Dementia

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Dementia

- Definition
- Diagnostic criteria
- Epidemiology
- Differential diagnosis typical features and treatment of certain dementia syndromes
- Cases

Dementia: Definition

- Dementia is a clinical syndrome characterised by a decline of intellectual function in comparison with the patient's previous level of cognition.
- Social and occupational activities and behaviour are also influenced.
- A decline in the activities of daily living (ADL) often accompanies first two.

Dementia: Criteria

- DSM IV Criteria for the dementia:
  - Development of multiple cognitive deficit including memory impairment and at least one of the following:
    - aphasia
    - apraxia
    - agnosia
    - executive functioning disturbance
  - The cognitive deficit must,
    - be sufficiently severe to cause impairment in occupational and social functioning.
    - represent a decline from a previous higher level of functioning.

Dementia: Criteria, definition of key terms

- **Aphasia:** is a language disorder that affects ability to comprehend or express spoken or written language or both.
- The term **apraxia** is defined as inability to correctly perform learned skilled movements with the arms etc.
  - no weakness,
  - no ataxia,
  - no seizure,
  - no involuntary movement
- **Agnosia** can be defined as inability to recognise familiar objects, faces, sounds or words.
- perception,
- memory,
- language
- intellectual function

normal

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    - be sufficiently severe to cause impairment in occupational and social functioning.
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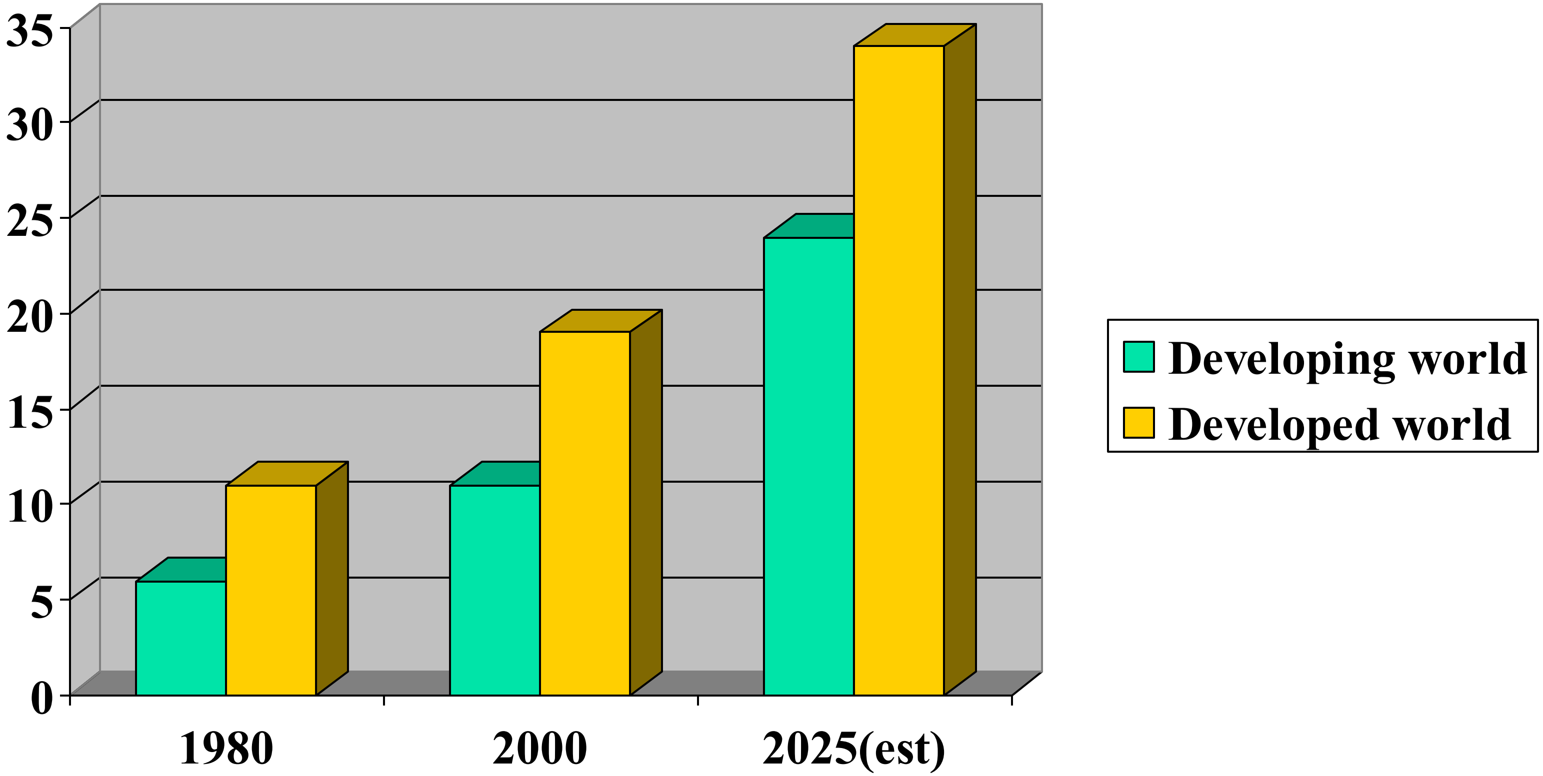
Dementia: Criteria

- DSM IV Criteria for the dementia:
  - Diagnosis should not be made if the cognitive deficits occur exclusively during the course of delirium.
  - Dementia may be etiologically related to a general medical condition, to the persisting effects of the substance abuse (including toxin exposure), or to a combination of these factors.

Dementia: Epidemiology II

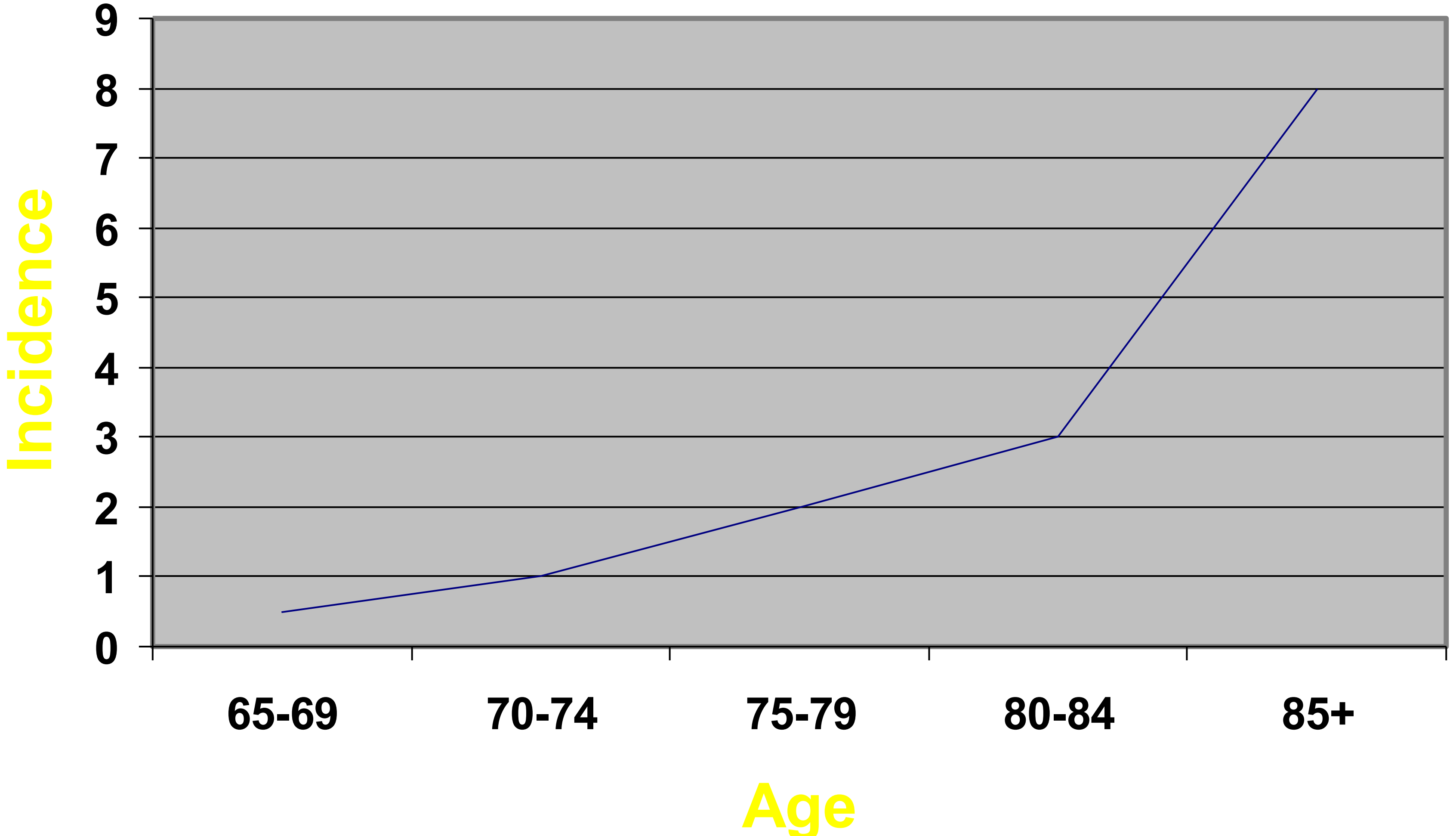


Prevalence increases with age

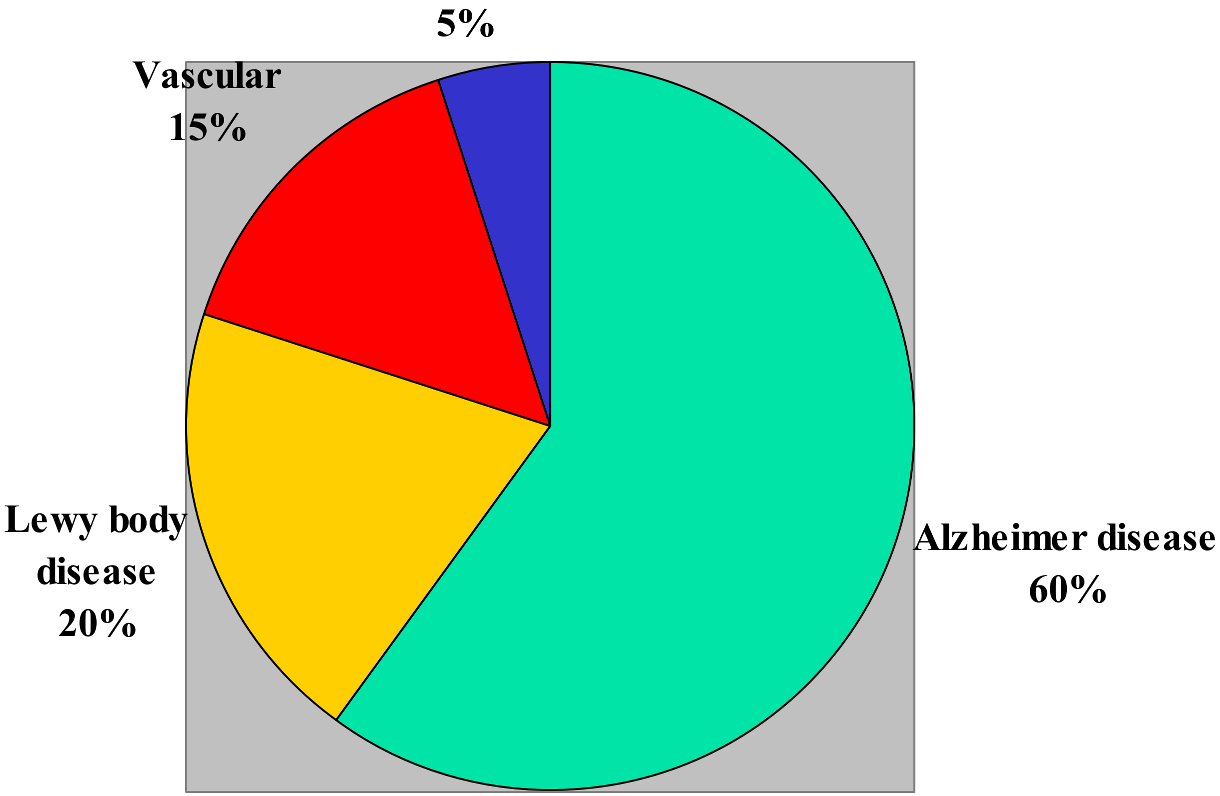
Age	**Prevalence***	**Age**	**Incidence**
>65	**5-10%**	**65-74**	**0.5-1%**
>75	**10-20%**	**75-84**	**2-4%**
>85	**25-50%**	**85+**	**6-8%**
>95	**40-70%**	**May level off or declince after age 100**	

*Lower numbers represent moderate to severe dementia

Incidence Of AD by Age



Dementia: Epidemiology III



Classification of dementias - I

- **Primary degenerative dementias**
  - **Dementia *pure*: neurodegenerative disorders primarily involving cerebral *cortex***
    - Alzheimer's disease
    - Focal degenerations
  - **Dementia *plus*: neurodegenerative disorders involving additional brain areas such as basal ganglia or other subcortical structures**
    - Dementia with Lewy bodies
    - Parkinson's disease
    - FTD-Parkinsonism-17; FTD with motor neuron disease
    - MSA
    - Corticobasal degeneration
    - PSP
    - Huntington diseae
    - Some forms of SCA
    - Familial multiple system taupathy
    - Progressive subcortical gliosis

Classification of dementias - II

- **Secondary forms of dementia**
  - Disorders damaging the brain tissue directly
    - Vascular-ischaemic causes
    - Infections
    - Demyelinating disorders
    - Inborn metabolic disorders
    - Traumatic brain injury
    - Post-radiation dementia
    - Some brain tumors
    - Parasitic cysts or brain abscess
  - Disorders changing intracranial contents and distorting brain structures
    - Normal pressure or obstructive hydrocephalus
    - Subdural or intraparenchymal haematoma
    - Primary or metastatic brain tumors
  - Systemic diseases or conditions affecting the brain
    - Metabolic-nutritional
    - Endocrine
    - Toxic
    - Systemic immune-mediated or inflammatory disorders

Dementia: Differential diagnosis Pseudo-dementia of depression

Clinical Picture	**Pseudo-dementia**	**Dementia**
Mode of onset	Rapid, with change in behaviour	Insidious, months and years
Mood/behaviour	Stable or apathy, depressed mood	Fluctuating, normal to apathy or irritable
Intellectual functions	Complains more, but neuropsychological testing, reveals good results.	Objective deficits on tests, but patients tend to minimize or rationalize errors.
Reason for consultation	Self-referral, anxious about AD	Patients are brought by their family members who notice change in the memory or behaviour.

Dementia: Differential diagnosis: Dementia vs Delirium

Feature	Dementia	Delirium
Onset	Insidious	**Sudden**
Duration	Months to years	Hours to days
Course	**Progressive**	Fluctuating
Attention	Normal	**Fluctuating arousal and inattention**
Speech	Normal	Slurred, incoherent
Language	Aphasic	Anomia, dysgraphia
Memory	**Learning deficit (AD)**	Encoding deficits
Cognition	Acalculia, concrete (AD)	Disorganized
Awareness	Impaired	Impaired
Motor signs	**None**	**Tremor, and asterixis**
EEG	**Mild-diffuse slowing**	**Moderate to severe diffuse slowing**

Dementia: Differential diagnosis: Cortical vs Subcortical

Feature	Cortical dementia	Subcortical dementia
Onset	Insidious	Insidious
Duration	Months to years	Months to years
Course	**Progressive**	Progressive or constant
Attention	Normal	Normal **(slow response time)**
Speech	Normal	Hyphophonic, dysarthric, mute
Language	Aphasic	Normal or anomic
Memory	**Learning deficit (AD)**	**Retrieval deficit**
Cognition	Acalculia, concrete (AD)	Slow
Awareness	Impaired	Usually preserved
Motor signs	**None**	**Tremor, chorea, rigidity, dystonia**
EEG	**Mild-diffuse slowing**	Normal-mild slowing

Disease Groups Can Present as Pure Dementia I

- **Space- Occupying Lesions**
  - Neoplasm
  - Normal-pressure hydrocephalus
  - Subdural hematoma
  - Parasitic cyst, brain abscesses
- **Infectious Organisms**
  - HIV
  - Syphilis
  - Herpes simplex
  - Lyme disease
  - Whipple's disease
- **Nutritional-Metabolic-Toxic**
  - Wernicke-Korsakoff disease
  - Chronic alcoholism
  - B12 deficiency
  - Pellegra
  - Organic solvent exposure
  - Heavy metal intoxication
  - Hepatic encephalopathy
- **Immune Inflammatory**
  - Paraneoplastic limbic encephalitis
  - Systemic lupus
  - Cerebritis associated with collagen-immune diseases

Disease Groups Can Present as Pure Dementia II

- Vascular Disease
  - Multiple infarcts
  - Binswanger's disease
  - Various arteritides
  - CADASIL*
- Storage Diseases
  - Metachromatic Leukodystrophy
  - Kuf's disease
- Prion Diseases
  - Creutzfeld-Jacob
  - Fatal familial insomnia
- **Primary (degenerative) Neuronal Diseases**
  - **Alzheimer's disease**
  - **Frontotemporal dementia**
  - **Lewy body disease**

* CADASIL: cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy.

Diseases that can present with sensory- motor deficits + dementia

- Parkinson’s disease
- Progressive supranuclear palsy
- Cortico-basal ganglionic degeneration
- Huntington’s disease
- Wilson’s disease
- Hallervorden-Spatz disease
- Spinocerebellar ataxias
- Amyotrophic lateral sclerosis
- Multiple sclerosis
- Gerstmann-Sträussler-Scheinker disease
- Kuru

Treatable Dementias

- <u>Thyroid disease</u>
- <u>B12 deficiency</u>
- Thiamine deficiency (Wernicke's encephalopathy)
- Pellegra
- Alcohol
- <u>Hepatic encephalopathy</u>
- <u>Normal- pressure hydrocephalus</u>
- <u>Sub-dural haematoma</u>
- Benign brain tumors
- Chronic meningitis
- Abscess
- Cyst

Alzheimer’s Disease (AD): Genetics, prevalence, risk factors I

- In 5-10 % of AD patients disease shows an autosomal dominant trait.
- It’s onset is at 30s or 40s.
- APP (chromosome 21), presenilin1(chromosome 14) and presenilin2 (chromosome 1) mutations
- All of them result in excessive production of insoluble ß amyloid .
- hIn patients with Down syndrome the AD pathology occurs when they are 30-40 years old because of te over-production of ß amyloid due to the existence of an extra chromosome 21.

Alzheimer's Disease (AD): Genetics, prevalence, risk factors II

- In 90-95 % of the patients AD does not show an autosomal dominant transmission.
- The disease onset is at about their 65s.
- But in this group, some of the patients come from the families where the prevalence of AD is higher than general populations (nondominant familial AD).
- The rest of the patients comes from families, their prevalence of AD is similar to that of the general population (sporadic AD).

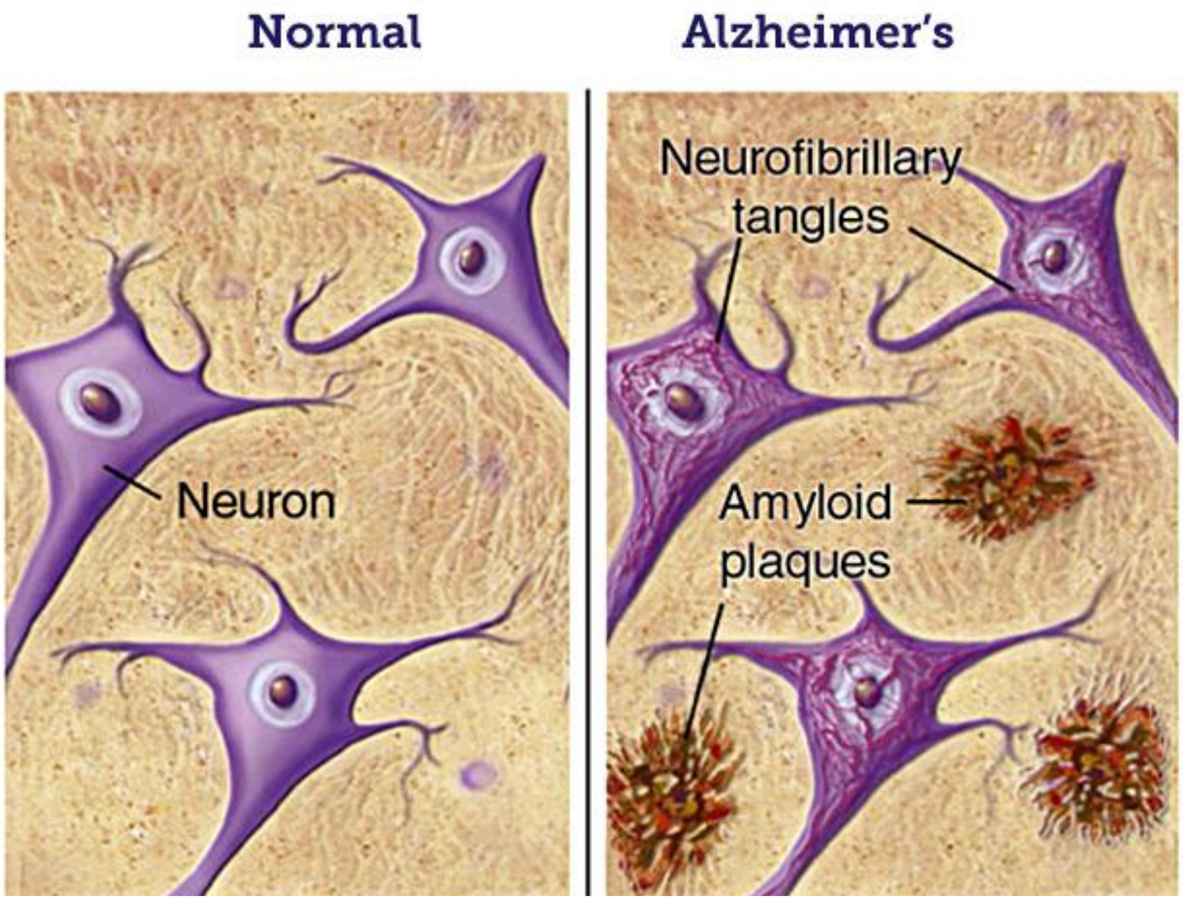
Alzheimer’s Disease (AD): Genetics, prevalence, risk factors III

- The most important risk factor for AD is age. Prevalence doubles for every 5 years after the age of 65 (10%) and reaches 40% among those older than 85.
- Head injury, female gender and a positive family history are other known risk factors.
- An additional risk factor has been linked to chromosome 19 that encodes apolipoprotein E (ApoE).
- The e4 allele frequency is 20% in the general population and 40% in AD.

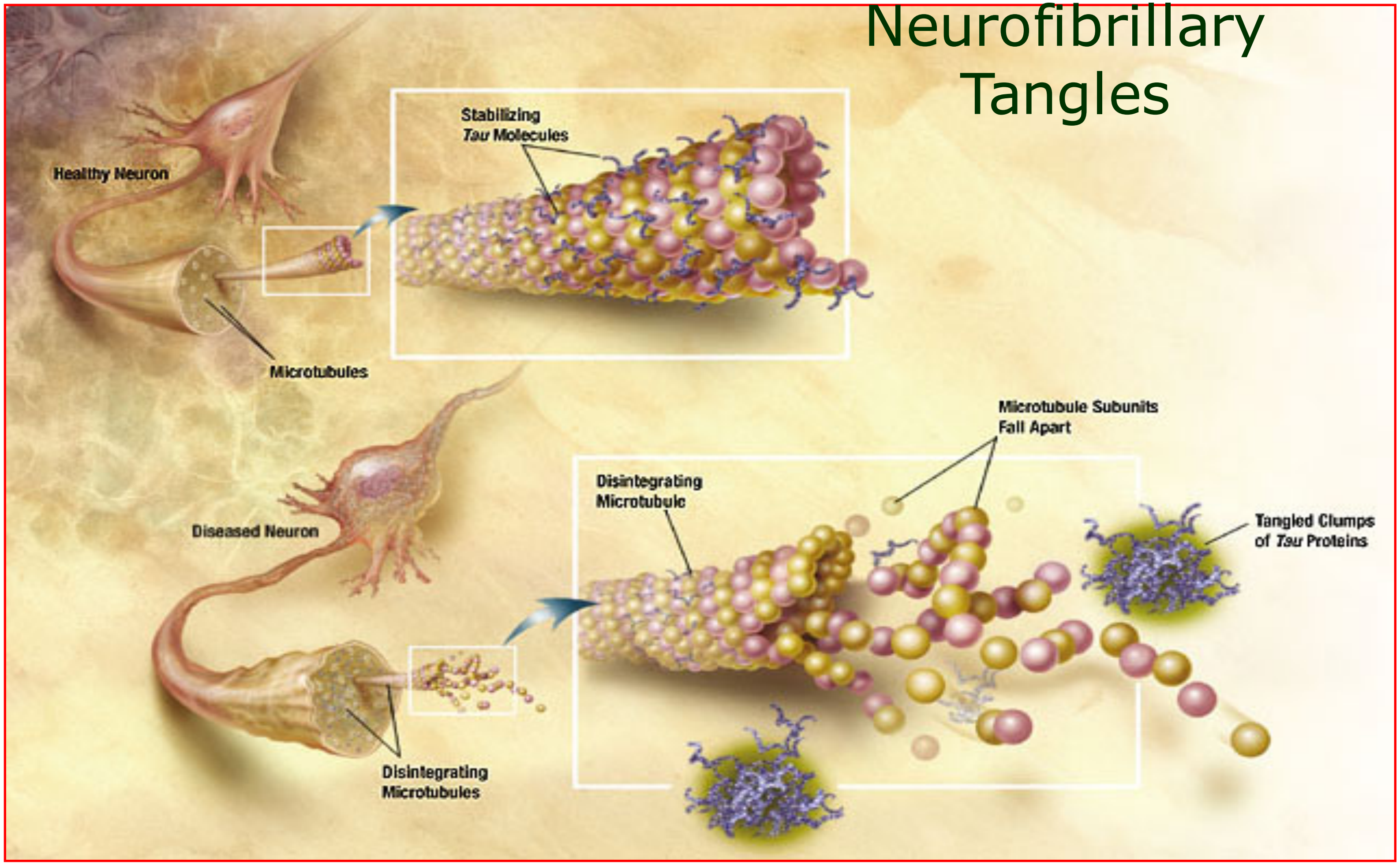
Alzheimer's Pathophysiology

- **Neuritic plaques** -*extracellular* - abnormal insoluble amyloid protein fragments
- **Neurofibrillary tangles** - *intracellular* - disturbed tau-microtubule complexes (hyperphosphorylated tau)
- Cholinergic system degeneration with significant loss of neurons in certain areas (such as Nucleus basalis of Meynert)
- Degeneration often begins in **enterorhinal cortex** and progresses to other limbic structures

Alzheimer's Pathophysiology



Neurofibrillary Tangles



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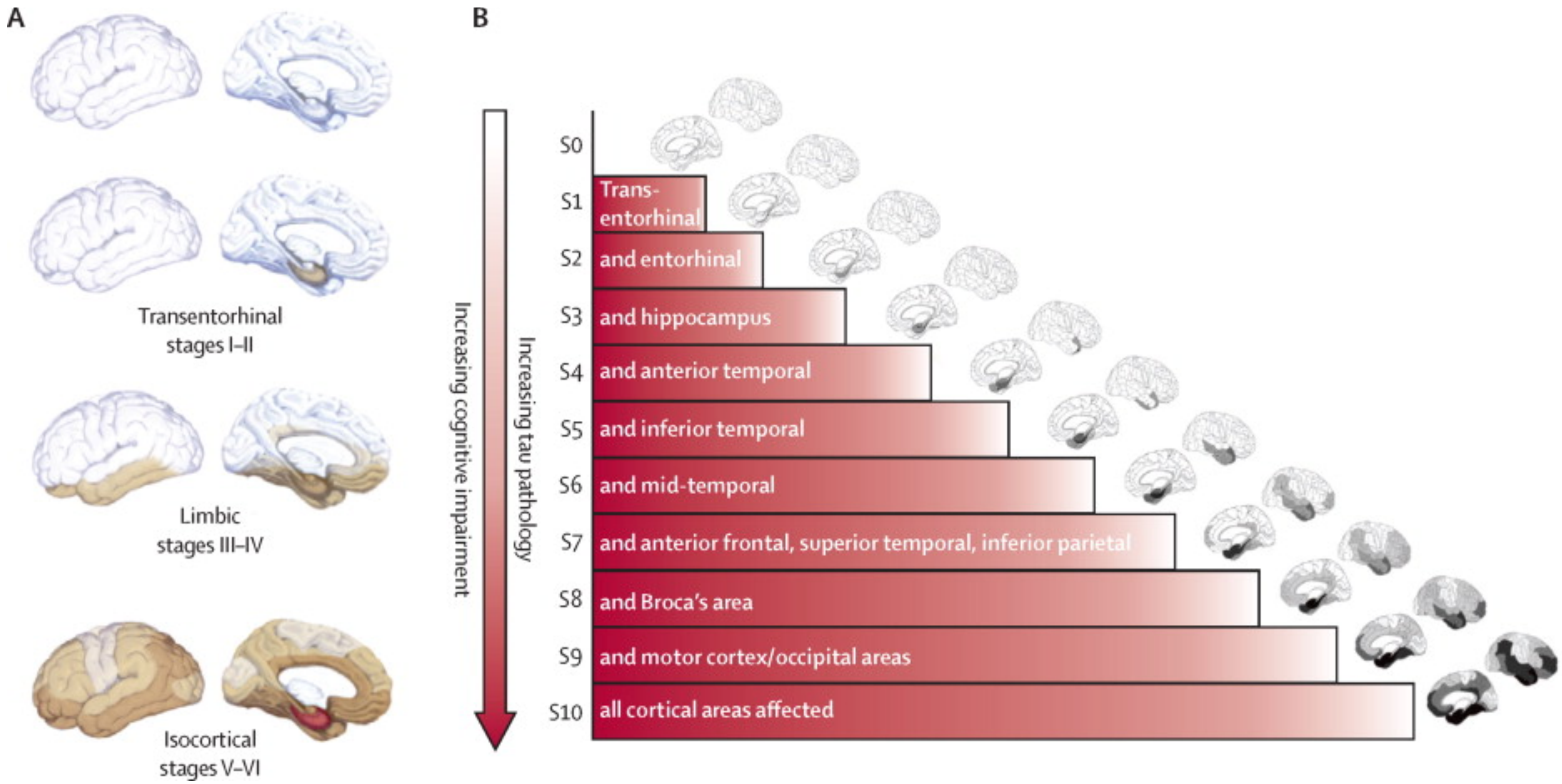
NIA/ADEAR

Progression of tau deposition in AD



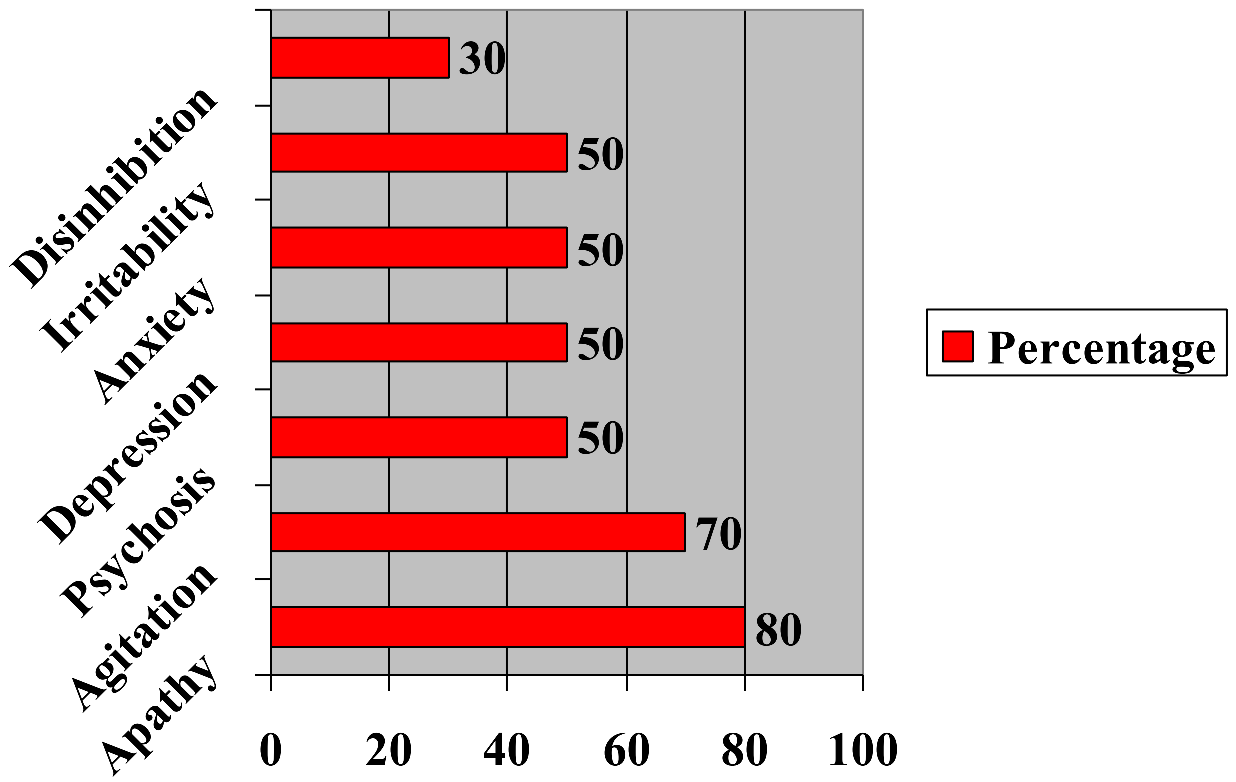
Braack and Braak (I-VI), and Delacourte staging (S1-10)

Villemagne 2015

AD: Clinical Picture (ABC's of AD)

- AD is an amnestic dementia with an insidious onset and indolent course.
- It causes disturbances in daily living <u>a</u>ctivities, <u>b</u>ehavioural symptoms and <u>c</u>ognitive decline.
- Diagnosis→ death about 15-20 years.
- Symptoms change as the pathology of the disease progresses.

Neuro-psychiatric Symptomatology in AD



AD: Initial Stage I

- **Memory problems**
  - forgets names, repeat themselves, misplaces their belongings, makes lists
  - may fluctuate in intensity, good for remote events and recent events with high emotional impact.
  - poor for ordinary recent events
  - clues and multiple choices are useful.

AD: Initial Stage II

- **Language and behavioural problems**
  - speech becomes less fluent and loses spontaneity.
  - difficulty in word finding.
  - Self awareness of impairment may elicit depression.
- may keep working, especially when he/she is protected by understanding staff in his/her office.
- may have some difficulties in choosing dress, complex financial tasks.
- may keep house, pay bill, drive car, participate social activities

AD: Intermediate Stage I

- Memory problems
  - recognition difficulties (forgets remote events)
  - forgets faces
  - inability to use clues or lists
  - spatial orientation disturbances (getting lost in unfamiliar environment)
  - inability to store new data (even for minutes)

AD: Intermediate Stage II

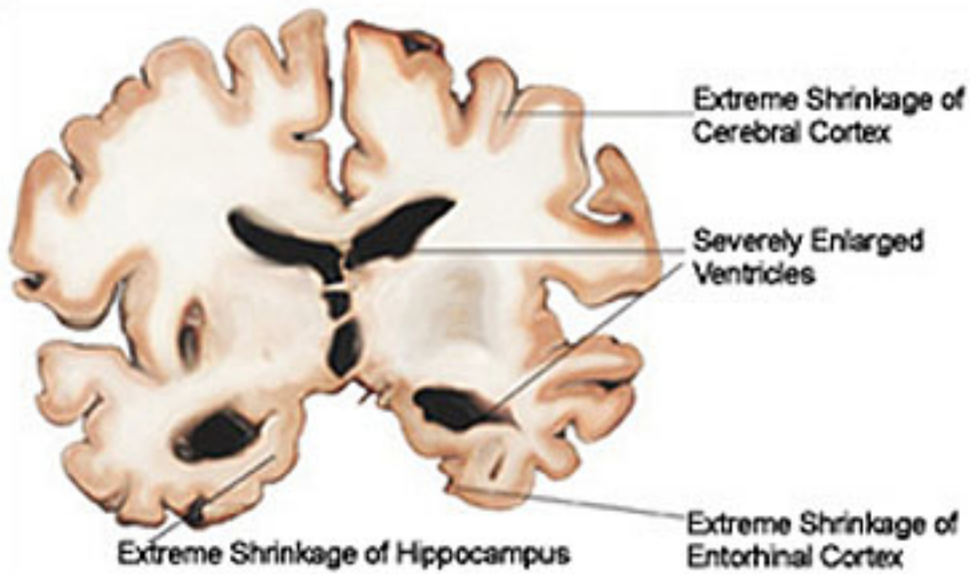
- Language and behavioural problems
  - word finding difficulty in ordinary conversations
  - increased misunderstanding
  - become indifferent to their symptoms, depression subsides.
  - paranoid ideation (spousal infidelity, stolen personal object due to misplacement)
  - sun downing (worsening of cognitive and behavioural symptoms at the end of the day)
  - Independency in housekeeping, dressing, bathing, grooming, paying bills are gradually lost

AD: Final Stage I

- Memory problems
  - living in past
  - inability to recognize family members
  - family members recognized as if they are not themselves (they recognized as their imitations)
  - getting lost even in familiar surroundings
  - inability recognize home and rooms

AD: Final Stage II

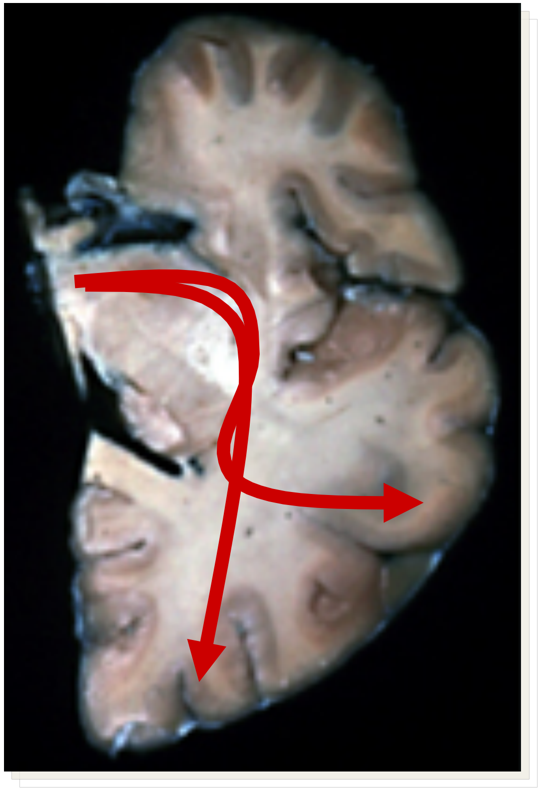
- Language and behavioural problems
  - incoherent speech
  - loss of speech
  - wandering
  - purposeless movements
  - crying
  - agitation
  - difficulties in moving and feeding, bathing, continence towards the end of stage
  - myoclonus, rigidity, gait difficulties
  - become bedridden and death due to infections or emboli.



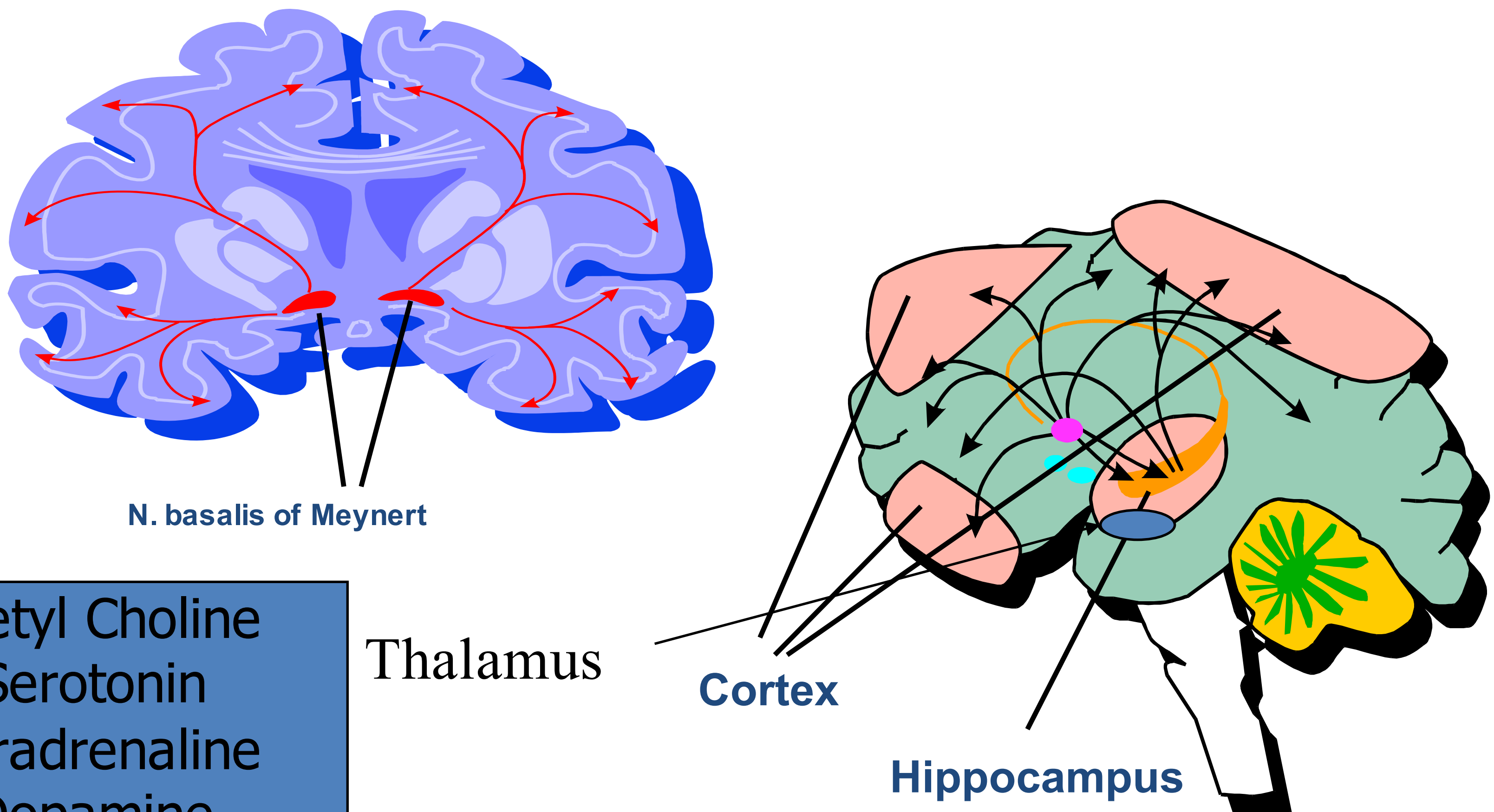
Severe Alzheimer’s Disease

Regional distribution of pathology

- Distribution of pathology in AD is not random, but starts in transentorhinal cortex and ends in neocortex

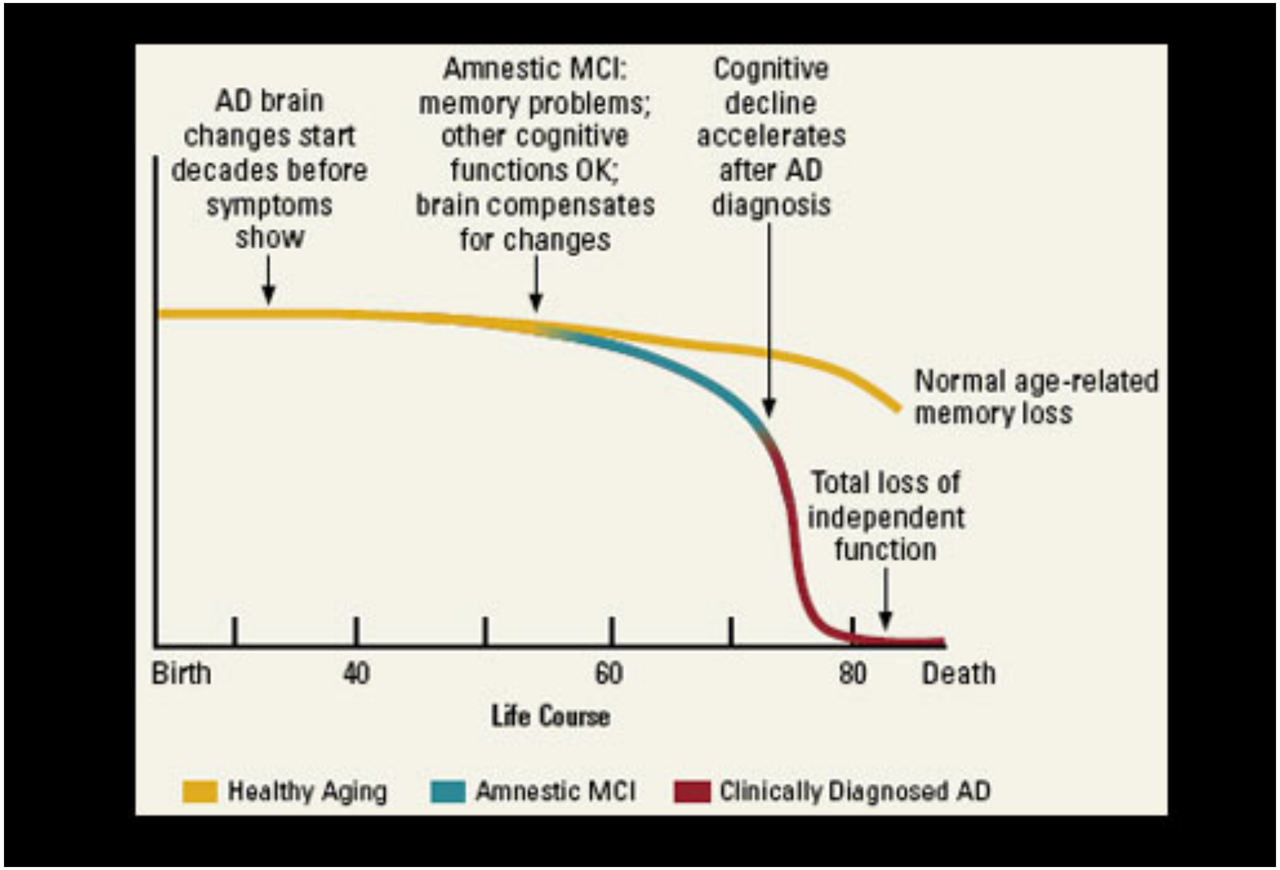


Affected neurotransmitter systems in AD



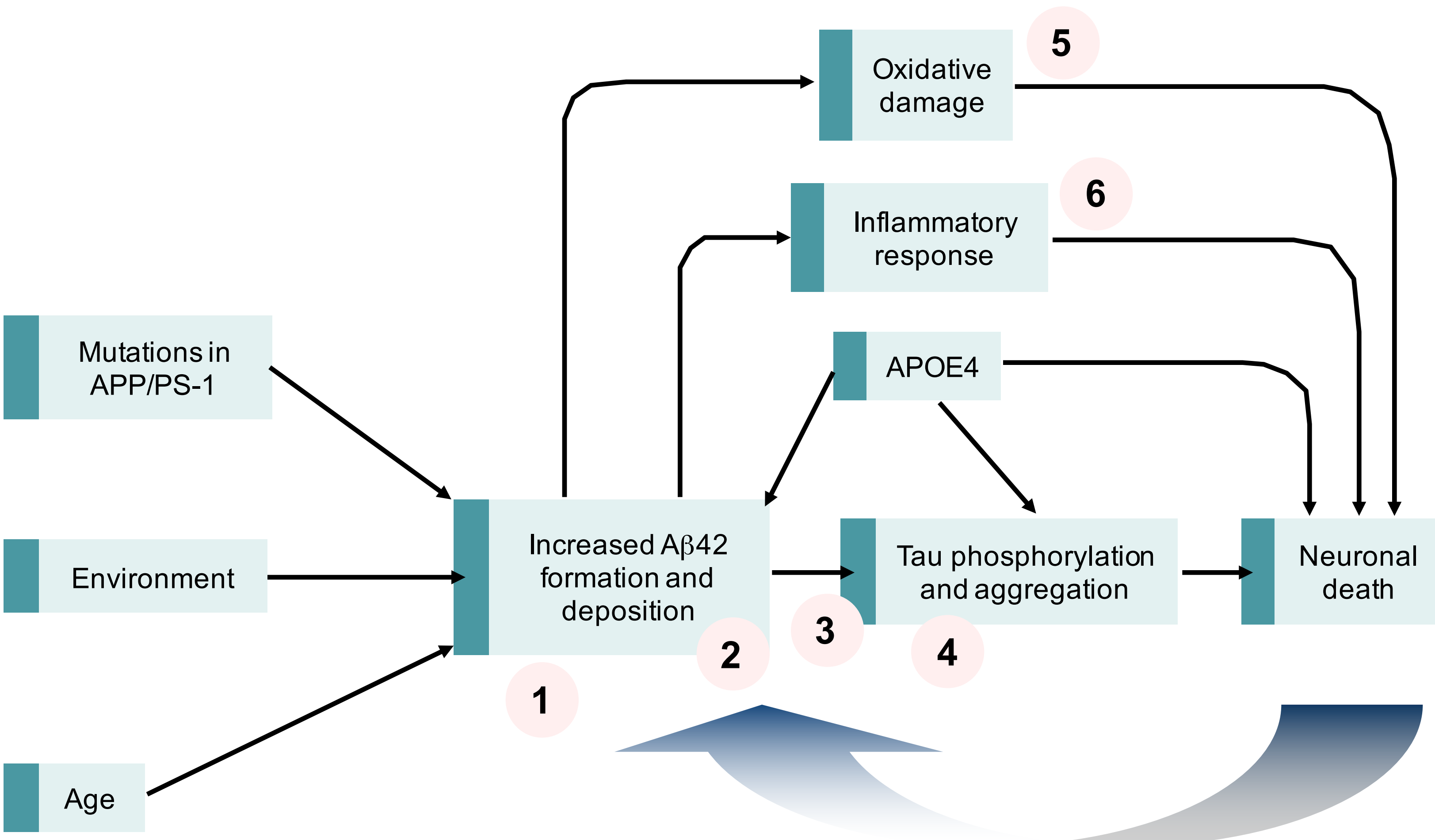
Acetyl Choline
Serotonin
Noradrenaline
Dopamine

Bartus et al., 1982; Cummings and Back, 1998, Perry et al., 1978



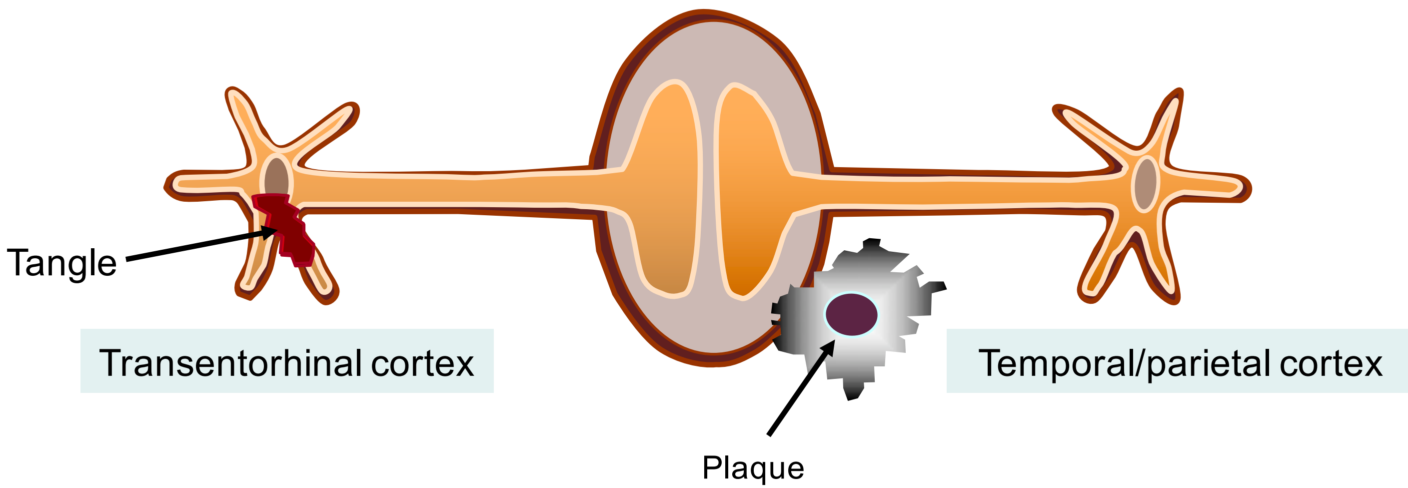
AD brain changes start decades before symptoms show
Amnestic MCI: memory problems; other cognitive functions OK; brain compensates for changes
Cognitive decline accelerates after AD diagnosis
Normal age-related memory loss
Total loss of independent function
Birth
40
60
80
Death
Life Course
Healthy Aging
Amnestic MCI
Clinically Diagnosed AD

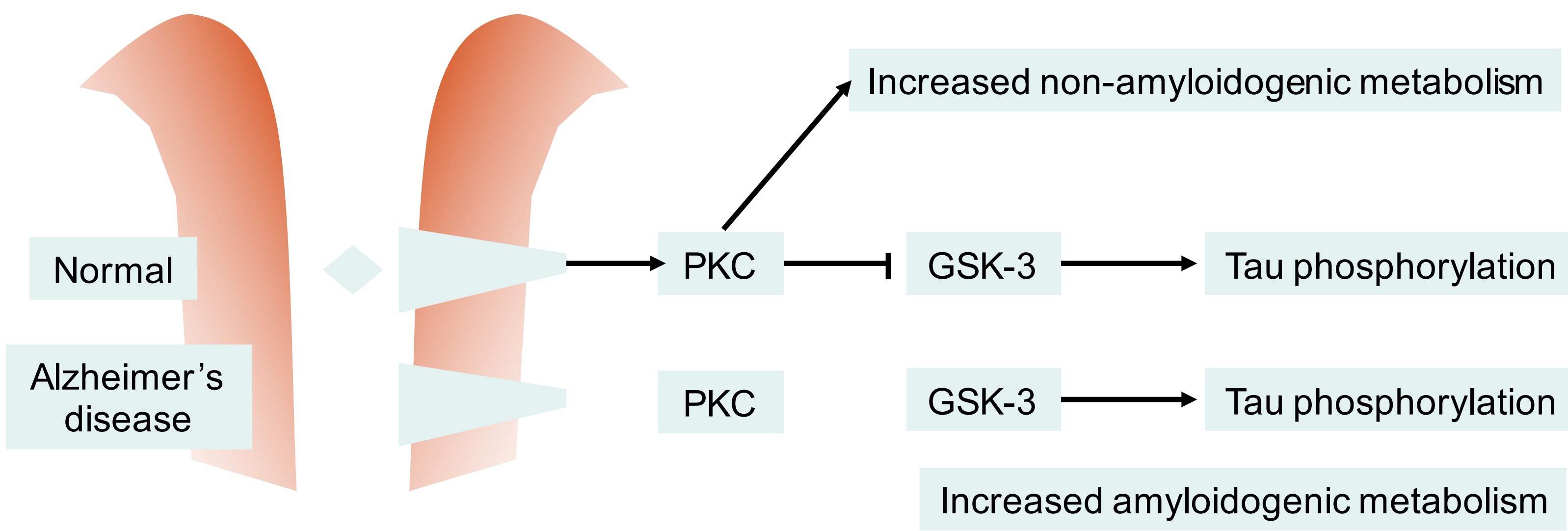
Synthesis (1)



5
Oxidative damage
6
Inflammatory response
Mutations in APP/PS-1
APOE4
Environment
Increased Aβ42 formation and deposition
Tau phosphorylation and aggregation
Neuronal death
Age
1
2
3
4

Synthesis (2)


Tangle
Transentorhinal cortex
Plaque
Temporal/parietal cortex


Increased non-amyloidogenic metabolism
Normal
PKC
GSK-3
Tau phosphorylation
Alzheimer's disease
PKC
GSK-3
Tau phosphorylation
Increased amyloidogenic metabolism

Clinical and laboratory diagnosis

- No lab. test for definitive diagnosis in a living patient.
- Biopsy or autopsy is gold standard
- The NINCDS-ADRDA criteria have been purposed to probable AD (PRAD).
- Post mortem confirmation studies revealed a 90 % or higher concordance with criteria in diagnosis of PRAD

NINCDS/ADRDA Criteria for Alzheimer's Disease I

- Criteria for clinical diagnosis of **Probable AD** include:
  - Dementia established by clinical exam and documented by, confirmed by further neuropsychological tests.
  - Deficits in two or more areas of cognition.
  - Progressive worsening of memory and other cognitive functions.
  - No disturbance of consciousness.
  - Onset between the ages of 40 and 90.
- Absence of systemic diseases or other brain diseases that could explain the cognitive changes.

The National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Associations 1984

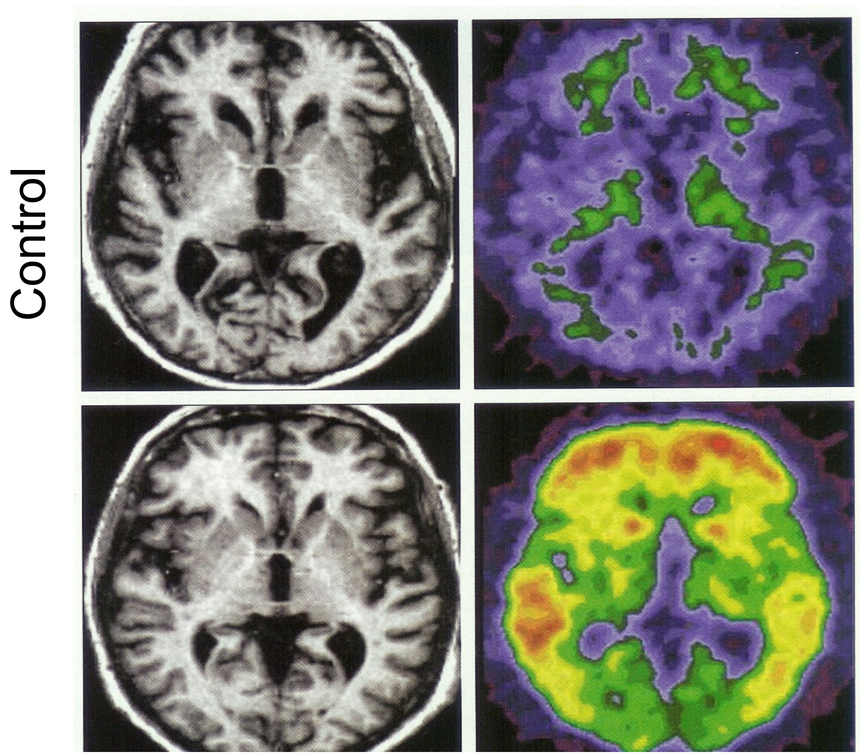
NINCDS/ADRDA Criteria for Alzheimer's Disease II

- The diagnosis of Probable AD is supported by:
  - Progressive deterioration of specific cognitive functions such as language, motor skills, and perception (aphasia, apraxia, agnosia, respectively).
  - Impaired activities of daily living.
  - Positive family history, particularly if documented neuropathologically.

- **Biomarkers**

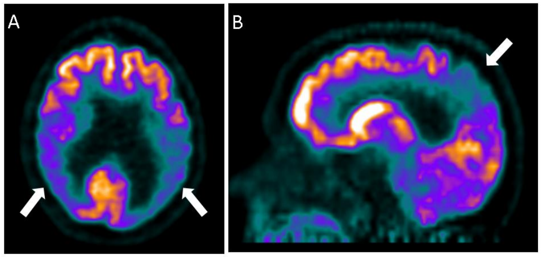
Biomarkers

- <u>Brain Aß amyloidosis</u>
  - PIB/florbetapir-PET



  - ↓ CSF Aß-42

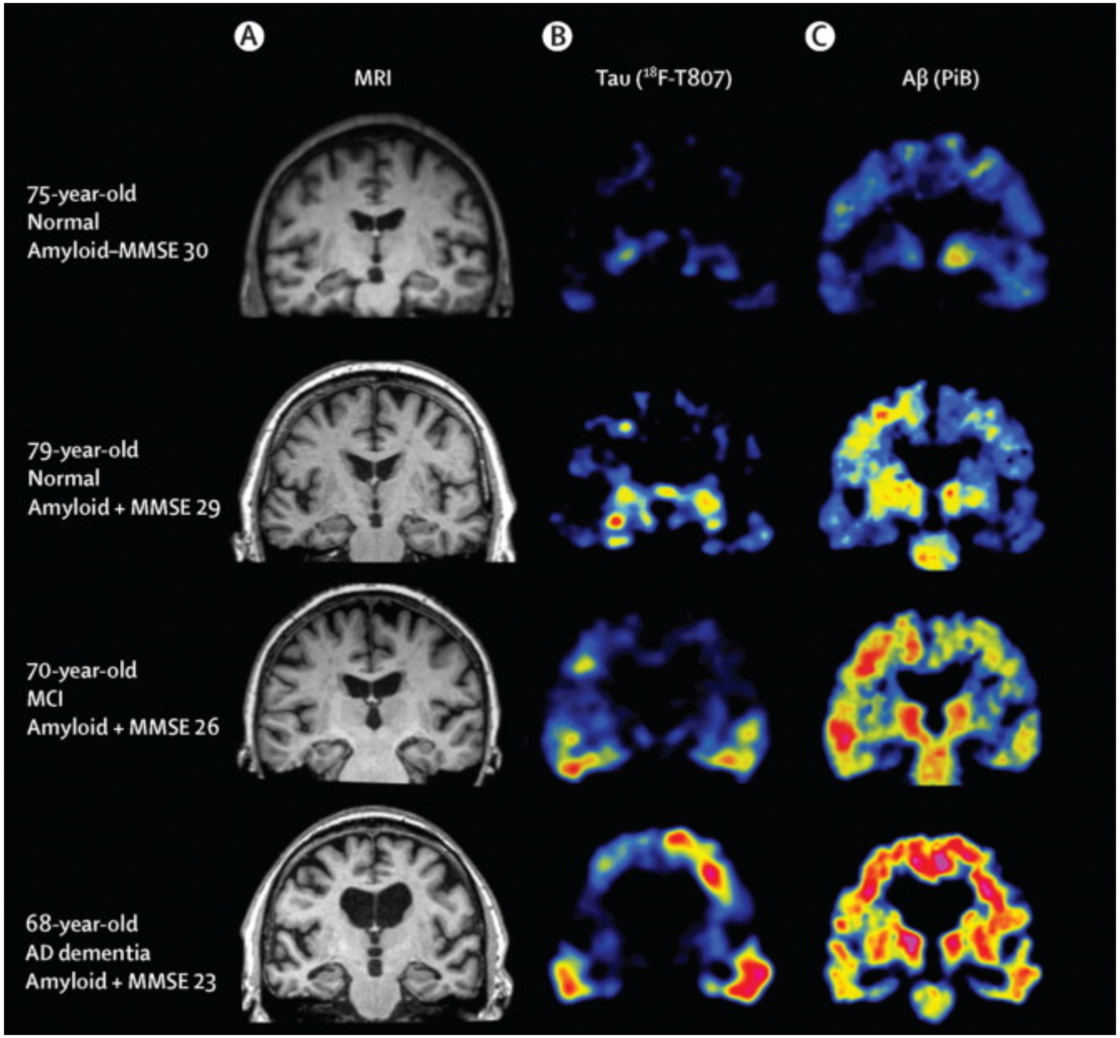
- <u>Neuronal injury</u>
  - FDG-PET



  - ↑ CSF-tau
  - MRI atrophy
    - Medial temporal lobes
    - Temporoparietal cortex

Biomarkers

- Brain Tau
  - Tau PET



Multimodal Imaging- tau and Aß

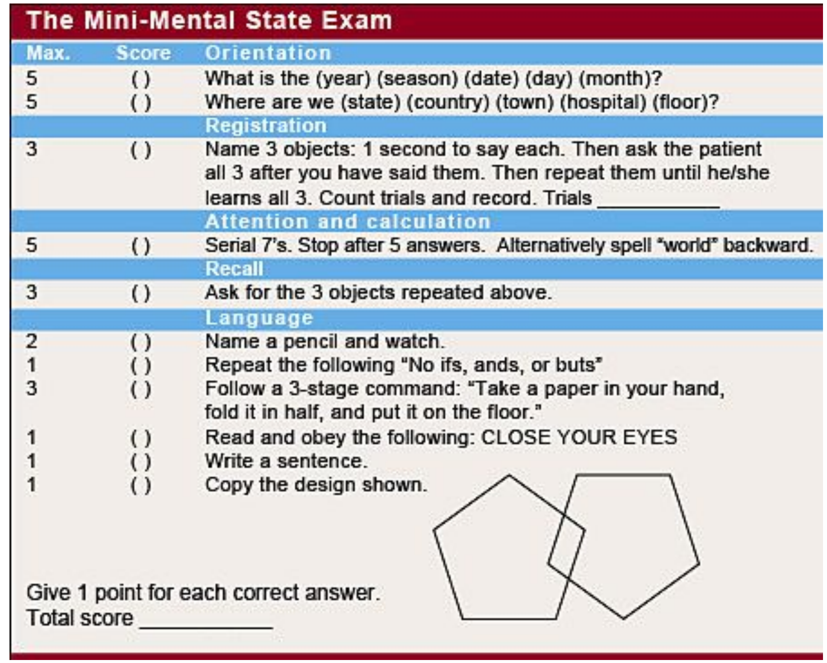
• Tau -/Aß -	■ Normal aging, depression, meds
• Tau +/Aß +	■ Alzheimer’s disease, AD/LBD
• Tau -/Aß +	■ Premorbid AD, normal aging
• Tau +/Aß -	■ CTE, FTD, MSA > AD

Laboratory tests

Routine	Optional
Blood glucose	
CBC	Chest X-ray
Vitamin B_{12} level	ECG
Thyroid function tests	EEG
AST, ALT	Drug levels
LDH	Urinalysis
BUN	HIV testing
Uric acid	Heavy metals in urine
Sedimentation rate	CSF analysis
Syphilis serology	PET/SPECT
CT, MRI	

Primary Care Screening Tools

- MMSE

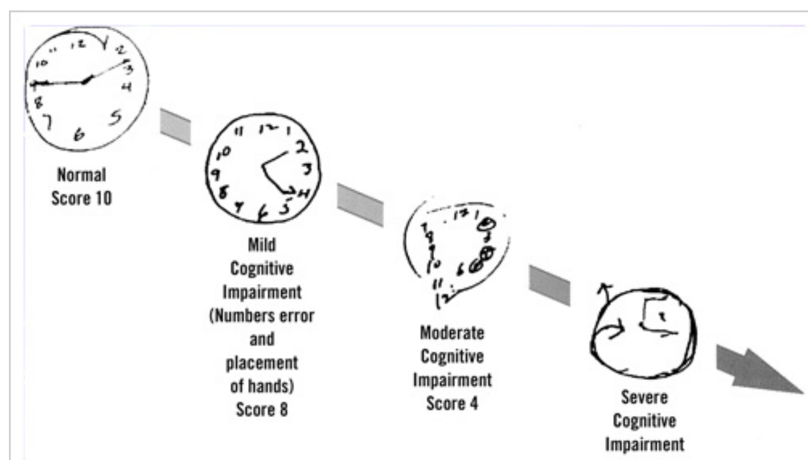


The Mini-Mental State Exam

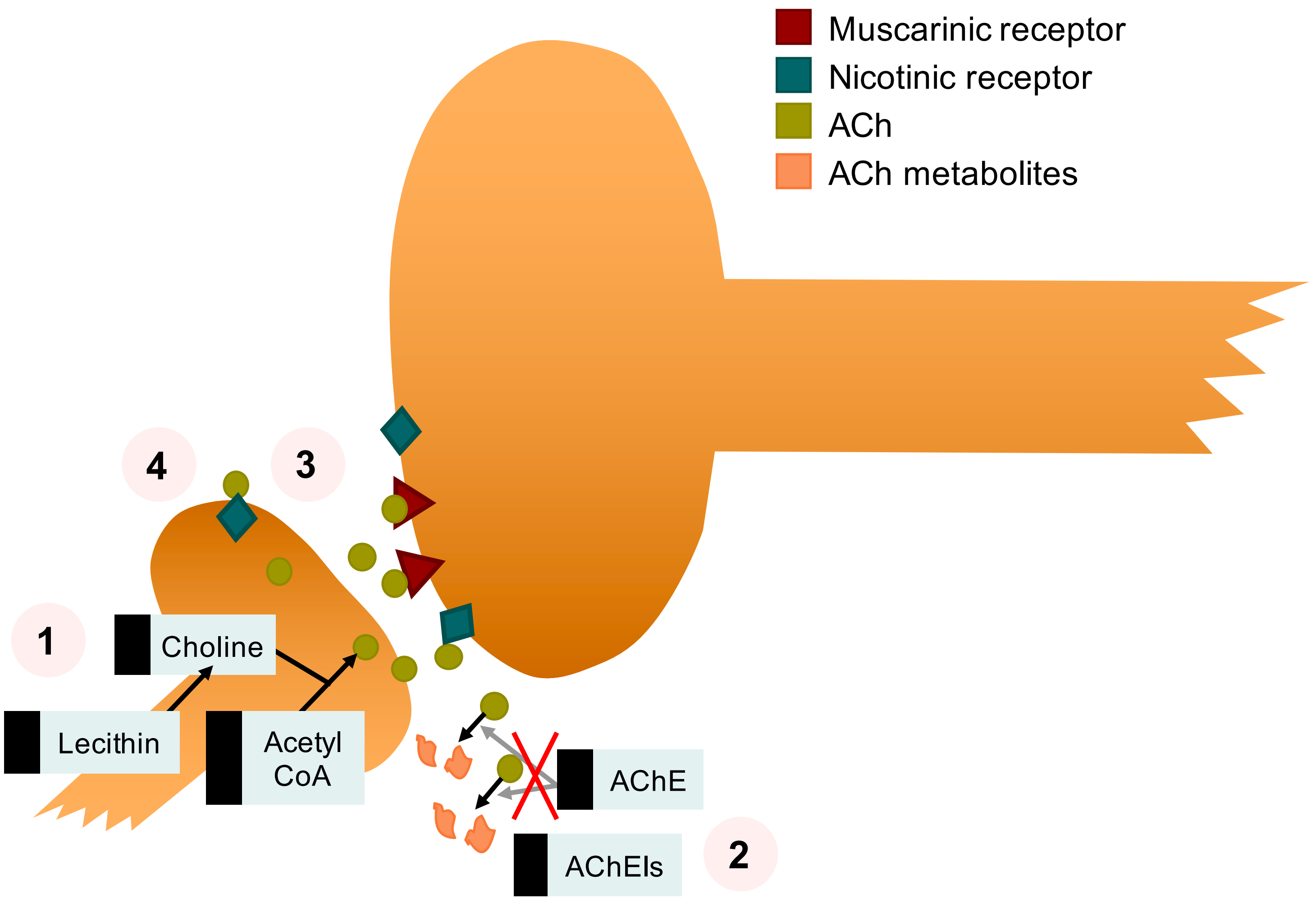
Max.	Score	Orientation
5	( )	What is the (year) (season) (date) (day) (month)?
5	( )	Where are we (state) (country) (town) (hospital) (floor)?
		Registration
3	( )	Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Then repeat them until he/she learns all 3. Count trials and record. Trials ___________
		Attention and calculation
5	( )	Serial 7's. Stop after 5 answers. Alternatively spell "world" backward.
		Recall
3	( )	Ask for the 3 objects repeated above.
		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.

Give 1 point for each correct answer.
Total score ___________

- Clock Test – easy to do, quick. Draw a clock, put numbers in correct locations, set hands to '10 til 2'.



Correcting cholinergic loss in AD



Treatment I

Acetylcholinesterase inhibitors

- Donepezil
- Rivastigmine
- Galantamine
- *have been shown to enhance cognitive performance in early disease.*

NMDA-antagonists

- Memantine *is approved for moderate disease. <u>However they do not cure!</u>*
- Treat concurrent depression, anxiety and sleep disorders. Neuroleptic use may be required for behavioral disturbance.
- Mangement of AD requires careful advice and counseling of the patient and family and shared care involving the family, caregivers, GPs, hospital specialist, and community psychiatric services.
- Long-term residential care is ofte required.

Treatment II

- Behavioural symptoms
  - Psychotic features
    - Typical neuroleptics (avoid in Lewy body dementia)
      - Haloperidol
      - Thioridazine
      - Chlorpromazine
      - Sulpiride
      - Pimoside
    - Atypical neuroleptics
      - Clozapine(!) agranulocytosis
      - Olanzapine
      - Risperidone
      - Quetiapine
  - Depressive features

    (Avoid antidepressants with prominent anticholinergic effect)
    - SSRI's
      - Fluoxetine
      - Sertraline
      - Citalopram

Treatment III

- SNRI’s
  - Venlafaxine
- Sleep disturbances
  - Trasodone
  - Anxiety
- benzodiazepines
- beta blockers

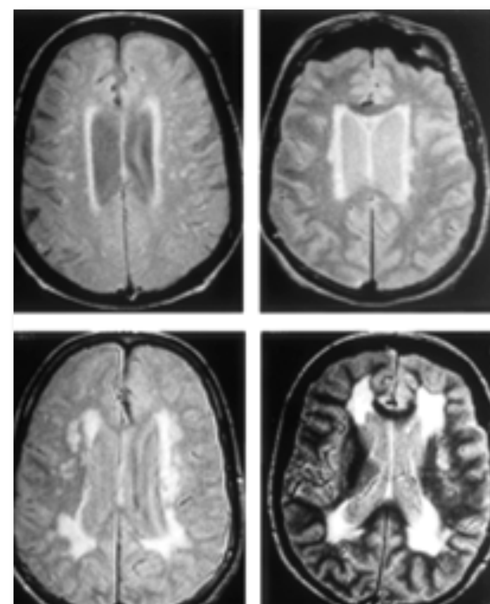
- Mood Stabilisers
  - Valproate Na
  - Gabapentine
  - Carbamazepine
  - Lithium

Non-AD dementia

- Multi-infarct dementia (VD)
- Mixed dementia
- Frontotemporal Dementia (FTD, M. Pick)
- Dementia with Lewy Bodies (LBD)

Multi-infarct dementia (VD)

- This is an **overdiagnosed condition** which accounts for less than 10% of cases of dementia.
- MID is caused by multiple strokes - SILENT STROKES
- Dementia occurs ’ **stroke by stroke ‘,** with progressive focal loss of function.
- **Clinical features of stroke profile** – hypertension, diabetes, etc. – are present. More often in males.
- Diagnosis is obtained from the history and confirmed by **CT or MRI scan** (the presence of multiple areas of infarction).
- **Treatment**: Maintain adequate blood pressure control, anti-platelet aggregants (aspirin).



Frontotemporal Dementia (FTD, M. Pick)

- Impairment of executive function
  - Initiation
  - Goal setting
  - planning
- Disinhibited behavior
- Cognitive testing may be normal/minimally abnormal; memory loss not prominent early feature
- 5-10% cases of dementia
- Onset usually 45-65

Frontotemporal Dementia (FTD, M. Pick)

- Subtype of frontal lobe dementia - Pick
- Pick bodies (silver staining intracytoplasmic inclusions in neocortex and hippocampus)
- Language abnormalities
  - Logorrhea (abundant unfocused speech)
  - Echolalia (spontaneous repetition of words/phrases)
  - Palilalia (compulsive repetition of phrases)

Frontotemporal Dementia (FTD, M. Pick)

Special forms

- primary progressive aphasia
- semantic dementia
- MRI and SPECT confirm focal changes.

Dementia with Lewy Bodies

- Cortical Lewy Bodies on path
- Overlap with AD and PD
- Fluctuations in mental status (may appear delirious)
- Early delusions and hallucinations
- Mild extrapyramidal signs
- Neuroleptic hypersensitivity!!!
- *Unexplained falls or transient changes in consciousness*

Progressive Supranuclear Palsy

- Uncommon
- Vertical supranuclear palsy with downward gaze abnormalities
- Postural instability
- Falls (especially with stairs)
- “surprised look”
- Difficulty with spilling food/drink

Normal pressure hydrocephalus

= term applied to the triad of:

1. Dementia
2. Gait disturbance
3. Urinary incontinence

occuring in conjunction with hydrocephalus and normal CSF pressure.

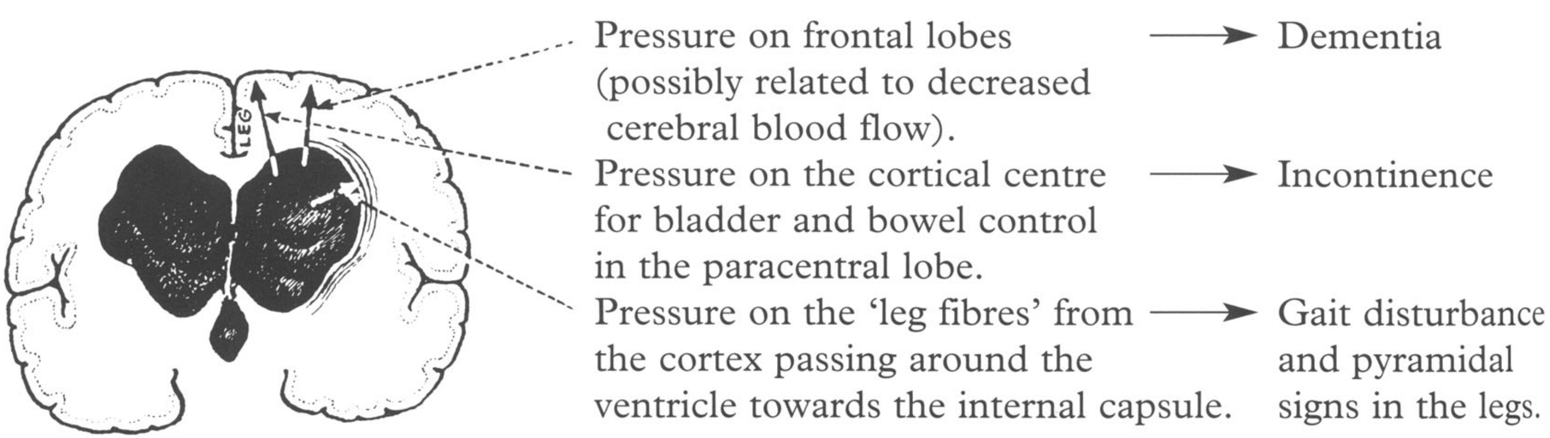
Two types:

- NPH with a preceding cause (SAH, meningitis, trauma, radiation-induced).
- NPH with no known preceding cause – idiopathic (50%).

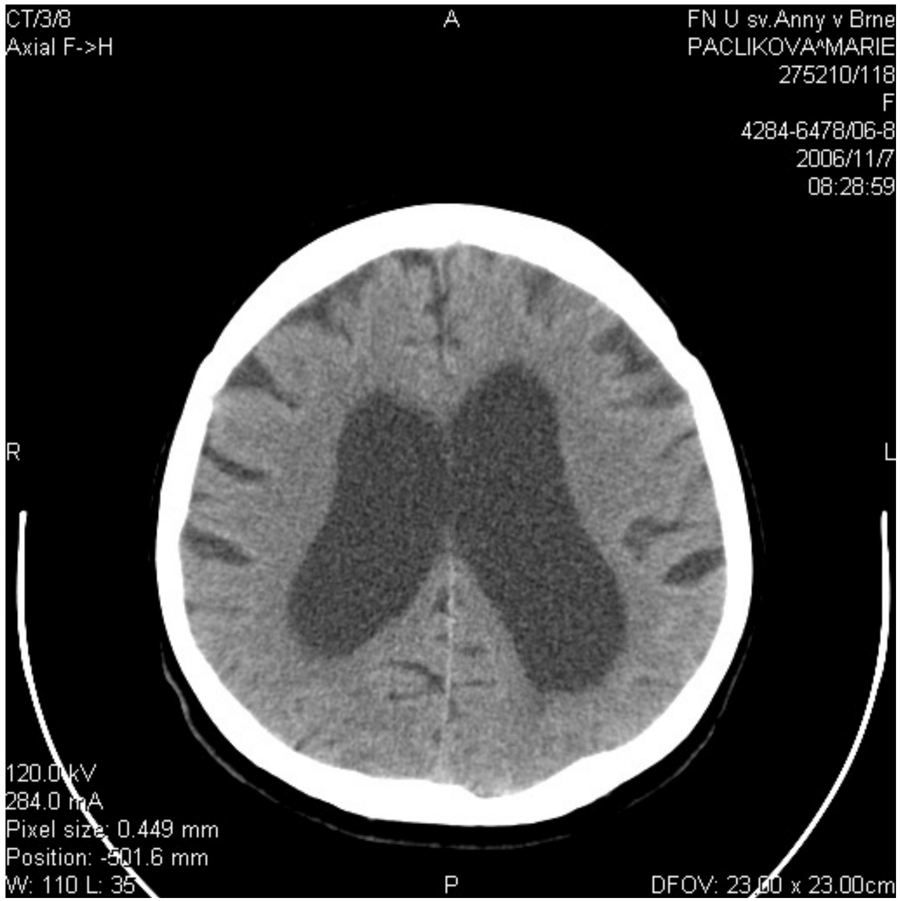
Normal pressure hydrocephalus

Aetiology is unclear.

It is presumed that at some preceding period, impedence to normal SCF flow causes raised intraventricular pressure and ventricular dilatation. Compensatory mechanisms permit a reduction in CSF pressure yet the ventricular dilatation persists and causes symptoms.



Normal pressure hydrocephalus



Degeneration of the basal ganglia

- Huntington’s disease
  - Rare: 5 in 100,000
  - abnormal ‘exaggerated movements
- Parkinson's disease
  - Common: 1 in 100 over age 65
  - General slowing of voluntary movements
- Both diseases involve the basal ganglia, but in large opposite ways

AIDS dementia complex

- Approximately two-thirds of persons with AIDS develop dementia, mostly due to AIDS dementia complex.
- In some patients HIV is found in the CNS at postmortem. In others an immune mechanism or an unidentified pathogen is blamed.
- Dementia is initially of a "subcortical " type.
- CT - atrophy; MRI - increased T2 signal from white matter.
- Treatment with Zidovudine (AZT) halts and partially revers neuropsychological deficit.

Trauma

- Reduction of intellectual function is common after severe head injury.
- Chronic subdural haematoma can also present as progressive dementia, especially in the elderly.
- *Punch-drunk encephalopathy* (dementia pugilistica) is the cumulative result of repeated cerebral trauma. It occurs in both amateur and professional boxers and it manifests by dysarthria, ataxia and expy signs associated with ’subcortical‘ dementia. There is no treatment for this progressive syndrome.

Tumor

- Dementia rarely may be due to intracranial tumour, especially when tumours occur in certain anatomical sites.
- Mental or behavioral changes occur in 50-70% of all brain tumours as distinct from dementia which is associated with frontal lobe tumours, III ventricle tumours and corpus callosum tumours.
- Cognitive impairment also occurs as a non metastatic complication of systemic malignancy.

Staging of Dementias

- MILD: difficulties with checkbook maintenance, complex meal preparations, complicated medication schedules
- MODERATE: difficulties with simple food preparation, household or yard work. May need some assistance with self-care
- SEVERE: Need considerable assistance with feeding, grooming and toileting
- PROFOUND: Largely oblivious to surroundings, totally dependent
- TERMINAL: Bed bound; require constant care

Case I

- Mr. Jones is a 72 y/o gentleman with progressive memory loss. He denies any problems. His son speeks about frequent falls and On exam, his BP is 170/90; he is oriented, scores 26/30 on the MMSE (0/3 recall and difficulty with the intersecting pentagon); he is unable to do the clockface.

Case I

- A few months later, his MMSE is 24/30; on exam he has some mild cogwheel rigidity and a slight shuffling gate, but no tremor. His daughter reports that he has been having vivid visual hallucinations and paranoid thought…

Dementia with Lewy Bodies

- Cortical Lewy Bodies on path
- Overlap with AD and PD
- Fluctuations in mental status (may appear delirious)
- Early delusions and hallucinations
- Mild extrapyramidal signs
- Neuroleptic hypersensitivity!!!
- *Unexplained falls or transient changes in consciousness*

Case II

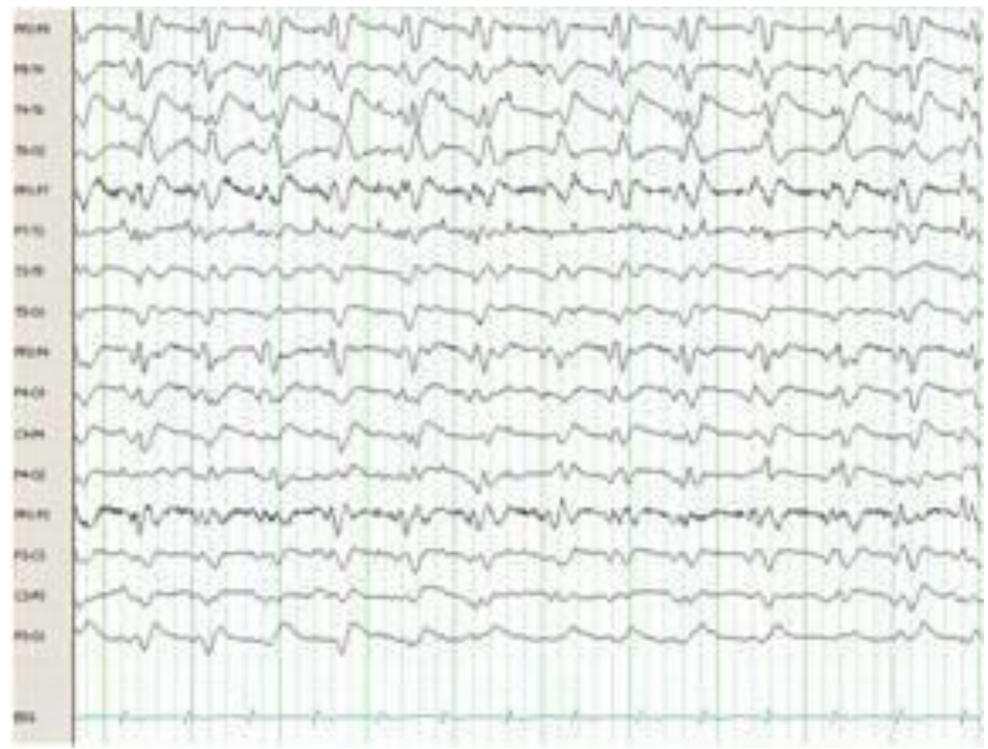
- A 54 y/o male without significant medical history with a <u>rapid progression of cognitive decline (3 weeks)</u>

- Neurological exam shows <u>impaired mental status, generalized ataxia, upper motor neuron signs and myoclonus</u>

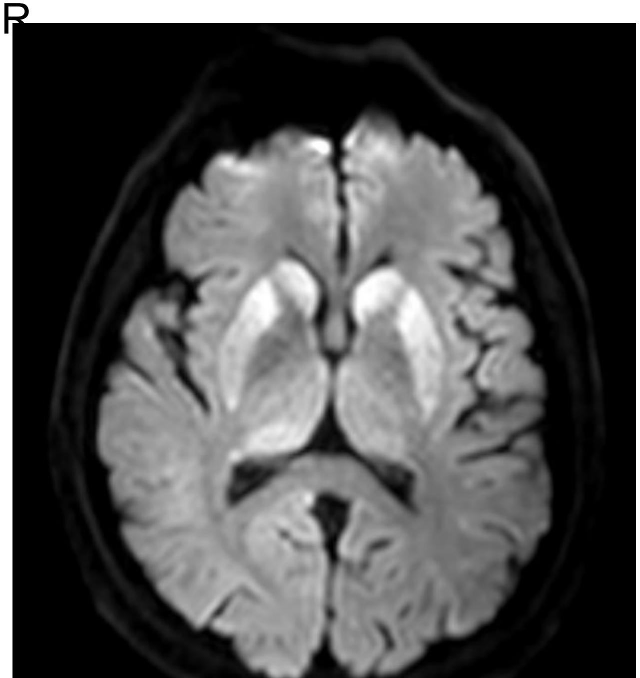
Significant Results

- CSF
  - Negative for 14-3-3 protein
  - Negative for Neuron-specific enolase
  - Positive for Total Tau

EEG: GPEDs

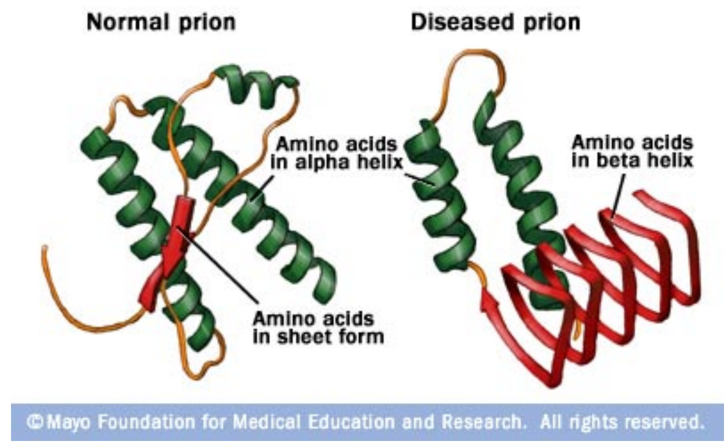


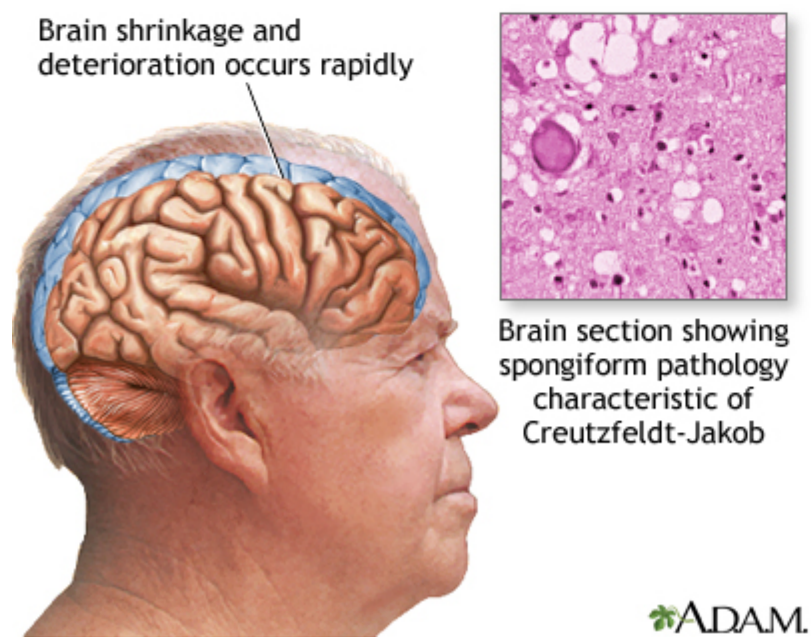
MRI: basal ganglia/cortical ribbon on FLAIR



Creutzfeldt-Jakob Disease

- Caused by the transformation of a normal cellular prion protien (PrP^c) into a disease causing prion (PrP^{Sc})
- Accumulation of PrP^{Sc} leads to neurodegeneration





3 CJD Subtypes

- Sporadic CJD (sCJD)
  - 85% of CJD cases
  - No known cause
  - Survival 4-8 months
  - 90% mortality at 1 year
  - Onset 55-75 years (median age 68, mean 61)
  - Include sporadic fatal insomnia (very rare)

3 CJD Subtypes

- Genetic CJD (gCJD)
  - Include: familial CJD, Gerstmass-Straussler-Scheinker syndrome and fatal familial insomnia
  - Mutation makes PrP more susceptible to change to PrP^{Sc}

  Familial CJD presents exactly like sCJD

  60% of genetic CJD cases have no family history

3 CJD Subtypes

- Variant Creutzfeldt-Jakob disease (vCJD)
- Bovine Spongiform Encephalopathy (BSE) has been strongly linked to the occurrence of vCJD in humans.
- 175 cases in UK and Ireland from October 1996 to March 2011; 3 cases in US.
- Containment of the BSE epidemic in cattle resulted in decline of cases of vCJD

CJD MRI findings now thought to be best test for CJD

sCJD and gCJD – cortical riboning and basal ganglia involvement on DWI

vCJD – Pulvinar sign on DWI and FLAIR is said to be 90% sensitive for vCJD

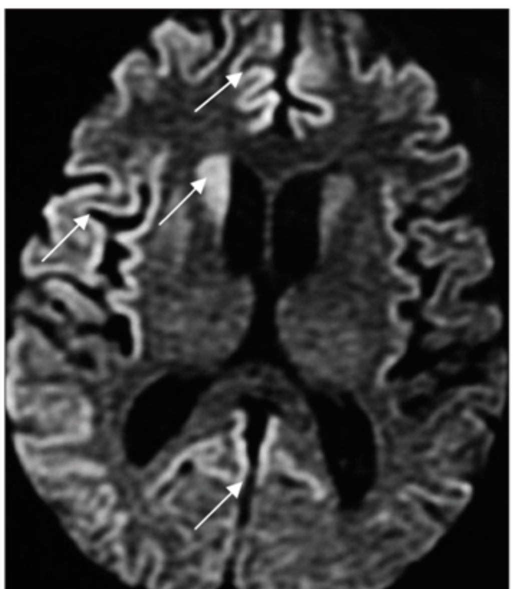
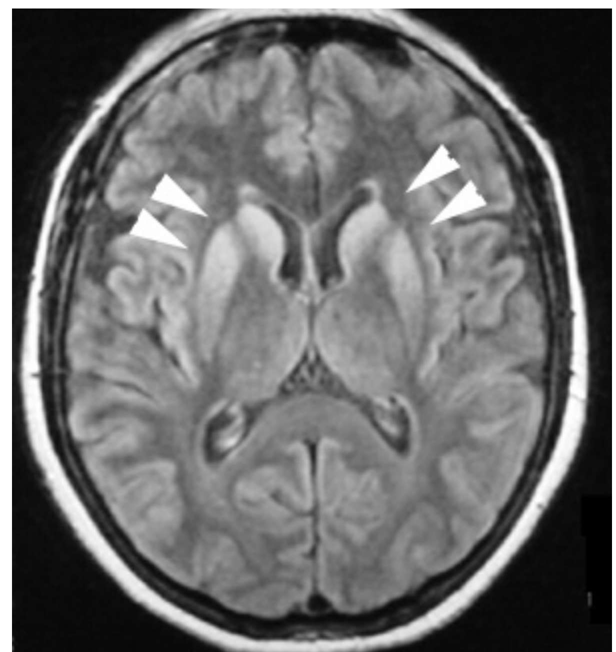
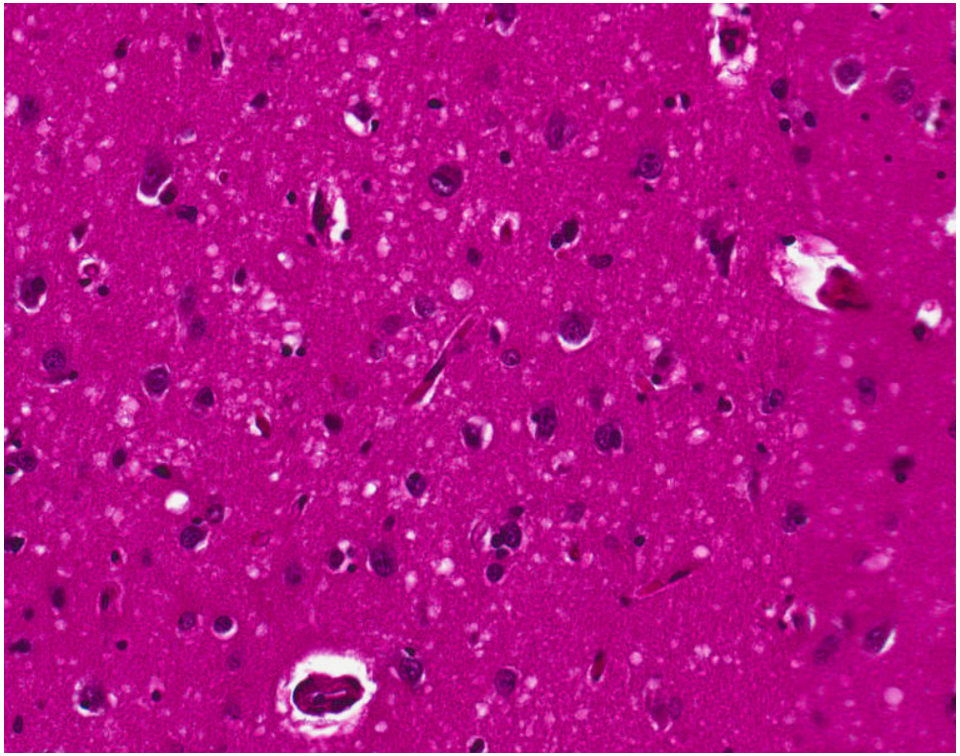


Fig 1. Axial brain MRI showing in the diffusion sequence hypersignal in the right caudate nucleus and frontal, temporal and occipital cortical gyri.



Definitive diagnosis of CJD can only be made through autopsy



Rapidly Progressive Dementia Differential Diagnosis

- VITAMINS:
- **Vascular**: multi-infarct, CNS vasculitis, intravascular lymphoma
- **Infectious**: Encephalitis (bacterial, viral, fungal, rickettsial); Infectious in older adults (UTI, PNA); Progressive multifocal leukoencephalopathy (PML), HIV dementia, Creutzfeldt-Jakob disease;
- **Toxic/Metabolic**: heavy metals, bismuth, drug rxn, electrolytes, Wilson's disease, vitamin deficiencies, uremic/hepatic encephalopathy

Rapidly Progressive Dementia Differential Diagnosis

- **Autoimmune**: CNS vasculitis, Hashimoto encephalopathy, sarcoid
- **Metastasis (neoplasm)**: lymphoma, paraneoplastic, primary tumor
- **Iatrogenic**: medications, hospitalization
- **Neurodegenerative**: CJD, Alzheimer disease, obstructive hydrocephalus
- **Systemic**: delirium, hypertensive encephalopathy, mitochondrial

WAKE
UP
AND
THANK YOU FOR
YOUR ATTENTION