

An Introduction to Major Neurocognitive Disorder (Dementia)

Yolin A. Bueno, MD.
Geriatric & Internal Medicine

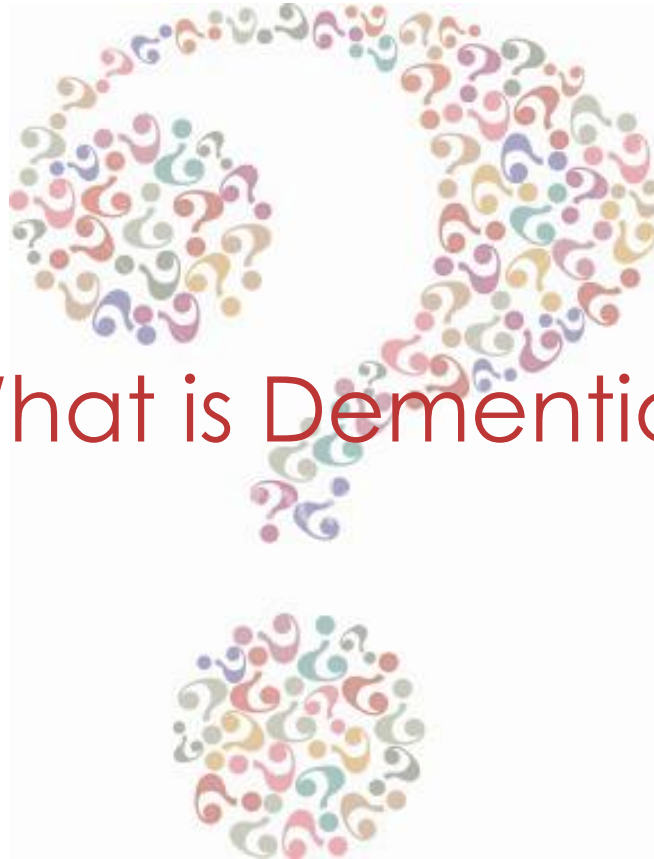


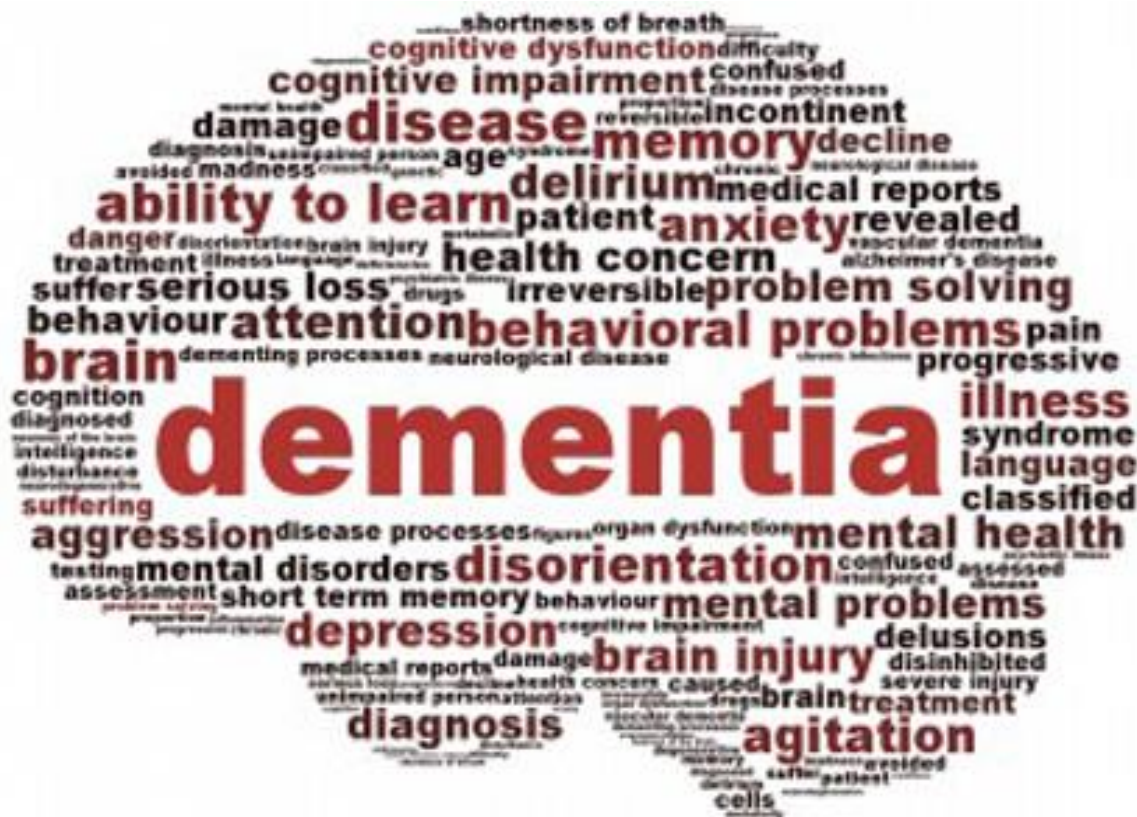
What we're about to cover

- An Introduction to Dementia
 - Neurocognitive Impairment Defined
 - Epidemiology and Social Impact
 - Types of Dementia and Causes
 - Risk Factors
- Is it Dementia?
 - Assessment
 - Listen and Observe
 - Cognitive Tests
 - Imaging and Lab Work
 - Differential Diagnoses
 - The Importance of Early Diagnosis
- What can we do?
 - Preventative Measures
 - Non-Pharmacological Approaches
 - Pharmacological Treatments
- Conclusions and Recommendations
- Helpful Resources



What is Dementia?





An Introduction to Dementia

Neurocognitive Disorder Defined

Dementia, formally known as **neurocognitive disorder (NCD)**, is the term used to describe in general several disorders that cause significant decline in one or more areas of cognitive functioning severe enough to result in functional decline.

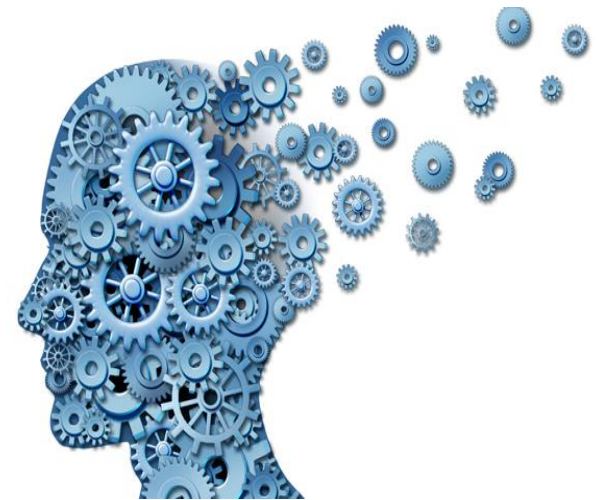


Neurocognitive Disorder Defined (cont.)

- While symptoms of dementia can vary greatly, at least two of the following core mental functions must be significantly impaired to be considered dementia:
 - Memory
 - Communication and language
 - Ability to focus and pay attention
 - Reasoning and judgment
 - Visual perception
- Dementia can be mild, moderate or severe. DSM-5 differentiates mild versus moderate NCD with regard to impairment in instrumental activities of daily living (IADLs) versus activities of daily living (ADLs), respectively.
- The majority of diagnosed patients have Alzheimer disease (AD)
- It also affects millions of caregivers
- Dementia and aging are not synonymous

And while this can be a scary diagnosis for patients, the good news is:

- Diagnostic and treatment advances have benefited many patients.
- Early and accurate diagnosis of dementia can minimize use of costly medical resources.



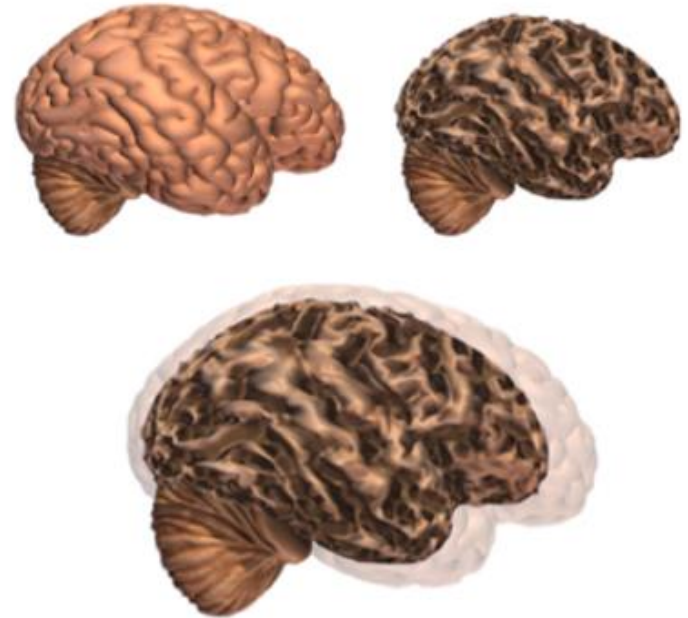
Epidemiology

Who? NCD mostly affects older adults. The disease prevalence doubles every 5 years after age 60; an estimated 45% or more of those who are ≥ 85 years old have AD.

What? There are multiple types of dementia including: mild cognitive impairment, AD, vascular dementia, lewy bodies, frontal temporal and huntingtons

How?

- Lewy bodies is now thought to be the second most common cause of dementia.
- Huntington disease, Parkinson disease, or other causes such as head injury and alcoholism account for other dementia syndromes.



Social Impact

- World Report on Alzheimer's 2010, total costs for dementia were \$604 billion annually.
- In 2013, the Alzheimer's Association reported family caregivers provided an estimated 17.7 billion hours of care, estimated to cost more than \$220.2 billion dollars in the United States alone.
- The emotional toll is immense for both patients and their families
- Nearly half of primary caregivers of patients with dementia experience psychologic distress, particularly depression, and have more physical health issues



Progression of Dementia

Stage 1: No cognitive impairment

Stage 2: Very mild cognitive decline

Individuals at this stage feel as if they have memory lapses, especially in forgetting familiar words or names or the location of keys, eyeglasses, or other everyday objects.

Stage 3: Mild cognitive decline

- Early-stage AlzD
- Friends, family, or coworkers begin to notice deficiencies.

Stage 4: Mod. cognitive decline (mild or early-stage Alzheimer disease)

- Decreased knowledge of recent occasions or current events
- Impaired ability to perform challenging mental arithmetic, eg, to count backward from 100 by 7s
- Decreased ability to perform complex tasks.



Progression of Dementia

Stage 5: Moderately severe cognitive decline (moderate or mid-stage Alzheimer disease) Major gaps in memory and deficits in cognitive function emerge. Some assistance with day-to-day activities becomes essential.

Stage 6: Severe cognitive decline (moderately severe or mid-stage Alzheimer disease) Memory difficulties continue to worsen, significant personality changes may emerge, and affected individuals need extensive help with customary daily activities. At this stage, individuals may:

- Lose most awareness of recent experiences, events, and surroundings
- Recollect their personal history imperfectly, although they generally recall their name

Stage 7: Very severe cognitive decline (severe or late-stage Alzheimer disease)

This is the final stage of the disease when individuals lose the ability to respond to their environment, to speak, and ultimately to control movement.



Types of Dementia (Cheat Sheet)

Syndrome	Onset	Cognitive Domains, Symptoms	Motor Symptoms	Progression	Imaging	Pharmacologic Treatment of Cognition
MCI	Gradual	Primarily memory	Rare	Unknown, 12%/yr proceed to AD	Possible global atrophy, small hippocampal volumes	Cholinesterase inhibitors (ChIs) possibly protective for 18 months (SOE=A) in subset of high-risk patients
Alzheimer's 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 AD	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 AD	Atrophy in frontal and temporal lobes	Not recommended per current evidence



Causes

Fig. A

Illustrates a normal vs. Alzheimer's inflicted brain. Amyloid plaques/oligomers or tau neurofibrillary tangles (or both) associated w/AD

Source: BrightFocus® Foundation

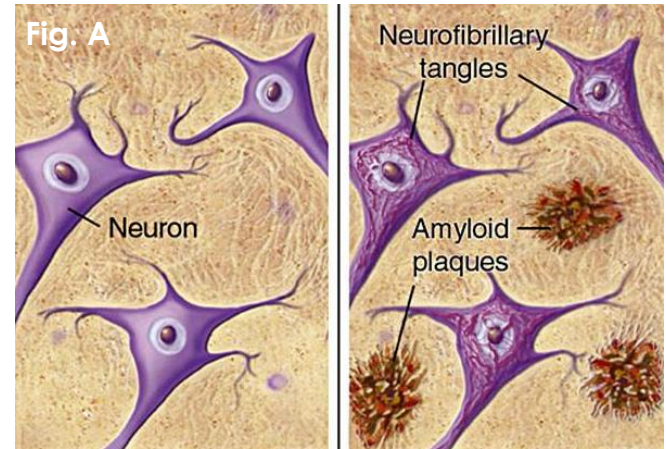


Fig. B

Illustrates Tau or ubiquitin proteins of frontotemporal dementia

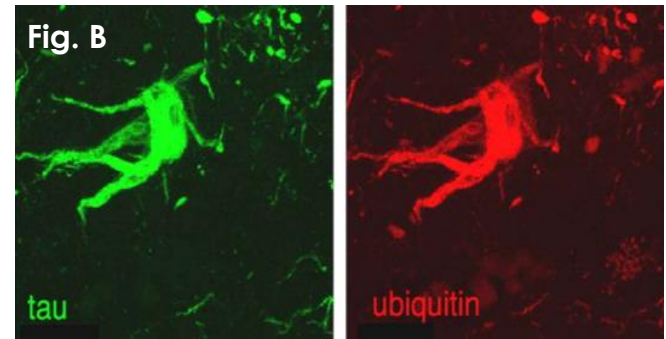
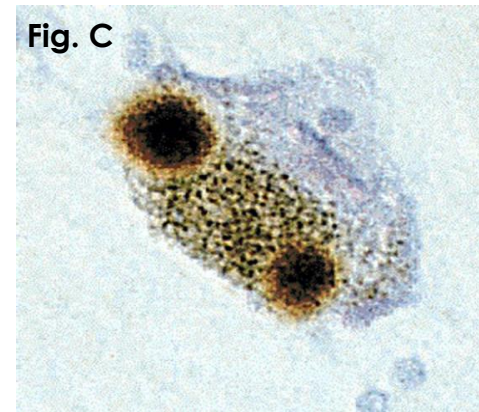


Fig. C

Illustrates a cytoplasmic α -synuclein inclusion bodies of Lewy body dementia and Parkinson dementia



Risk Factors

The two greatest risk factors for AD are age and family history.

Other risk factors include:

Definite

- Age
- Family history
- APOE4 allele
- Down syndrome

Possible

- Head trauma
- Fewer years of formal education
- Late-onset major depressive disorder
- Cardiovascular risk factors (obesity, HTN, DM, HLDP)



Case Study



In addition to repeating the MMSE in 6 months, which one of the following is the most appropriate intervention?

- A. Increase lisinopril dosage to achieve target blood pressure <math><140/90\text{ mmHg}</math>.
- B. Refer for physical therapy assessment.
- C. Refer for cognitive rehabilitation.
- D. Prescribe daily *Ginkgo biloba*.
- E. Prescribe daily vitamin E.



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Is it Dementia?

Assessment: Listen + Observe

- Cognitive and functional assessments should be conducted in the patient's native language, if at all possible. (In the face of cognitive decline, dementia patients commonly retain the greatest fluency in their native language)
- A comprehensive physical examination should include a neurologic and mental status evaluation.
- Both the patient and a reliable informant should be interviewed
- A Functional Activities Questionnaire should be performed
- Cognitive performance is influenced by number of years of formal education.
- PCPs: be alert to the early symptoms and to subjective complaints from patient or family member concerning cognitive decline



Assessment: Cognitive Tests

Subtle Signs of Cognitive Change

- Missing deadlines
- Behavioral changes
- Difficulty managing complex tasks such as finances
- Giving up a hobby or interest that may have become too challenging

Screening Instruments

Instrument Name	Items Scoring	Domains Assessed	Available at (accessed Jan 2016)
Mini-Cog	2 items Score = 5	Visuospatial, executive function, recall	http://geriatrics.uthscsa.edu/tools/MINICog.pdf
St. Louis University Mental Status (SLUMS) Examination	11 items Score = 30	Orientation, recall, calculation, naming, attention, executive function	http://medschool.slu.edu/agingsuccessfully/pdfsurveys/slumsexam_05.pdf
Montreal Cognitive Assessment (MoCA)	12 items Score = 30	Orientation, recall, attention, naming, repetition, verbal fluency, abstraction, executive function, visuospatial	www.mocatest.org
Folstein Mini-Mental Status Examination (MMSE)	19 items Score = 30	Orientation, registration, attention, recall, naming, repetition, 3-step command, language, visuospatial	www.minimental.com (for purchase)
Functional Activities Questionnaire	10 items Score = 30	Informant based, executive functioning, activities of daily living, attention, concentration, memory, home safety	www.healthcare.uiowa.edu/familymedicine/fpinfo/Docs/functional-activities-assessment-tool.pdf



Assessment: Imaging and Lab Work

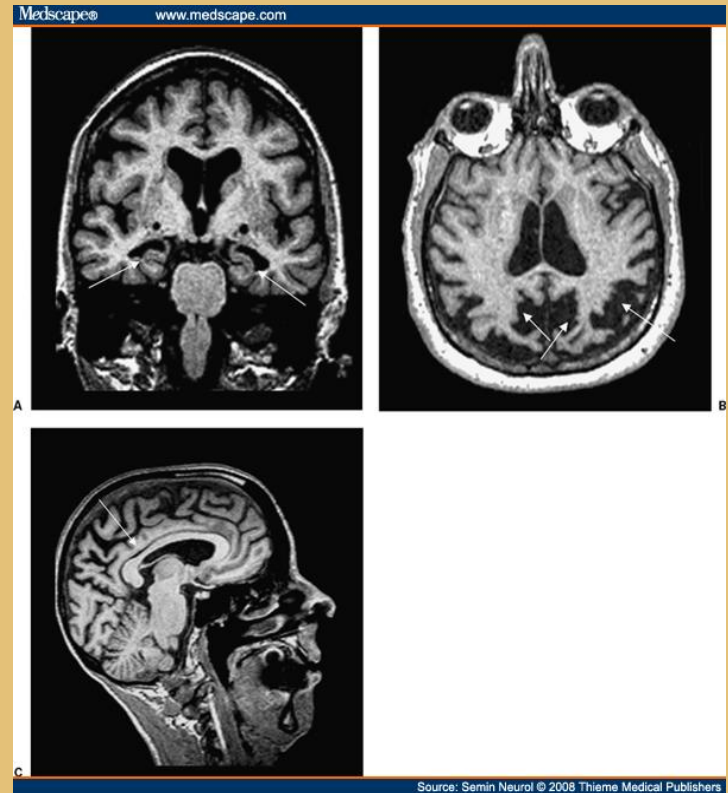
Types of Imaging

- MRI and (CT) may identify non-degenerative and potentially treatable causes of dementia.
- Pittsburgh Compound-B (PIB) ligand for positron emission tomography imaging in Alzheimer's disease, will improve our ability to differentiate among the neurodegenerative dementias.
- High-resolution volumetric MRI has increased the capacity to identify the various forms of the frontotemporal lobar degeneration spectrum and some forms of parkinsonism or cerebellar neurodegenerative disorders,
- Diffusion-weighted MRI can help in the early diagnosis of Creutzfeldt-Jakob disease. Although only clinical assessment can lead to a diagnosis of dementia, neuroimaging is clearly an invaluable tool for the clinician in the differential diagnosis.



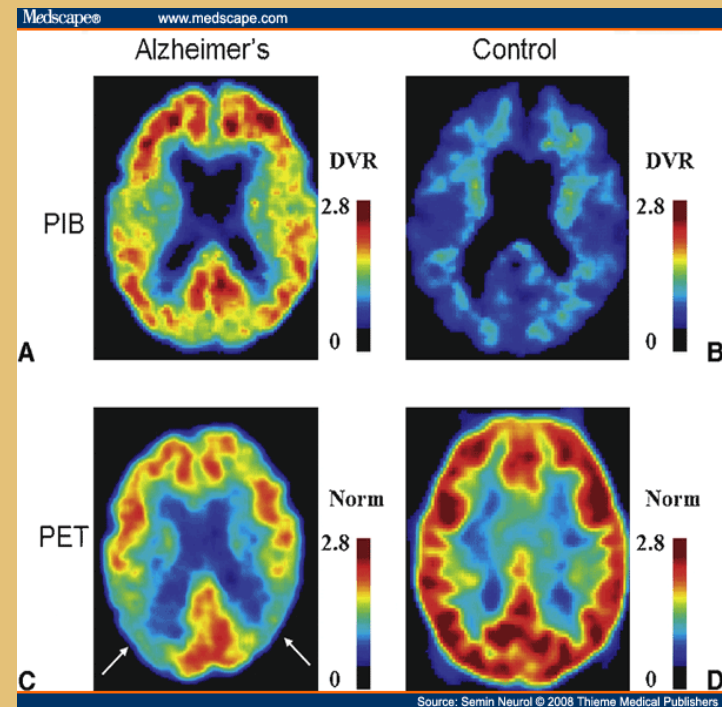
Imaging: MRI of AD

- A. Coronal image showing bilateral hippocampal atrophy (arrows) in an 83-year-old woman (MMSE score 21).
- B. Axial image showing biparietal and posterior cingulate atrophy (arrows) in a 62-year-old woman with early age of onset AD (MMSE 22).
- C. Sagittal image showing thinning of the posterior body of the corpus callosum (arrow), associated with significant parietal and posterior frontal atrophy in a 59-year-old woman with early onset AD (MMSE 21).



Imaging: PET with AB amyloid ligand Pittsburgh Compound-B

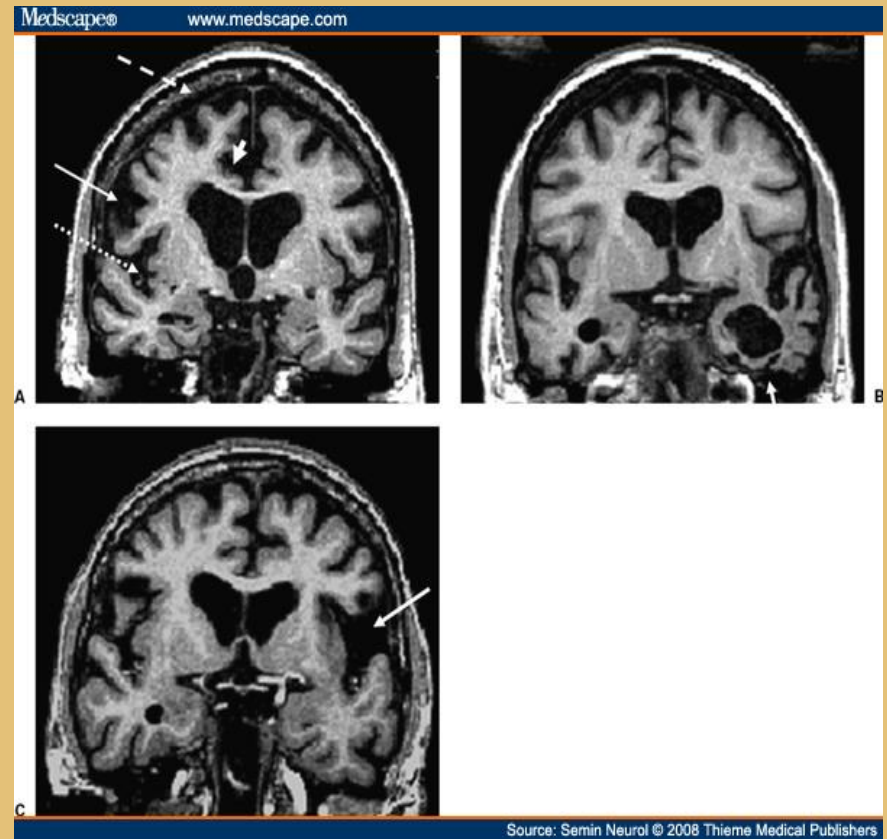
- A. A 67-year-old man with moderate AD. AD has increased tracer binding in the frontal, posterior cingulate, parietal and temporal cortices, and the striatum. Patient with AD demonstrates prominent hypometabolism, particularly in parietal cortex
- B. A 73-year-old cognitively normal woman, cognitively normal control does not demonstrate tracer uptake in the cortex. Normal control shows normal glucose metabolism.



Imaging: MRI of FTP Dementia

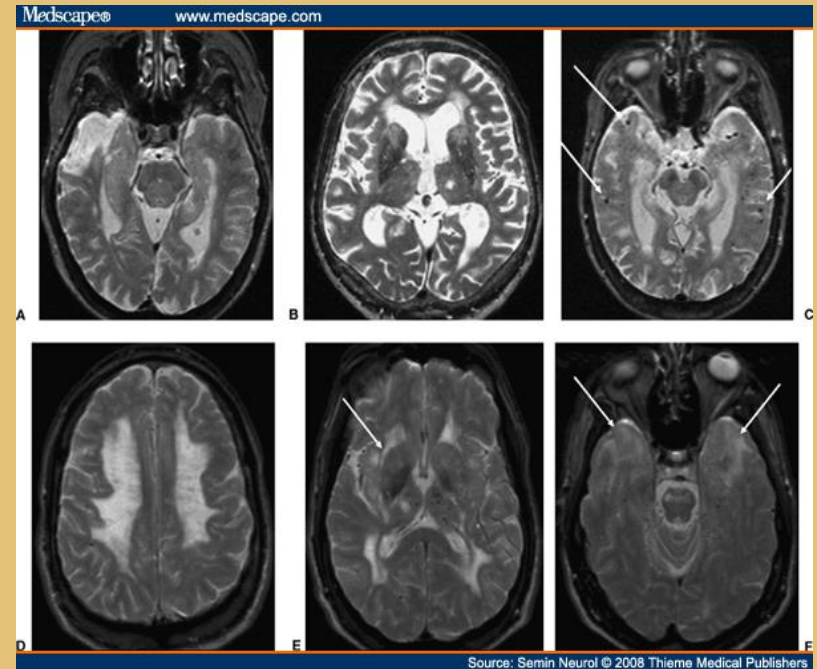
Brain coronal T1-weighted MRI from patients with different clinical presentations of frontotemporal lobar degeneration.

- A. BvFTD in a 62-year-old man, MMSE score 24. atrophy of the left temporal lobe
- B. SD in a 66-year-old man, MMSE 26. prominent atrophy in the left perisylvian region
- C. PNFA in a 66-year-old woman, MMSE 28. Note the bilateral gray matter loss in the inferior frontal gyrus, superior frontal gyrus, the insula (dotted arrow), and the anterior cingulate



Imaging: MRI of Vascular Dementia

- A. 84-year-old woman with cognitive deficits (MMSE 26, which 2 years later declined to 15). T2-weighted MRI shows chronic right temporal pole infarction and only mild left hippocampal atrophy.
- B. A 79-year-old man with behavioral, frontal-executive, and memory problems (MMSE 19). T2-weighted MRI shows chronic left thalamic lacunar stroke, bilateral caudate and frontal white matter small vessel disease, as well as bifrontal atrophy.
- C. A 72-year-old woman with memory impairment (MMSE 24) diagnosed with mixed AD-VaD. T2-weighted MRI shows bilateral hippocampal atrophy and multiple microhemorrhages (focal hypointensities, arrows) suggestive of amyloid angiopathy.
- F. Subcortical white matter of temporal poles and the pons



Differential Diagnosis

- Delirium
- Depression
- Medication Side Effects
- Sensory deficiencies
- Hypothyroidism
- B-12 deficiency



The Importance of Early Diagnosis

- A better chance of benefiting from treatment
- More time to plan for the future
- Lessened anxieties about unknown problems
- Increased chances of participating in clinical drug trials, helping advance research
- An opportunity to participate in decisions about care, transportation, living options, financial and legal matters.
- Time to develop a relationship with doctors and care partners
- Benefit from care and support services, making it easier for them and their family to manage the disease.
- Alzheimer's Navigator can help identify needs and create actions plans.



Case Study



Which one of the following is most likely to indicate pathologic neurologic decline?

- A. Taking longer to complete routine tasks
- B. Forgetting to pay mortgage and credit card bills
- C. Having a complaint about memory
- D. Experiencing difficulty retrieving names



Case Study



Which one of the following is most likely to indicate pathologic neurologic decline?

- A. Taking longer to complete routine tasks
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What can we do?

Preventative Measures

Possible Protective Factors

- NSAIDs
- Diet
- Antioxidants
- Intellectual activity
- Physical activity
- Statins
- Marriage?!

https://www.medscape.com/viewarticle/890916?src=WNL_infoc_180121_MSCPEDIT_TEMP2&uac=178656CR&impID=1538021&faf=1



"Okay, we grew old together
— now what?"



Non-pharmacological Approaches

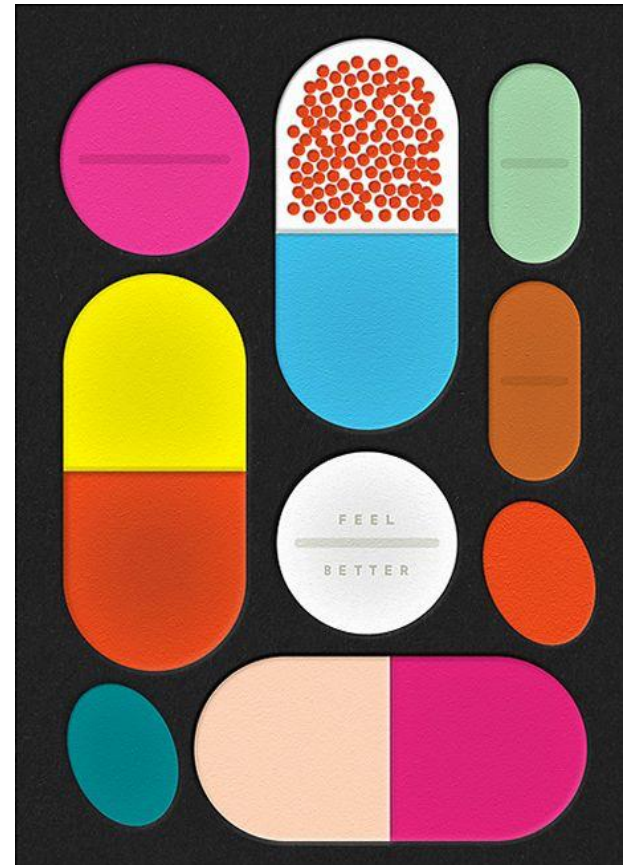
- Addressing sensory deficits
- Familiarity
- Calm environment
- Simple and compassionate communication
- Other therapies: art and music
- Adequate rest
- Monitor personal comfort
- Avoid confrontation
- Redirect the person's attention
- Acknowledge requests
- Don't take behavior personally
- Adult day care
- Frequent orientation (ex: Calendar or newspaper)
- Use support community
www.ALZConnected.com



Pharmacological Treatments

Before beginning treatment, keep in mind general issues:

- Polypharmacy; interactions and adverse events are likely.
- Medications with anticholinergic effects can worsen cognitive impairment and lead to delirium.
- Any nonessential medications with CNS adverse events should be considered carefully.
- Best strategy, “start low and go slow”. The goal is to identify the lowest effective dosage,
- Before starting any treatment, identify and treat any underlying medical conditions that might impair cognition.



Case Study



Which one of the following is the most appropriate next step?

- A. Increase lisinopril to 40 mg.
- B. Refer for retinal screening.
- C. Check hemoglobin A_{1c} level.
- D. Screen for depression and cognitive impairment.



Case Study



Which one of the following is the most appropriate next step?

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Pharmacological Treatments (cont.)

Generic	Brand	Approved for	Side effects
Donepezil	Aricept	All stages	N/V, loss of appetite, increased frequency of bowel movements
Galantamine	Razadyne	Mild to Moderate	N/V, loss of appetite, increased frequency of bowel movements
Memantine	Namenda	Moderate to severe	Headache, constipation, confusion, dizziness
Rivastigmine	Exelon	Mild to Moderate	N/V, loss of appetite, increased frequency of bowel movements
Memantine + donepezil	Namzaric	Moderate to severe	N/V, loss of appetite, increased frequency of bowel movements, headache, constipation, confusion, dizziness



Pharmacological Treatments (cont.)

Antidepressants

- Considered for AD patients with depressive symptoms depressed mood, appetite loss, insomnia, fatigue, irritability, and agitation.
- SSRIs in disinhibitions and compulsive behaviors associated with FTD?
- Patients with dementia are at risk of falls, and the use of SSRIs and SNRIs can possibly exacerbate these risks, especially those with greater anticholinergic tone (eg, paroxetine).



Case Study



Which one of the following regimens should be prescribed to help manage the patient's symptoms?

- A. Begin haloperidol at a low dosage, increase the dosage until symptoms are controlled, then taper as soon as possible.
- B. Begin quetiapine at a low dosage, increase the dosage until symptoms are controlled, then taper as soon as possible.
- C. Begin duloxetine at a low dosage, increase the dosage until symptoms are controlled, then taper as soon as possible.
- D. Prescribe lorazepam at a low dosage as needed.



Case Study



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Pharmacological Treatments (cont.)

Psychoactive Medications

- Limited evidence that first- and second-generation antipsychotics help control these symptom.
- Recent trials have revealed that all antipsychotics increase the risk of “all-cause” mortality in the setting of dementia (SOE=A)
- To help mitigate these risks, frequent attempts to taper off each medication should be undertaken (SOE=A).
- Carbamazepine and valproic acid are possible alternatives for managing irritability and agitation
- The use of benzodiazepines and medications with anticholinergic effects should be avoided.
- Antidepressants with sedating effects such as mirtazapine and trazodone can be considered in management of insomnia.



Conclusions + Recommendations

Call for Action

- There is evidence that earlier diagnosis can be achieved through practice based educational programs in primary care.
- It is a myth that there is no point in early diagnosis, since “nothing can be done”.
- Discuss with patients potential preventative measures
- We have to educate affected patients and their families on natural progression of Dementia and provide them with helpful resources
- Before beginning treatment, keep in mind general issues
- Realistic expectations need to be set with patients and caregivers



Helpful Resources

NCD Screening Instruments

Mini-Cog™

Instructions for Administration & Scoring

ID: _____ Date: _____

Step 1: Three Word Registration

Look directly at person and say, "Please listen carefully. I am going to say three words that I want you to repeat back to me now and try to remember. The words are [select a list of words from the versions below]. Please say them for me now." If the person is unable to repeat the words after three attempts, move on to Step 2 (clock drawing).

The following and other word lists have been used in one or more clinical studies.^{1,3} For repeated administrations, use of an alternative word list is recommended.

Version 1	Version 2	Version 3	Version 4	Version 5	Version 6
Banana	Leader	Village	River	Captain	Daughter
Sunrise	Season	Kitchen	Nation	Garden	Heaven
Chair	Table	Baby	Finger	Picture	Mountain

Step 2: Clock Drawing

Say: "Next, I want you to draw a clock for me. First, put in all of the numbers where they go." When that is completed, say: "Now, set the hands to 10 past 11."

Use preprinted circle (see next page) for this exercise. Repeat instructions as needed as this is not a memory test. Move to Step 3 if the clock is not complete within three minutes.

Step 3: Three Word Recall

Ask the person to recall the three words you stated in Step 1. Say: "What were the three words I asked you to remember?" Record the word list version number and the person's answers below.


Word List Version: _____ Person's Answers: _____

Scoring

Word Recall: _____ (0-3 points)	1 point for each word spontaneously recalled without cueing.
Clock Draw: _____ (0 or 2 points)	Normal clock = 2 points. A normal clock has all numbers placed in the correct sequence and approximately correct position (e.g., 12, 3, 6 and 9 are in anchor positions) with no missing or duplicate numbers. Hands are pointing to the 11 and 2 (11:10). Hand length is not scored. Inability or refusal to draw a clock (abnormal) = 0 points.
Total Score: _____ (0-5 points)	Total score = Word Recall score + Clock Draw score. A cut point of <3 on the Mini-Cog™ has been validated for dementia screening, but many individuals with clinically meaningful cognitive impairment will score higher. When greater sensitivity is desired, a cut point of <4 is recommended as it may indicate a need for further evaluation of cognitive status.

NCD Screening Instruments

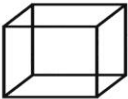
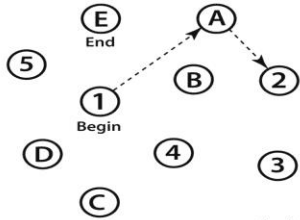
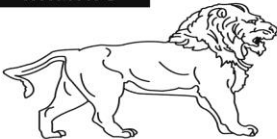
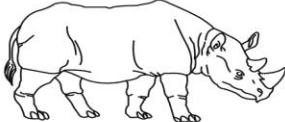
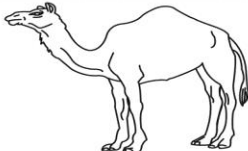
MMSE\$1

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day of the week? Month?"
5		"Where are we now: State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials: _____
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, ...) Stop after five answers. Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL



NCD Screening Instruments

MoCA Free!

MONTREAL COGNITIVE ASSESSMENT (MOCA) Version 7.1 Original Version		NAME:	Education:	Date of birth:																			
		Sex:		DATE:																			
VISUOSPATIAL / EXECUTIVE		 Copy cube <input type="checkbox"/>		Draw CLOCK (Ten past eleven) (3 points) <input type="checkbox"/>																			
		<input type="checkbox"/>		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> Contour Numbers Hands																			
				___/5																			
NAMING																							
																							
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MEMORY		Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.		<table border="1"> <tr> <td></td> <td>FACE</td> <td>VELVET</td> <td>CHURCH</td> <td>DAISY</td> <td>RED</td> </tr> <tr> <td>1st trial</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>2nd trial</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>			FACE	VELVET	CHURCH	DAISY	RED	1st trial						2nd trial					
	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		[] FBACMNAAJKLBAFAKDEAAAJAMOF AAB																			
				___/1																			
Serial 7 subtraction starting at 100		[] 93 [] 86 [] 79 [] 72 [] 65		___/3																			
		4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt																					
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		<table border="1"> <tr> <td>FACE</td> <td>VELVET</td> <td>CHURCH</td> <td>DAISY</td> <td>RED</td> </tr> <tr> <td>[]</td> <td>[]</td> <td>[]</td> <td>[]</td> <td>[]</td> </tr> </table>		FACE	VELVET	CHURCH	DAISY	RED	[]	[]	[]	[]	[]								
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Optional		Multiple choice cue																					
ORIENTATION		[] Date [] Month [] Year [] Day [] Place [] City		___/6																			
© Z.Nasreddine MD		www.mocatest.org		Normal ≥ 26 / 30																			
Administered by: _____				TOTAL ___/30																			
				Add 1 point if ≤ 12 yr edu																			





Thank you.



Sources



From the AMERICAN GERIATRICS SOCIETY

Geriatrics Evaluation & Management Tools

