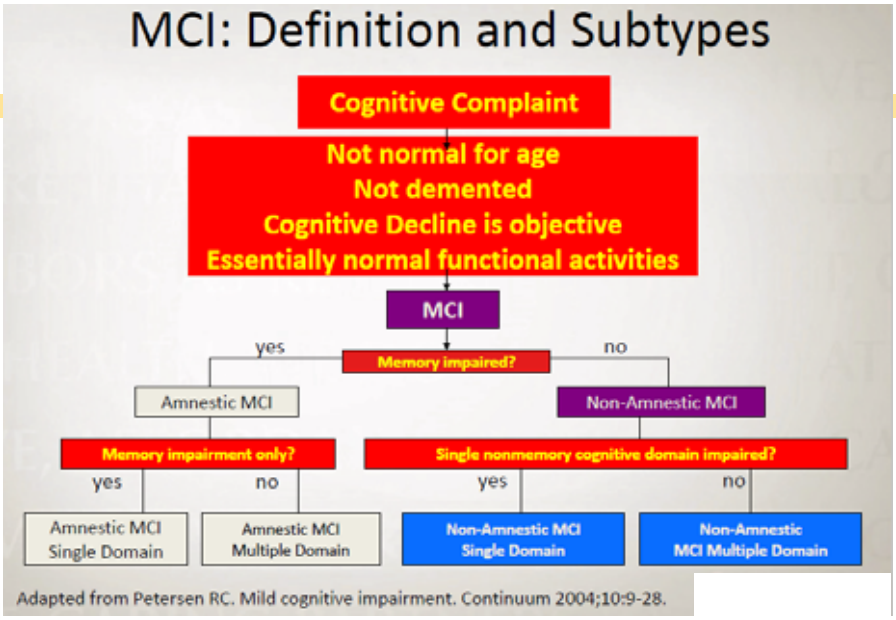
11

- A significant cognitive decline from a previous level of performance in one or more cognitive domains
- The cognitive deficits interfere with independence of everyday activities (i.e. iADLs)
- This is not delirium or another mental disorder

Adapted from the American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders: **DSM-5**. Washington, D.C: American Psychiatric Association.

LECOM HEALTH

12



LIGHT

LECOM HEALTH

Epidemiology: MCI

13

- Studies vary significantly due to:
  - Diagnostic criteria
  - Measuring instruments
  - Definitions
  - Use of population vs clinic-based samples
- Prevalence rate 2-4% to greater than 20%

LIGHT

LECOM HEALTH

Pathology: MCI

14

- Neuropathological studies suggest that MCI represents an early clinical expression of age-related neurodegenerative disease.
- Common autopsy findings have AD pathology, cerebrovascular disease, mixed type.

LIGHT

LECOM HEALTH

Evaluation: MCI

15

- The cornerstone of any evaluation of someone with memory loss is the clinical interview.

LIGHT

LECOM HEALTH

The HPI is critical!

16

- Ask a close informant
- Duration, rate, smoothness?
- Associated symptoms
  - Headache, trouble with vision, speech, strength, coordination, gait
- What domains are affected?
  - Repeats self? Forgets recent things? Appointments? Month & year? Trouble with appliances? Trouble planning? Change in personality, judgment, behavior? Navigation problems? Hallucinations? Word finding problems?
- How is function affected?
  - Finances, chores, hobbies, driving, occupation, social

LIGHT

LECOM HEALTH

Fill out the picture

17

- Medical problems and risk factors?
- Neurologic history (stroke, trauma, infection)?
- Educational background?
- Family history?
- Alcohol and drugs?
- Medications?

Remember, your first goal is to exclude readily treatable causes…

LIGHT

LECOM HEALTH

Example of Mild Cognitive Complaints

18

- A 64 yo overworked accountant is behind in his work and overwhelmed. He worries that his memory is failing and that he can't keep up with his responsibilities.
- He's using lists and GPS more and more. He came close to missing an important appointment, but was reminded of it, at the last minute.
- Assessment: normal MRI, but low scores in executive functioning and memory.

LIGHT

LECOM HEALTH

Example of Mild Cognitive Complaints

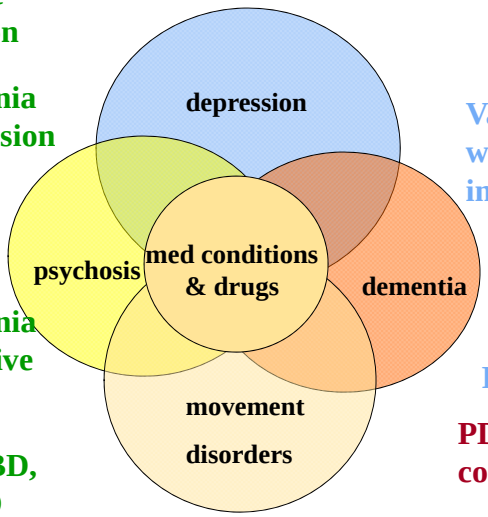
19

- A 68 yo attorney is forgetting appointments and relying more on her GPS.
- Her car, in neutral, rolled out of the driveway and hit a car.
- She paid a large bill twice and never recorded it in her checkbook.
- Assessment: apparent mild decline in memory storage and executive function

LIGHT

LECOM HEALTH

OVERVIEW: Consider main syndrome & comorbid conditions



Psychotic depression

Schizophrenia with depression

Schizophrenia with cognitive deficits

PDD, LBD, AD, VaD with psychotic sx

Schizophrenia with movement disorders

Depression with dementia ("pseudodementia")

Vascular depression with mild cognitive impairment

MCI with depression

Dementia with depression

PD with depression

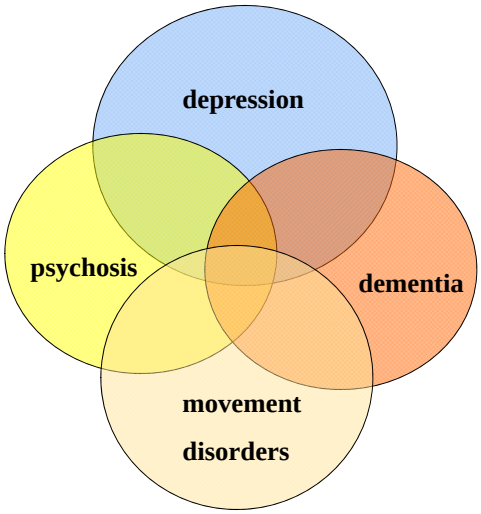
PDD, LBD, PD+ with cognitive deficits

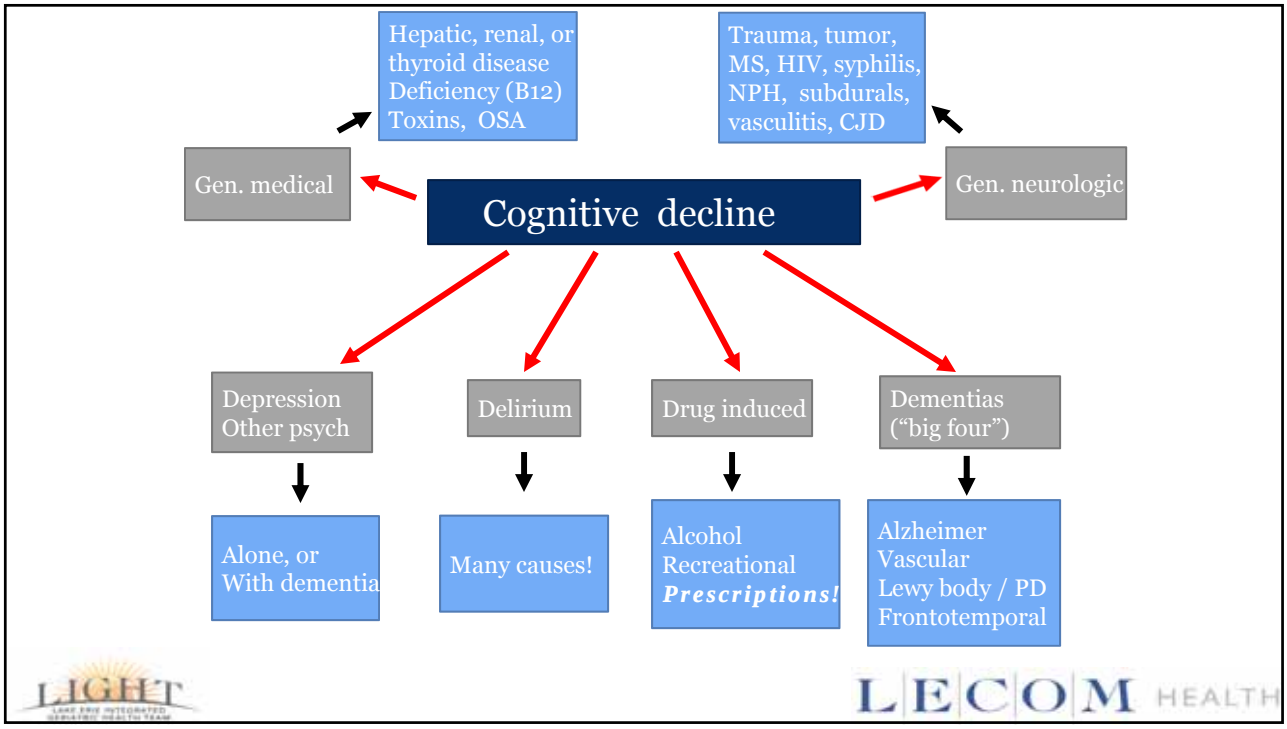
PDD, LBD, AD with movement sx

LIGHT

LECOM HEALTH

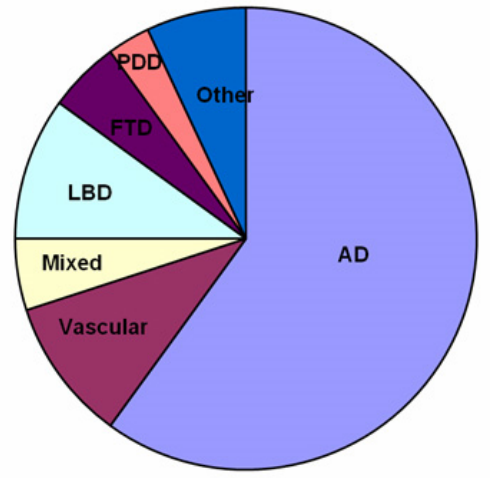
SYMPTOM OVERLAP: OVERVIEW





"Primary" dementias: the big ones

23



- AD= Alzheimer's
- LBD= Lewy Body dementia
- PDD= Parkinson disease dementia
- FTD= Frontotemporal dementia
- Vascular

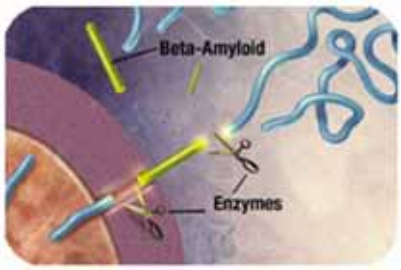
LIGHT

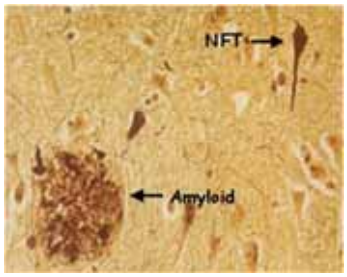
LECOM HEALTH

Alzheimer Disease (AD)

24

- Commonest neurodegenerative and dementing disease
- Prevalence doubles every 5 years after 65; ~50% of those older than 85





LIGHT

LECOM HEALTH

AD Risk Factors

25

- Age!!
- Mild cognitive impairment (MCI)
- ApoE-e4 positivity
- Family hx in first degree relative (especially if younger onset)
- Vascular risk (diabetes, heart disease, etc.)
- Low education and physical/social activity
- Female sex

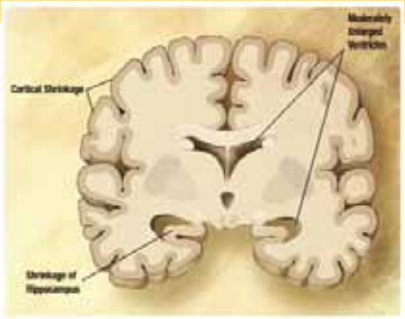
LIGHT

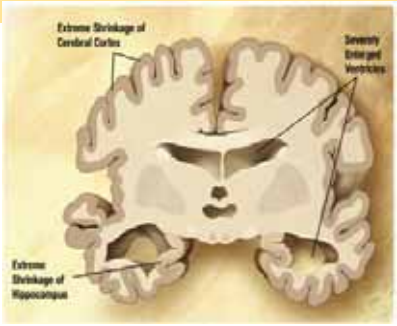
LECOM HEALTH

Mild-moderate AD

Severe AD

26





LIGHT

LECOM HEALTH

AD Clinical Features

27

- Earliest cognitive symptoms are usually poor short term memory; loss of orientation
- Smooth, usually slow decline without dramatic short-term fluctuations
- Other domains involved with time
- So common that many variations are seen

LIGHT

LECOM HEALTH

AD: Behavioral & Psych

28

- Depression, anxiety
- Irritability, hostility, apathy
- Delusions, hallucinations
- Sleep-wake changes
- Sundowning
- Agitation

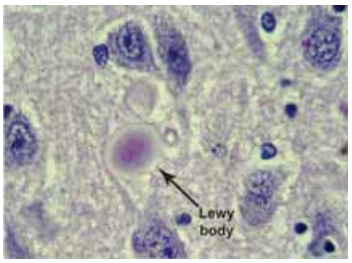
LIGHT

LECOM HEALTH

Dementia with Lewy Bodies (DLB)

29

- Relatively earlier occipital and basal ganglia degeneration
- Similar to Parkinson disease dementia
- α-synuclein aggregates into Lewy bodies
- Concurrent AD pathology is common



LIGHT

LECOM HEALTH

DLB Clinical Features

30

- Dementia (early on, visuospatial and executive) PLUS
  - Core features
    - Parkinsonism
    - Recurrent early visual hallucinations
    - Fluctuations (clue: recurrent delirium evaluations)
  - Suggestive features include REM sleep disorder (dream enactment) & neuroleptic sensitivity

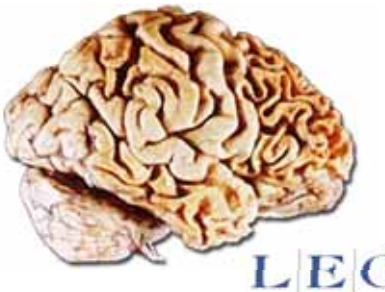
LIGHT

LECOM HEALTH

Frontotemporal Dementia (FTD)

31

- Average age of onset 58, rather than very old
- Often familial (30-50%)
- Overlap with progressive supranuclear palsy, ALS, and corticobasal degeneration
- Pathologic aggregates of tau or TDP-43



LIGHT

LECOM HEALTH

FTD clinical features

32

- Behavior and personality change (may be initially misdiagnosed as a psychiatric disorder)
- Executive dysfunction
- Progressive non-fluent aphasia
- May see parkinsonism or muscle weakness

LIGHT

LECOM HEALTH

Vascular Dementia

33

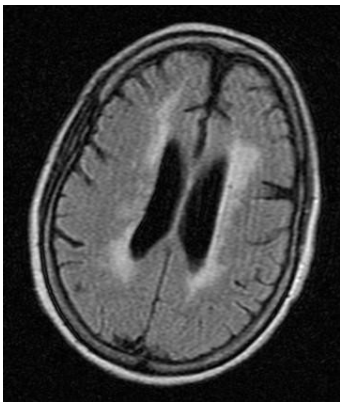
- Suspect when
  - Abrupt onset and/or stepwise decline
  - Fluctuating course
  - H/o stroke
  - Focal neurologic symptoms or signs
- Usually see bilateral infarcts
- Often associated with executive dysfunction, gait disorder, apathy, incontinence

LIGHT

LECOM HEALTH

"…evidence of chronic small vessel ischemic disease involving subcortical white matter"

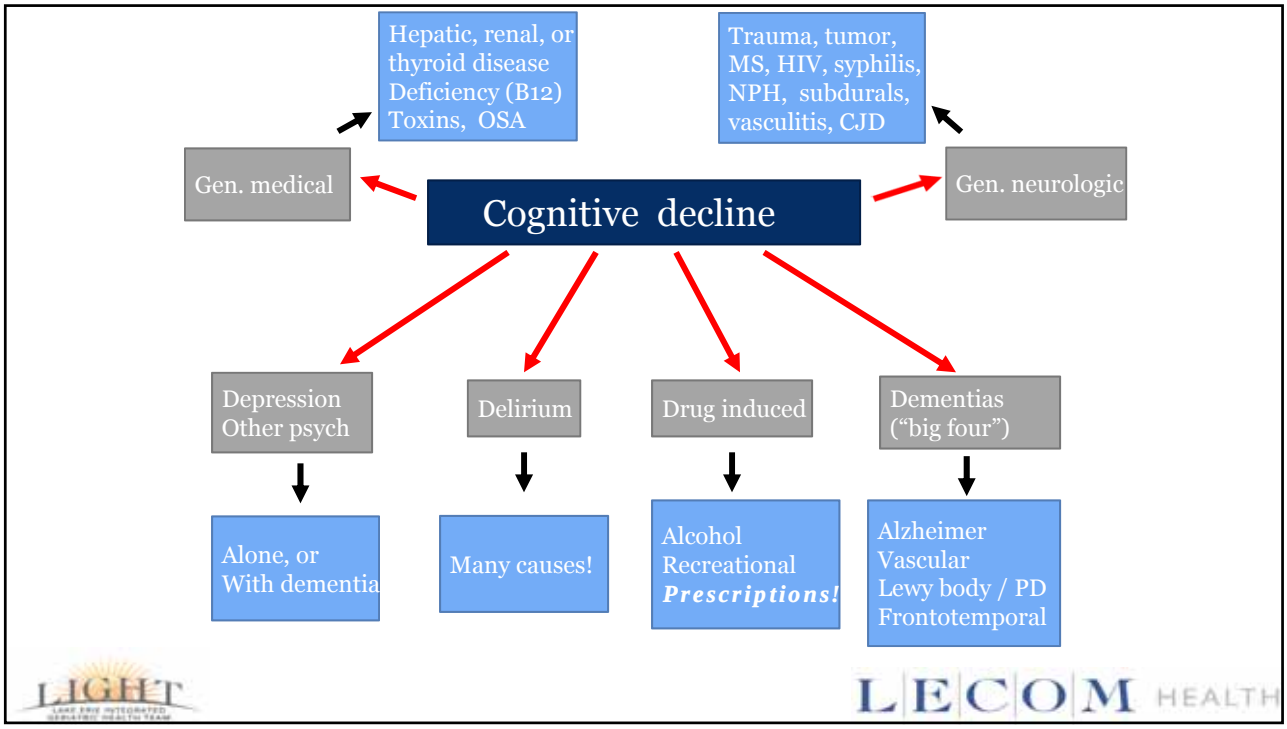
34



- This is nondiagnostic and very common with age
- Changes may or may not be symptomatic
- ≠ "Vascular dementia"
- Don't tell patients "Your scan showed strokes."

LIGHT

LECOM HEALTH



Differential diagnosis in dementia: More common treatable causes

36

- Structural brain lesion (subdural bleed)
- Thyroid disease
- B12 deficiency
- Untreated sleep apnea
- Depression or anxiety
- Alcoholism
- Meds: Benzos, opioids, anticholinergics (diphenhydramine, bladder drugs, tricyclics), neuroleptics, dopaminergics, other sedatives

LIGHT
LECOM HEALTH

Examination

37

- General neurologic exam
  - Any focalities that suggest stroke?
  - Signs of parkinsonism or a gait disorder?

- Cognitive screen
  - Mini-mental (MMSE)
  - Mini-cog
  - Montreal Cognitive Assessment (MoCA)
  - SLUM

Scale	Time to Administer, min*	Memory: Orientation	Memory: Registration Recall	Memory: Remote/ Over Learned Memory	Praxis, Visuospatial	Aphasia, Verbal Fluency	Attention	Abstraction	Executive Functioning Functional Status
Subjective questions to patient and informant	1-2								
6-Item Screener	1-2	X	X						
Clock Drawing	1-3				X				
3-Word Recall	3		X						
Mini-Cog	3-4		X		X				
Memory Impairment Screen	4		X						
Brief Alzheimer Screen	3-5	X	X			X	X		
AD8	3-5	X	X						X
General Practitioner Assessment of Cognition	4-5	X	X		X				X
Blessed Orientation Memory Concentration Test†	4-6	X	X				X		
Hopkins Verbal Learning Test	5		X						
Abbreviated Mental Test	5-7	X	X	X			X		
Informant Questionnaire for Cognitive Decline in the Elderly	5-7	X		X	X				X
Telephone Interview for Cognitive Status	7-9	X	X	X			X	X	
7-Minute Screen	7-9	X	X		X	X			
Montreal Cognitive Assessment	10	X	X		X	X	X	X	
Short Cognitive Evaluation Battery	8-12	X	X		X	X			
Short and Sweet Interview for Dementia	10	X	X		X	X	X		
Short Test of Mental Status†	10-12	X	X	X	X		X	X	
Mini-Mental State Examination	7-10	X	X		X		X		
Blessed Information Memory Concentration Test†	10-12	X	X	X			X		
Functional Activities Questionnaire†	10-15	X			X		X		X
Modified Mini-Mental State Examination	10-15	X	X	X	X	X	X	X	
Montreal Cognitive Assessment	10	X	X		X	X	X	X	X
Cognitive Assessment Screening Test	15‡	X		X	X				X
Cambridge Cognitive Examination	20	X	X	X	X	X	X	X	X
Psychogeriatric Assessment Scales	20-30‡	X	X	X	X		X		X

Holsinger et al JAMA. 2007;297(21):2391-2404

Diagnostic testing

39

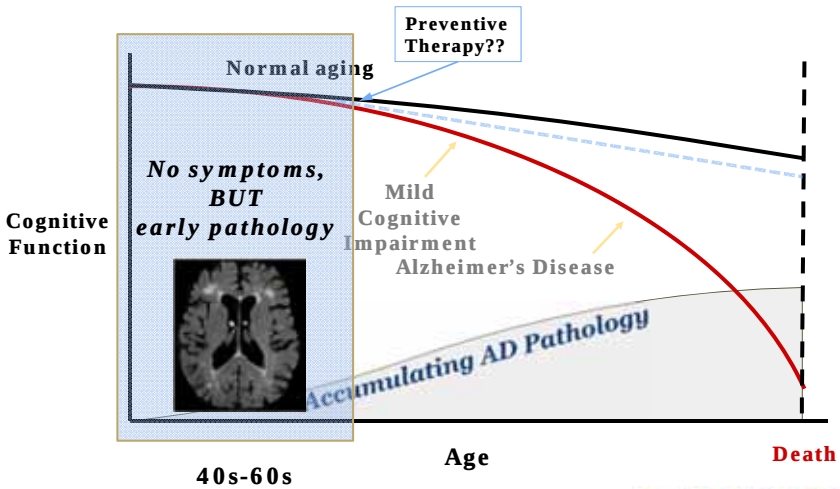
- There is no "dementia test panel"
- For slowly progressive "typical" dementia in adults >65, most essential tests: **B_{12}, TSH, brain image (CT is ok)**
- Neuropsychology testing can help but not mandatory
- FDG- PET approved to differentiate AD from FTD
- Amyloid-PET has just been approved
- PET studies have little value in most cases and are expensive
- For younger patients, or rapid or atypical course, workup may be "tiered" to target range of diagnoses, emphasizing treatable causes

LIGHT

LECOM HEALTH

Preclinical Stages of Alzheimer's Disease

40

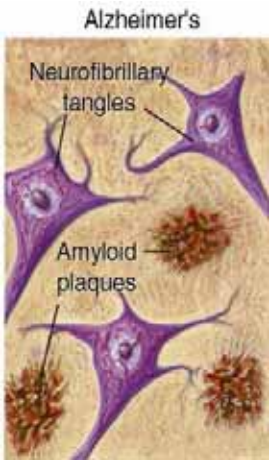


LIGHT

LECOM HEALTH

Identifying Asymptomatic At-Risk Adults

41



- ***Neuroimaging***
  - Magnetic resonance imaging (MRI)
    - Structure – atrophy, white matter hyperintensities
    - Function – cerebral blood flow
  - Positron emission tomography (PET)
    - FDG-PET – glucose uptake patterns
    - Amyloid imaging – amyloid burden
- ***Cerebrospinal fluid biomarkers***
  - β-amyloid, tau
- ***Cognitive tests***
- ***Genetic tests (APOE4 allele)***

LIGHT

LECOM HEALTH

Alzheimer's Disease Neuroimaging Initiative (ADNI)

42

- Currently in its third phase (ADNI, ADNI-GO, ADNI-2)
- Older controls (n=150), MCI (n=450), AD (n=150), subjective memory complaint (n=100)
- Developed standardized MRI, PET, CSF methods
- Identified earliest biomarker changes in AD pathology
- Elucidated patterns & rates of change of imaging & CSF biomarkers in controls, MCI, & AD pts
- Identified at-risk participants for clinical trials

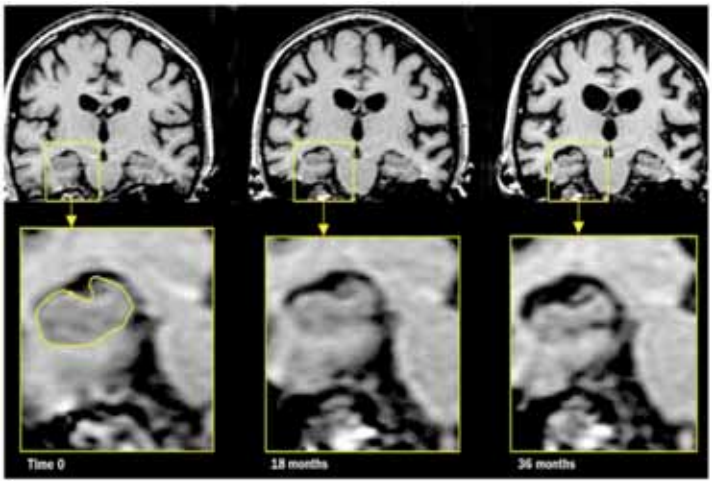
LIGHT

Weiner MW et al.. *Alz Dementia* 8 (2012):S1-S68.

LECOM HEALTH

Hippocampal Atrophy in AD

43

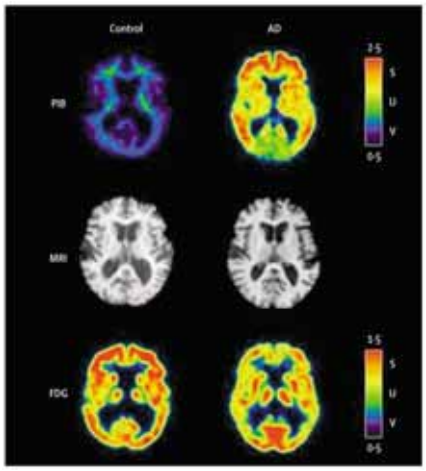


Scheltens et al. *Lancet Neurol* 2002;1:13-20.

Neuroimaging for Alzheimer's Disease

44

Control AD



PIB-PET: Greater amyloid deposition

MRI: Greater atrophy

FDG-PET: Reduced glucose uptake

Blennow K et al. *Lancet* 2006; 368: 387–403

Treatment: MCI

45

Summary

46

Table 3—Diagnostic Features and Treatment of Dementia Syndromes

Syndrome	Onset	Cognitive Domains, Symptoms	Motor Symptoms	Progression	Imaging	Pharmacologic Treatment of Cognition
Mild cognitive impairment	Gradual	Primarily memory	Rare	Unknown, 12% per year proceed to Alzheimer disease	Possible global atrophy, small hippocampal volumes	Cholinesterase inhibitors (ChIs) possibly protective for 18 months (SOE=A) in subset of high-risk patients
Alzheimer disease	Gradual	Memory, language, visuospatial	Rare early, apraxia later	Gradual (over 8–10 years)	Possible global atrophy, small hippocampal volumes	ChI for mild to severe (SOE=A); memantine for moderate to severe stages
Vascular dementia	May be sudden or stepwise	Depends on location of ischemia	Correlates with ischemia	Gradual or stepwise with further ischemia	Cortical or subcortical changes on MRI	Consider ChI for memory deficit only (SOE=C); risk factor modifiers
Lewy body dementia	Gradual	Memory, visuospatial, hallucinations, fluctuating symptoms	Parkinsonism	Gradual but faster than Alzheimer disease	Possible global atrophy	ChI (SOE=B); ± carbidopa/levodopa for movement
Frontotemporal dementia	Gradual; age <60 years	Executive, disinhibition, apathy, language, ± memory	None	Gradual but faster than Alzheimer disease	Atrophy in frontal and temporal lobes	Not recommended per current evidence