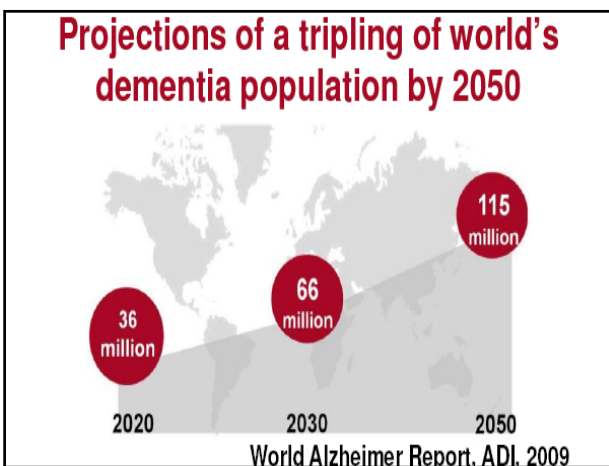
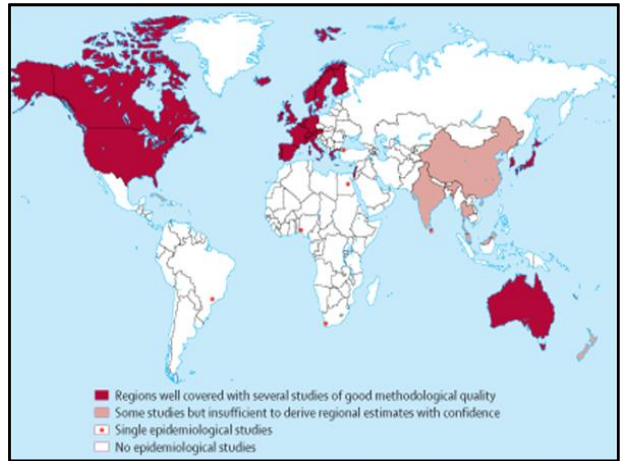


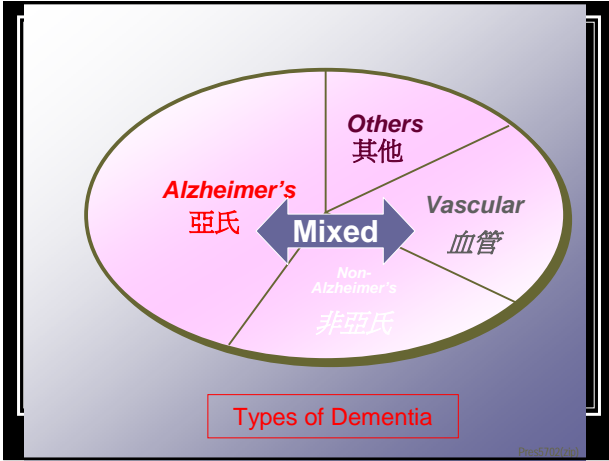
**Clinical approach
to
Alzheimer's & non-Alzheimer's
disease**

Dr Kin-Wah Liu
Specialist in Geriatric Medicine,
Prince of Wales Hospital

Created by Malaysian art director Walter Teoh in support of World Alzheimer's Day 2009.

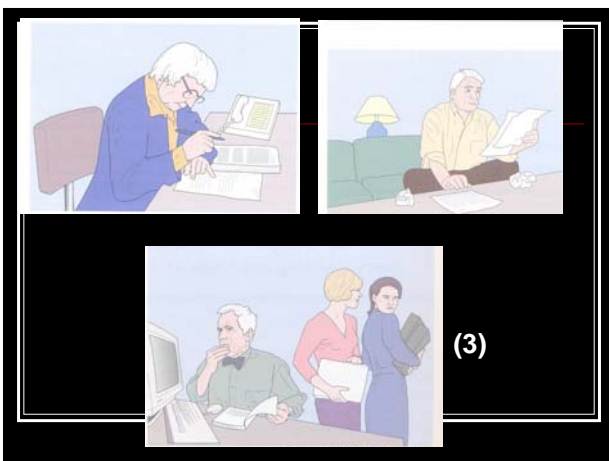


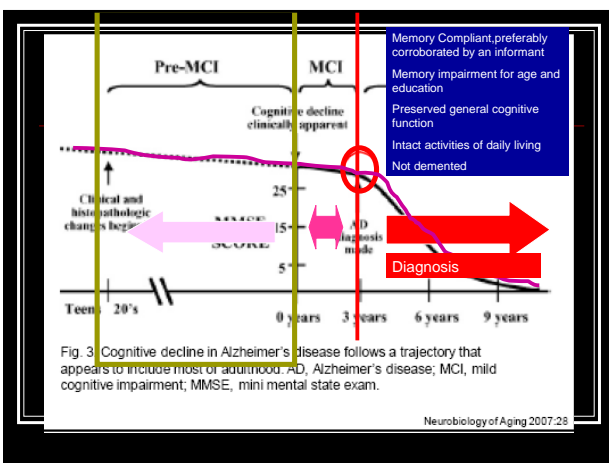
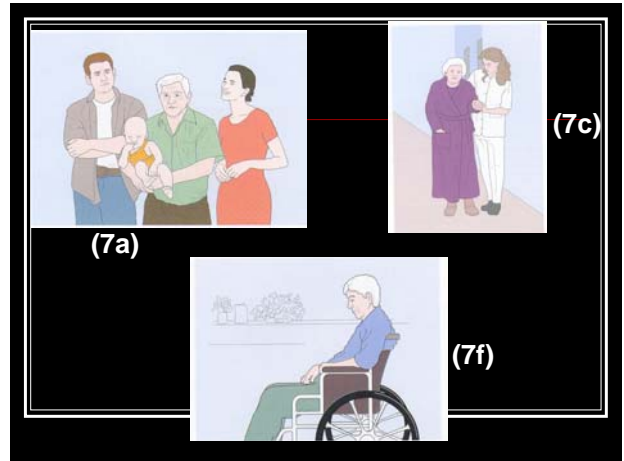
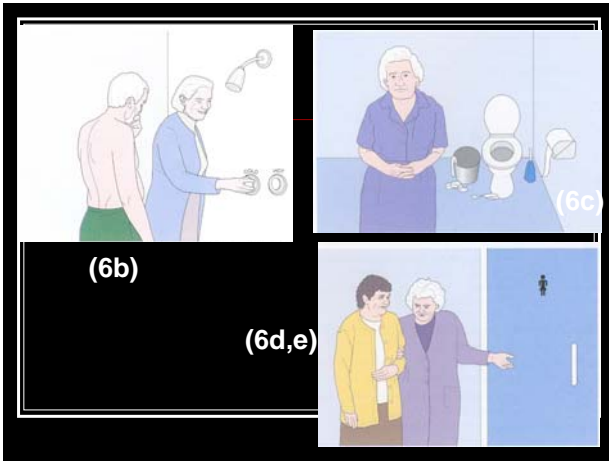
	2005		2020		2050	
	Prevalence	Incidence	Prevalence	Incidence	Prevalence	Incidence
'000 people						
Australia	195.4	60.2	301.3	91.1	664.1	199.7
China (inc Macao)	5,541.2	1,721.0	9,596.3	2,916.7	27,004.4	8,269.0
Hong Kong SAR	59.7	18.5	109.2	32.6	332.0	99.6
India	3,248.5	1,026.8	5,541.8	1,714.4	16,290.1	4,974.6
Indonesia	606.1	191.4	1,016.8	314.1	3,042.0	932.0
Japan	1,871.2	570.2	3,251.3	983.4	4,873.1	1,417.7
Malaysia	63.0	20.1	126.8	39.0	453.9	138.8
New Zealand	38.2	11.8	54.8	16.6	117.6	35.5
Pakistan	330.1	107.3	566.6	179.3	1,916.2	584.3
Philippines	169.8	54.8	316.3	99.2	1,158.9	353.9
Singapore	22.0	6.8	52.6	15.7	186.9	56.7
South Korea	246.3	75.5	542.2	164.3	1,569.9	475.4
Sri Lanka	86.0	26.9	148.0	45.1	409.0	125.0
TADA Chinese Taipei	138.0	43.1	253.4	76.6	659.3	199.4
Thailand	229.1	71.4	450.2	137.2	1,233.2	377.0
ADI Asia Pacific	12,844.3	4,005.9	22,327.6	6,825.2	59,910.6	18,238.7
Non-ADI Asia Pacific	859.3	276.2	1,399.6	437.1	4,730.9	1,448.6
Total region	13,703.6	4,282.1	23,727.1	7,262.3	64,641.5	19,687.3



FAST (Global Deterioration Scale)

Functional Assessment Staging Test
for
Alzheimer's Disease





- ### DSM-IV
- 1) **Memory impairment**
 - 2) **Aphasia**
Apraxia
Agnosia
 Disturbance in **executive functioning** (planning, organizing, sequencing, abstracting)
 - 3) Gradual onset and continuing
 - 4) Not due to: a) other CNS diseases (CVA, parkinson's, huntington's, sdh, nph, brain tumour)
 b) systemic (hypothyroidism, B12 def, hypercalcemia, HIV)
 c) substance-induced
 - 5) **Exclude delirium**
 - 6) **Exclude psychiatric diseases** (major depression, schizophrenia)



GPCOG Informant Interview

B. Informant Description (GPCOG Informant interview)

	Yes	No	Don't know	N/A
Compared to a few years ago.....				
1. Does the patient have more trouble remembering things that have happened recently?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Does he or she have more trouble recalling conversations after a few days?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. When speaking, does the patient have more difficulty in finding the right word or tend to use the wrong words more often?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Is the patient less able to manage money and financial affairs (e.g. paying bills, budgeting)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Is the patient less able to manage his or her medication independently?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Does the patient need more assistance with transport (either private or public)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

- ### Dementia Screen
- CBP, ESR
 - RFT, LFT
 - Ca/P
 - MSU: R/M, C&ST
 - B12, Folate
 - Thyroid function
 - ?VDRL
 - CXR
 - CT Brain

- ### Clinical tools
- MMSE
 - Clock face
 - Geriatric Depression Scale
 - Clinical Dementia Rating Scale

Table 10.1 MMSE Scores for Adults Living (Cronbach's α = 0.91)

MMSE (Folstein, et al.)	MMSE (Cantonese version)	Score
1. What is the year?	甚麼年(份)	10
2. What is the month?	甚麼月	10
3. What is the day?	甚麼日	10
4. Name three objects, taking one second for each.	命名三樣物件 (每樣物件, 請記下名稱, 請注意每一秒)	30
5. Read an item. Give one point for each correct answer. Stop after five correct. (Maximum: 5/5)	讀出五個字, 每個字一分, 讀出五個字後, 就停止 (每讀對一個字, 就給一分, 最高可得五分)	5
6. Read the names of three objects learned for Question 5. Give one point for each correct answer.	讀出五個字的名字 (每讀對一個字, 就給一分)	3
7. Read a sentence and a watch. What the patient cannot hear or see point.	讀出兩句說話 (每句一分)	2
8. How the patient responded "Yes, No, or Not?"	讀出三句說話 (每句一分)	3
9. How the patient followed a three-stage command "Take the paper to your right hand. Fold the paper in half. Put the paper on the floor."	按指令一步一步做, 包括由右邊拿紙張, 折紙張, 字一折紙張成一半, 然後將紙張放在地上	3
10. How the patient read and drew the following "CLOSE YOUR EYES"	讀出兩句說話, 然後照樣去畫 (每句一分)	2
11. How the patient writes a sentence of his/her choice. (The sentence should contain a subject and an object and should make sense. Ignore spelling when scoring)	讀出兩句說話, 寫一個完整的句子 (每句一分)	1
12. Copy a intersecting pentagon	照樣作圖, 畫一個由兩個五邊形交疊而成的圖	5

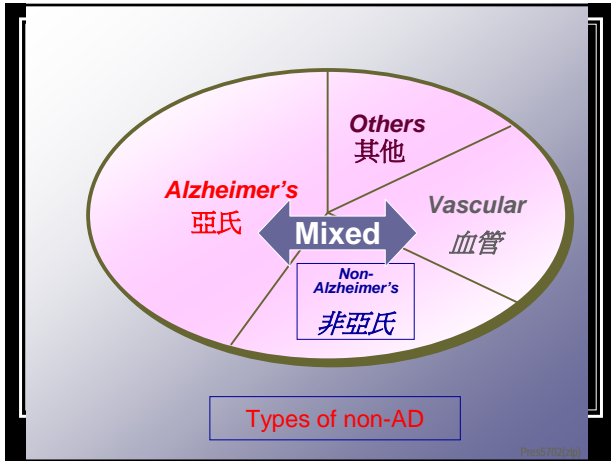
MMSE
mini-mental state examination

Cut-off Point:
Nil education: <18
1-2 yrs: <20
>2 yrs: <22

The image shows a page from the MMSE manual with various test items. At the bottom right, there is a box that says "Cut-Off Score: ≤ 7".

- Tips 1**
- 1) Ask family for substantially noticeable memory decline in the past 1-2 yrs
 - 2) Blaming close family members for taking his/her belongings usually money
 - 3) Age window for onset: 75-80 yr
 - 4) Disclosing the diagnosis

- Tips 2**
- 1) Simple tests
 - 2) MMSE for baseline documentation
 - 3) Clock test very sensitive for early AD with typical pattern



Non-Alzheimer Degenerative Dementia
(Curr Opin Neurol 1998, 11:417 - 427)

Frontotemporal(behavioral)
Cerebral Lewy Body Disease(CVH)
Progressive Supranuclear Palsy(Ocular, bulbar)
Corticobasal Degeneration(Apraxia)

Clinical Dementia Rating 1 (Mild Dementia)		None 0	Questionable 0.5	Mild 1	Moderate 2	Severe 3
Memory	No memory loss, or slight inconsistent forgetfulness	Consistent slight forgetfulness; partial recollection of events; "benign" forgetfulness	Moderate memory loss; more marked for recent events; defect interferes with every day activities	Severe memory loss; only highly learned material retained; new material rapidly lost	Severe memory loss; only fragments remain	
Orientation	Fully oriented	Fully oriented except for slight difficulty with time relationships	Some difficulty with time relationships, oriented for place and person at examination, but may have geographic disorientation	Usually disoriented to time, often to place	Oriented to person only	
Judgment and problem solving	Solves everyday problems and handles business and financial affairs well; judgment good in relation to past performance	Slight impairment in solving problems, similarities and differences	Moderate difficult in handling problems, similarities, and differences; social judgment usually maintained	Severely impaired in handling problems, similarities and differences; social judgment usually impaired	Unable to make judgments or solve problems	
Community affairs	Independent function at usual level in job, shopping and volunteer and social groups	Slight impairment in these activities	Unable to function independently at these activities although may still be engaged in some; appears normal to casual inspection	No pretense of independent function outside home. Appears well enough to be taken to functions outside a family home	No pretense of independent function outside home. Appears too ill to be taken to functions outside a family home	
Home and hobbies	Life at home, hobbies, and intellectual interests well maintained	Life at home, hobbies, and intellectual interests slightly impaired	Mild but definite impairment of function at home, more difficult chores abandoned; more complicated hobbies and interests abandoned	Only single chores preserved; very restricted interests, poorly maintained	No significant function in home	
Personal care	Fully capable of self-care	Fully capable of self-care	Needs prompting	Requires assistance in dressing, hygiene, keeping of personal affairs	Requires much help with personal care; frequent incontinence	

Mr. Ho

- 67 yrs old
- Education up to secondary school
- Retired teacher for few years
- Hypertension for >10 yrs
- Poor memory for 2 years
- Poor calculation
- Hot temper according to wife
- Independent ADL
- P/E unremarkable

Progress

- Admitted in 3/2006 due to AROU with urosepsis
- Developed delirium in ward
 - agitation with irrelevant speech
- Complex visual hallucination
 - seeing "ants crawling on the wall and body" and "ancestors who had passed away".

Progress

- Cry out with arms thrashing about during sleep for 2-3 years
 - ?REM related behavioral disorder (REMBD)
- Decline in ADL
 - Incontinence sometimes

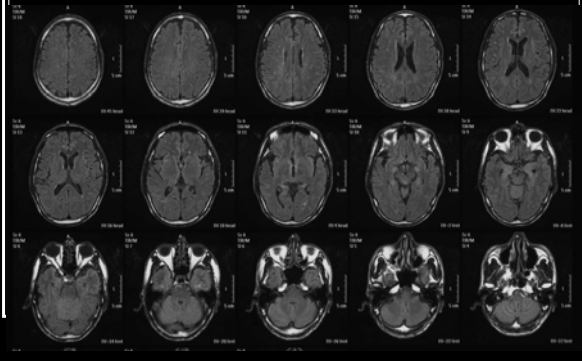
Progress

- Parkinsonism features noted during follow up
 - Masked face
 - Cogwheel rigidity of upper limbs
 - Brisk reflexes
 - Palmomental reflex not present
- Geriatric Depression scale 7/15

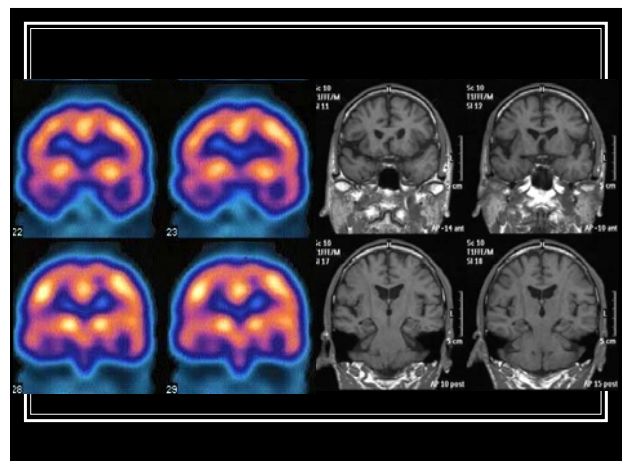
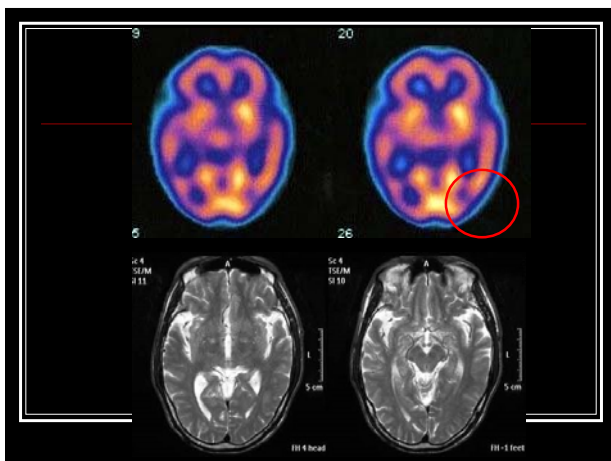
Visuo-constructive abilities in clock drawing and pentagon copying of a DLB and AD patient for comparison.

AD	DLB
MMSE 18/30 Orientation 5/10 Short term memory 0/3	MMSE 20/30 Orientation 8/10 Short term memory 2/3

< 5 lacunar infarcts,
no significant small vessel disease



MRA – No large vessel disease



What is Lewy bodies (LB)?

- Lewy bodies are neuronal cytoplasmic inclusions
- composed of abnormally phosphorylated **proteins** aggregated with **ubiquitin** and **alpha-synuclein** (**presynaptic protein**)



Named after Dr. Frederick Lewy who first described LBs in 1912 in idiopathic parkinson's disease patient

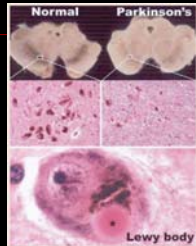


Table 4 Revised criteria for the clinical diagnosis of dementia with Lewy bodies (DLB)

- 1. Core features** (essential for a diagnosis of possible or probable DLB)
 - Dementia defined as progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuospatial ability may be especially prominent.
- 2. Core features** (two core features are sufficient for a diagnosis of probable DLB, one for possible DLB)
 - Fluctuating cognition with pronounced variations in attention and alertness
 - Recurrent visual hallucinations that are typically well formed and detailed
 - Spontaneous features of parkinsonism
- 3. Supportive features** (If one or more of these is present in the presence of one or more core features, a diagnosis of probable DLB can be made. In the absence of any core features, one or more supportive features is sufficient for possible DLB. Probable DLB should not be diagnosed on the basis of supportive features alone.)
 - REM sleep behavior disorder
 - Severe neuroleptic sensitivity
 - Low dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET imaging
- 4. Supportive features** (commonly present but not proven to have diagnostic specificity)
 - Repeated falls and syncope
 - Transient, unexplained loss of consciousness
 - Severe autonomic dysfunction, e.g., orthostatic hypotension, urinary incontinence
 - Hallucinations in other modalities
 - Systematized delusions
 - Depression
 - Relative preservation of medial temporal lobe structures on CT/MRI scan
 - Generalized low uptake on SPECT/PET perfusion scan with reduced occipital activity
 - Abnormal (low uptake) MIBG myocardial scintigraphy
 - Prominent slow wave activity on EEG with temporal lobe transient sharp waves
- 5. A diagnosis of DLB is less likely**
 - In the presence of cerebrovascular disease evident as focal neurologic signs or on brain imaging
 - In the presence of any other physical illness or brain disorder sufficient to account in part or in total for the clinical picture
 - If parkinsonism only appears for the first time at a stage of severe dementia

4. Supportive features

- Repeated falls and Syncope
- Transient loss of consciousness
- Severe autonomic dysfunction
 - Postural hypotension, urinary incontinence
- Systematized delusions
- Hallucinations in other modalities
- Depression
- Relative preservation of medial temporal lobe structures on CT/MRI scan
- Generalized low uptake on SPECT/PET perfusion scan with reduced occipital activity
- Abnormal (low uptake) MIBG myocardial scintigraphy
- Prominent slow wave activity on EEG with temporal lobe transient sharp waves



Pictures taken from a video in a sleep laboratory of older men who have RBD. These men throw punches while dreaming of fighting during REM sleep.

www.nature.com/.../images/nature04287-f4.0.jpg

- REM sleep behaviour disorder (REMBD)

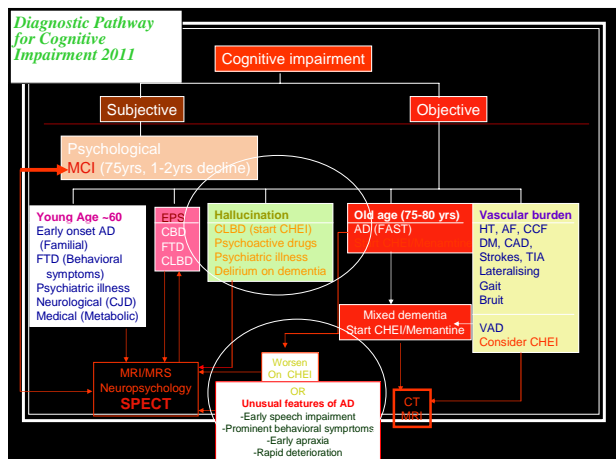
- Excessive muscle tone and undesirable behavioural manifestation during REM sleep
- Prevalence of RBD range from 0.4% of persons age 70 years or older to 0.5% of the general population .

5. Features Making the Diagnosis Less Likely

- a. cerebrovascular disease evident as focal neurologic signs or on brain imaging
- b. any other physical illness or brain disorder sufficient to account in part or in total for the clinical picture
- c. Parkinsonism for the first time at a stage of severe dementia

DLB vs Alzheimer's Disease

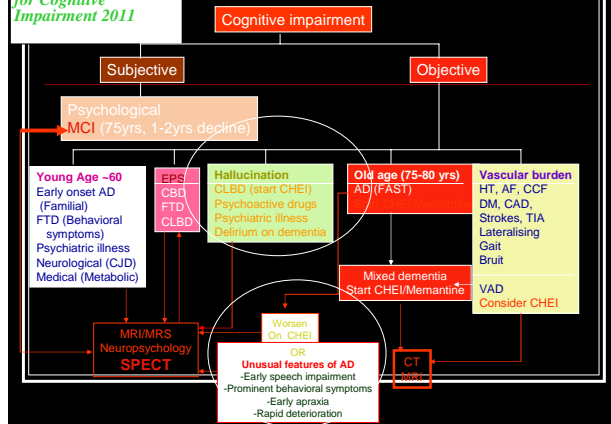
- Memory problems occur later in DLB
- Visuospatial ability worsened early in DLB (thus more fall in DLB)
- Attention more affected in DLB
- More fluctuation in DLB
- More rapid progression DLB
- Hallucinations & delusions more common in DLB
- Parkinson symptoms at onset in DLB



Non-responding to CHEI!

Non-AD
eg. Frontotemporal Dementia

Diagnostic Pathway for Cognitive Impairment 2011



Behavioral characteristics

- Disinhibition, impulsivity,
- Inertia,
- Loss of personal and social awareness
- Loss of insight
- Mental rigidity and inflexibility
- Hyperorality
- Utilization behaviour
- Stereotypies and rituals

