

+ Objectives

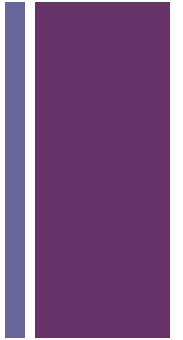


- Differentiate delirium from dementia
- Differentiate MCI from Dementia
- Become familiar with common dementia syndromes, and available treatments

+ Delirium

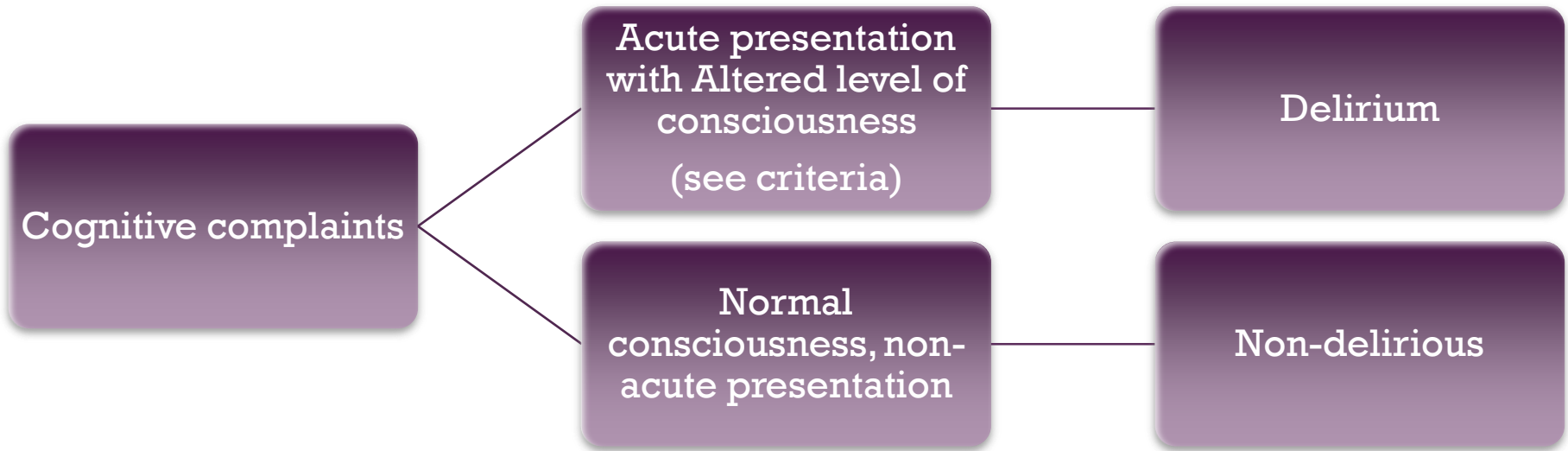
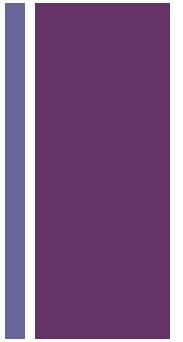
- *The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* diagnostic criteria for delirium is as follows:
 - Disturbance in attention (ie, reduced ability to direct, focus, sustain, and shift attention) and awareness.
 - Change in cognition (eg, memory deficit, disorientation, language disturbance, perceptual disturbance) that is not better accounted for by a preexisting, established, or evolving dementia.
 - The disturbance develops over a short period (usually hours to days) and tends to fluctuate during the course of the day.
 - There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by a direct physiologic consequence of a general medical condition, an intoxicating substance, medication use, or more than one cause.

+ Delirium



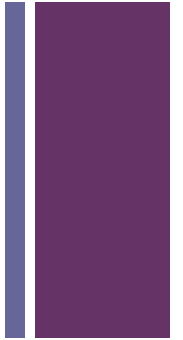
- Delirium, usually encompasses: “Acute confusional state” and “encephalopathy”

+ Dementia or Delirium?



The term “Delirium”, usually encompasses the terms of “acute confusional state” and “encephalopathy”.

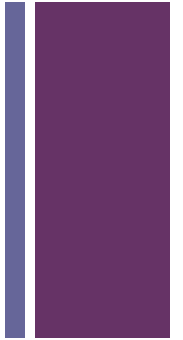
+ Delirium



It is not normal to have delirium, while this statement is obvious, patients' who have symptoms of delirium are dismissed as being sleepy, tired, or just age related changes.

BEING OLD \neq Being confused or mentally impaired

+ Delirium



■ Important clues to recognize delirium:

- Patient will not be able to give you a history
- Rapid development of symptoms (hours or days).
- Change in level of consciousness
- When the patient appears awake, assess level of attention
- Poor content of conversation and/or other cognitive deficits (memory loss, disorientation, abnormal language), neuropsychiatric symptoms such as hallucinations (visual, auditory somatosensory...etc) and delusions of harm.

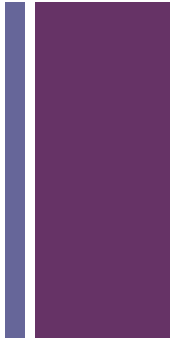
The opposite, hypervigilance, may occur in substance withdrawal (eg: alcohol or sedative).

+ Causes of Delirium

- Metabolic, examples include dehydration, hyponatremia, hypocalcemia, abnormal thyroid functions, liver and/or renal impairments, hypoglycemia .
- Toxic: ETOH and drugs of abuse.
- Infectious: UTI, pneumonia, or infections that result in systemic manifestations.
- Side effects of drugs or the abrupt discontinuation of certain drugs like benzodiazepines.
- Post surgery (anesthetics, pain)
- Disorders of the central nervous system (large strokes, Post-seizures, infections)



What can look like delirium?



- Non-convulsive seizures
- Sundowning behavior
- Dementia
- Psychiatric disorders
- Aphasias
- Transient Global Amnesia

+ Delirium management



The choice of the investigations should be guided by your history and clinical examination findings

There many causes of delirium, so an initial investigation may include (but not limited to) the following:

CBC, electrolytes, urea, creatinine, LFT, ESR, TSH +/- Auto-immune evaluation

Arterial blood gases

Urinalysis and toxicology screen

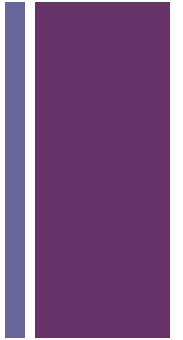
Chest X-ray, EKG

CT head, EEG, Lumbar Puncture

+ Dementia-Major Neurocognitive Disorder (DSM V)

- Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains*:
 - - Learning and memory
 - - Language
 - - Executive function
 - - Complex attention
 - - Perceptual-motor
 - - Social cognition
- The cognitive deficits interfere with independence in everyday activities
- The cognitive deficits do not occur exclusively in the context of a delirium
- The cognitive deficits are not better explained by another mental disorder (eg, major depressive disorder, schizophrenia)

+ Major Dementias



■ Neurodegenerative:

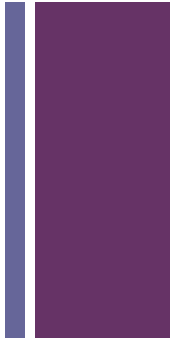
- Alzheimer's Disease
- Lewy Body Dementia
- Parkinson's Disease Dementia
- Frontotemporal Dementia
- Huntington's Disease

■ Other:

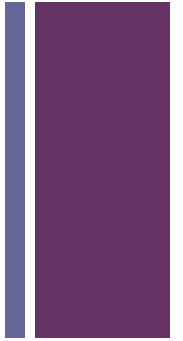
- Vascular Dementia
- Normal Pressure Hydrocephalus
- Creutzfeldt-Jakob Disease
- Wernicke-Korsakoff Syndrome
- Secondary to infection or systemic illness

+ Case

- 73 year old male retired judge.
- Presents with 1 year history of cognitive concerns
 - Trouble recalling names
 - He can completely forget a discussion
 - Forgets the location of previously placed tools
 - Only recalls fragments of a previous doctor visit 2 weeks earlier.
 - Does not follow the dates as accurately as he used to and indicates that this is because he is retired.
 - Sometimes he is repetitive with questions.
- Confusion about how to do things especially when tired.
- His ability to use household appliances is also affected.
- Tried putting on his shirt while still on the hanger



+ Alzheimer's Disease

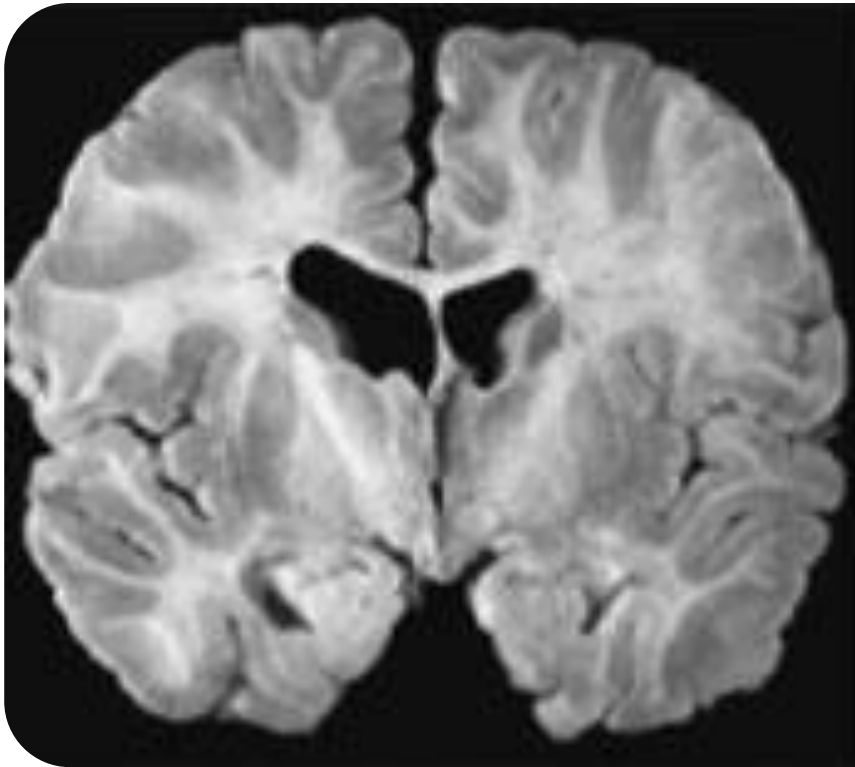


- Uncommon under the age of 60.
- Decreased memory and new learning is the hallmark of the condition
- Language impairment: Word finding difficulties with circumlocution and anomia.
- Executive dysfunction
- Apraxia, Unawareness of illness
- Visual-spatial impairments
- Passivity, apathy > agitation
- Delusions
- Depression
- Circadian rhythm disturbances (sundowning)
- Weight loss

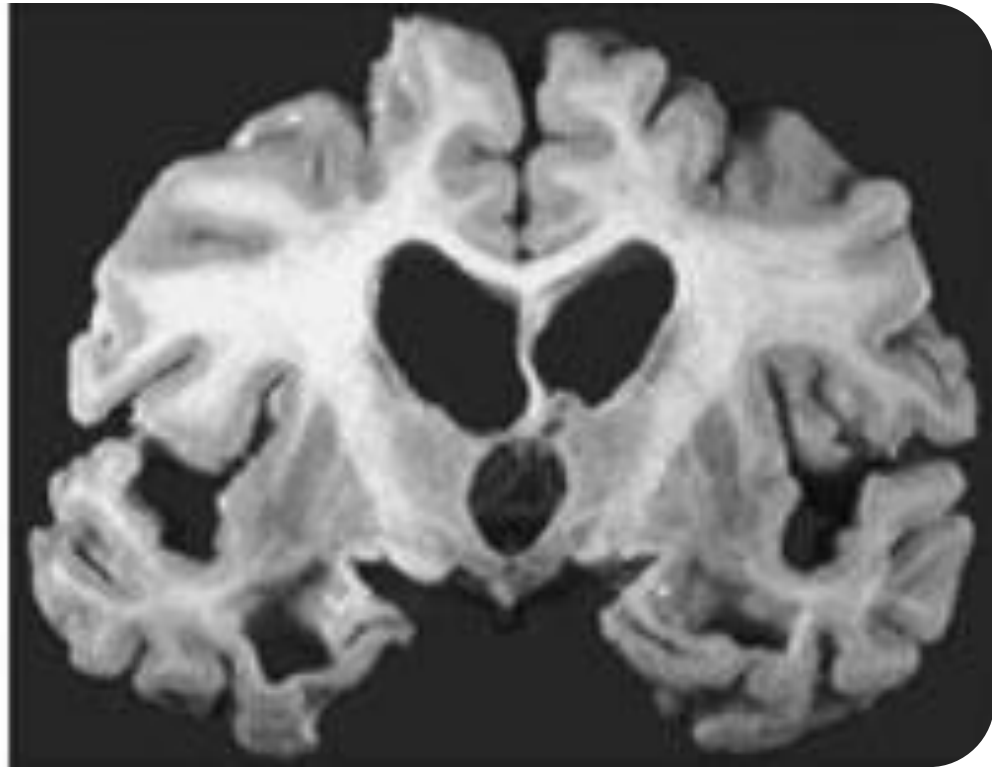
+ Risk Factors for AD



- Major risk factors
 - Increasing age
 - (APOE ϵ 4) The E4 allele for Apolipoprotein E on chromosome 19
 - Down Syndrome
 - Specific inherited types
- Mid-life vascular risk factors (DM, HTN, Hyperlipidemia, Lack of exercise)
- Brain trauma

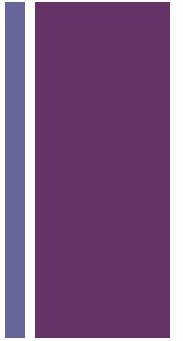


Normal



Atrophic

+ Mild Cognitive Impairment



Normal

MCI

Dementia

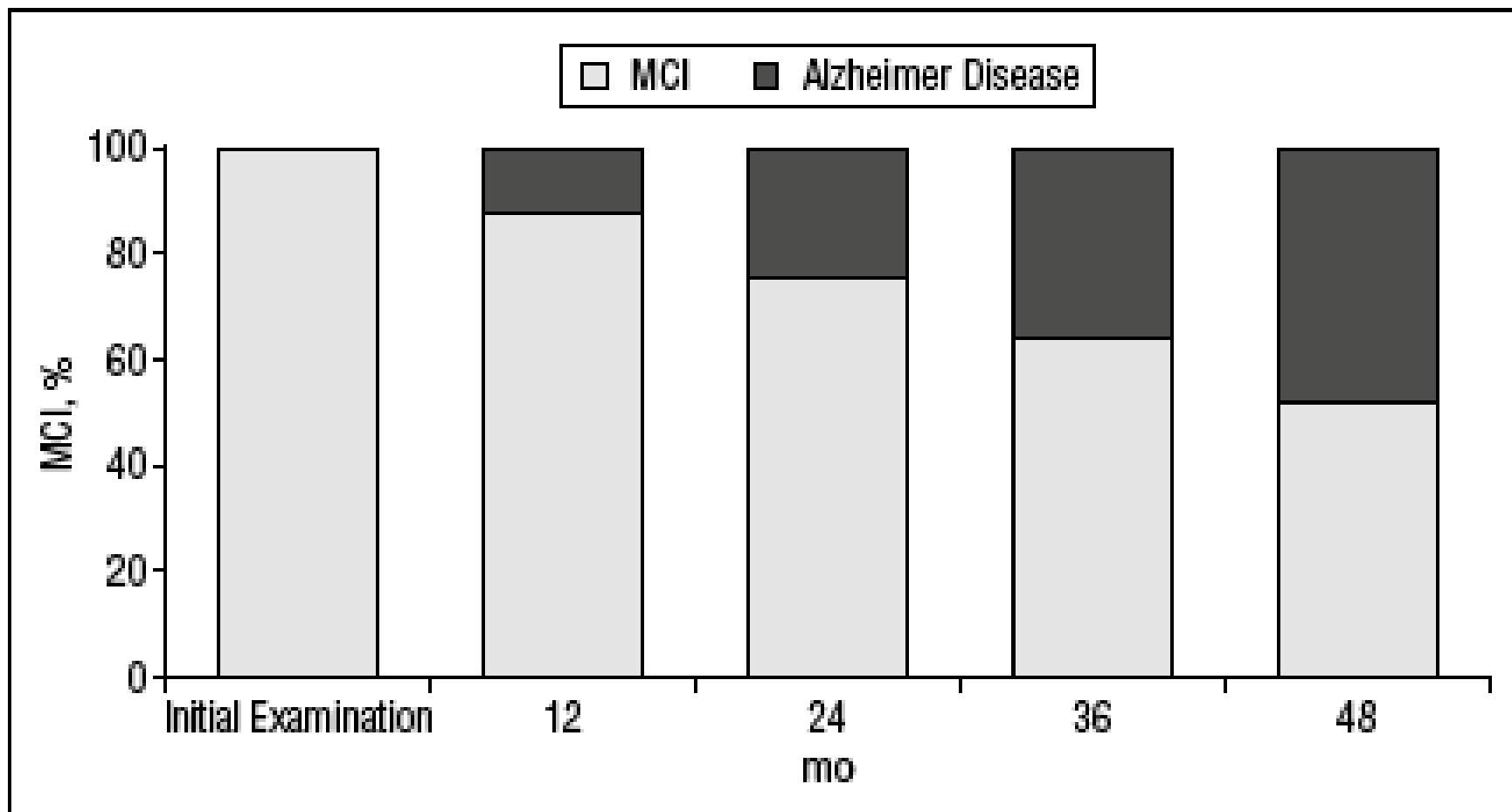
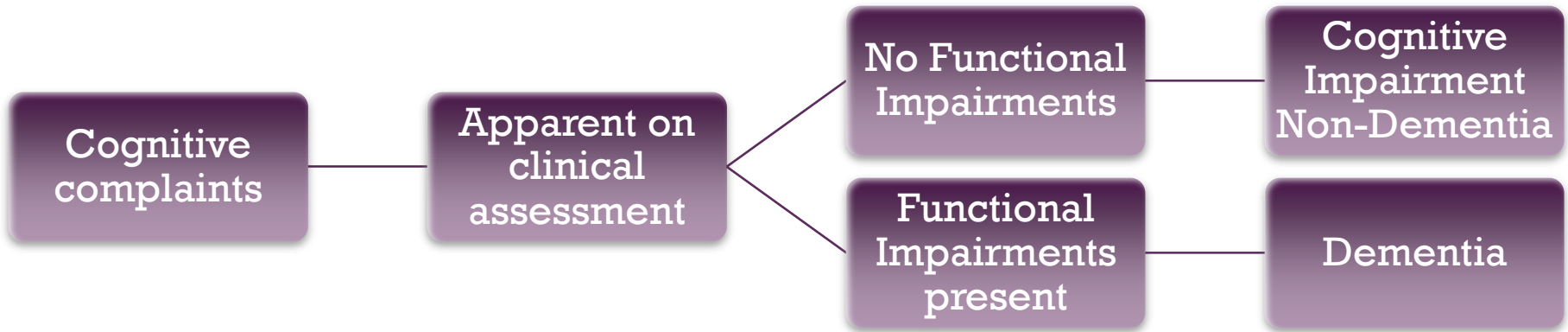
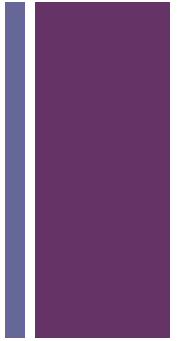
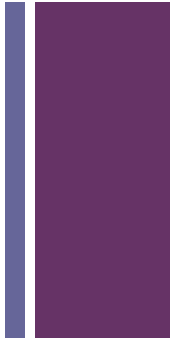


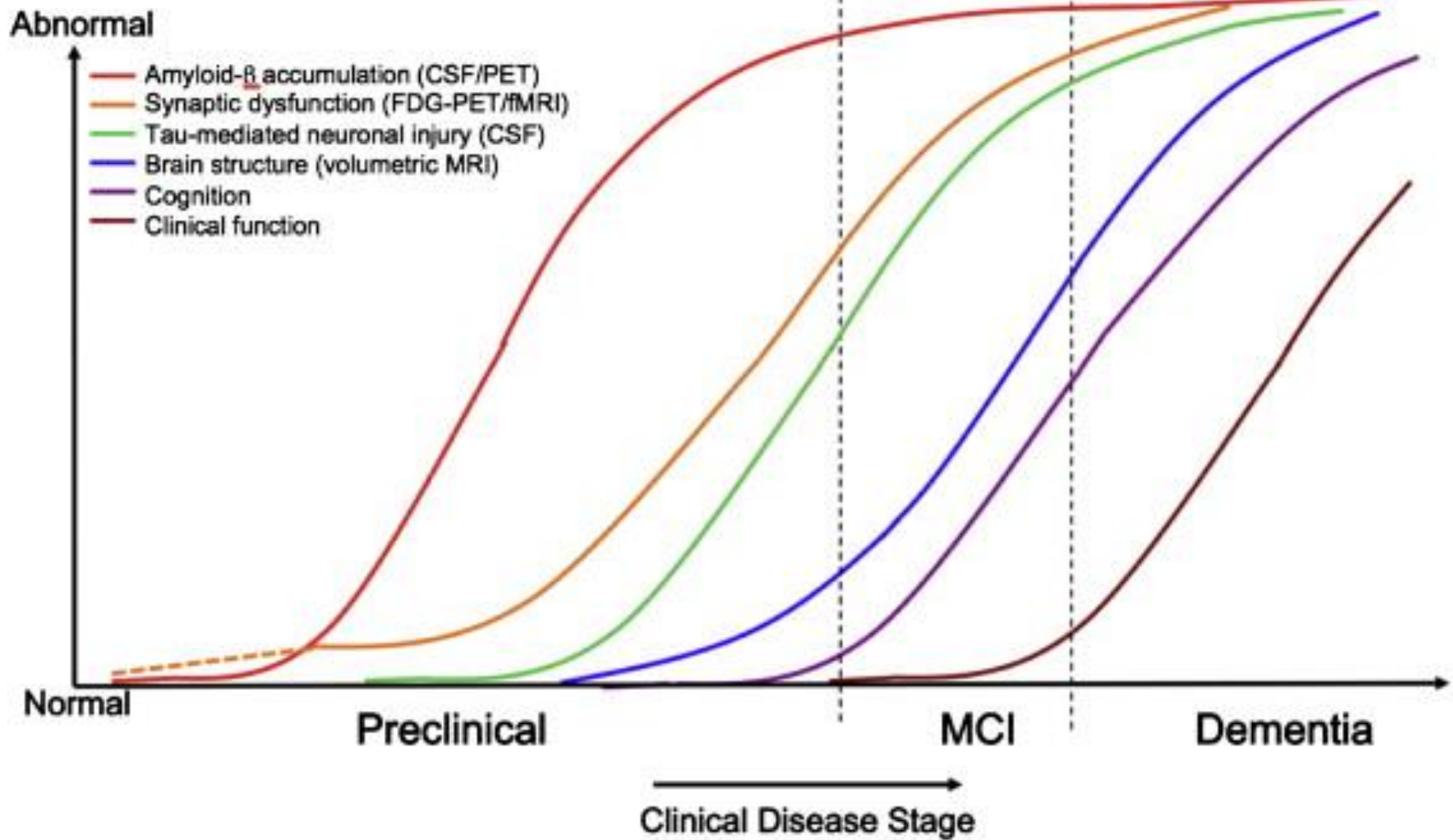
Figure 2. Annual rates of conversion from mild cognitive impairment (MCI) to dementia over 48 months.

+ Dementia or Cognitive Impairment?





- Defects in the mechanisms for clearing amyloid beta results in its accumulation and form senile plaques
- Abnormal accumulation of hyperphosphorylated tau protein results in accumulation and the formation of neurofibrillary tangles.
- Tangles and plaques are pathological hallmarks in Alzheimer's disease
- The resultant loss of neurons and synapses is responsible for the clinical profile
- The neuronal loss in the basal forebrain region is responsible for a cholinergic deficit.

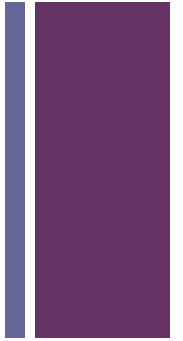


Reisa A. Sperling et al. **Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease**

Alzheimer's & Dementia, Volume 7, Issue 3, 2011, 280 - 292

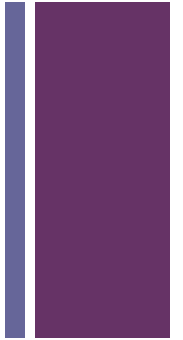
<http://dx.doi.org/10.1016/j.jalz.2011.03.003>

+ Diagnosis



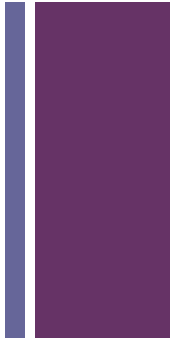
- Diagnosis is clinical
- Rely on history and cognitive/neuropsychological assessments that demonstrates a slowly progressing cognitive disorder which causes impairments in daily life.
- Brain structure on MRI may demonstrate medial temporal atrophy bilaterally
- PET scans can demonstrate decreased metabolism in temporal and parietal regions
- Cerebrospinal fluid might show low Amyloid beta, and elevated Tau (not specific)

+ Lewy Body Dementia



- Second most common cause of “degenerative” dementia.
- Core clinical features includes visual hallucinations, parkinsonism, and fluctuations in cognitive ability and level of consciousness.
- Other symptoms include visual spatial impairment > short term memory, sensitivity to neuroleptics, REM sleep behavior disorder and autonomic dysfunction

+ Lewy Body Dementia



- Pathologically there are “Lewy Bodies” present in neurons, which are the result of abnormal synuclein protein accumulation.
- Diagnosis is primarily clinical
- PET scan may show decreased occipital lobe metabolism
- Myocardial scintigraphy may be abnormal due to abnormal cardiac sympathetic innervation
- Parkinson’s Disease Dementia is similar to LBD. The difference is that a clear history of PD with NO cognitive impairment precedes the development of dementia by at least a year.

+ Vascular Dementia



- Occurs secondary to
 - A single stroke in a region important to cognition such as hippocampus or thalamus, or a large stroke that affects multiple lobes.
 - Recurrent strokes that accumulate over time, there is a step-wise development of cognitive deficits.
 - Slowly progressing cognitive deficits due to subclinical progressing of small vessel disease
- Associated with vascular risk factors (HTN, DM, Hyperlipidemia, & smoking)
- Frequently coexists with Alzheimer's disease

+ Frontotemporal Dementia

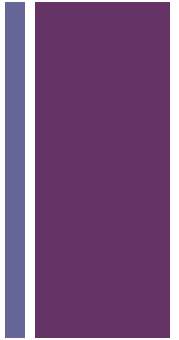


- Mean age of onset is 58
- Preferentially involves the frontal and temporal lobes, symptoms depend on the region (lobe) involved, therefore there are variants::
- Behavioral Variant
- Primary Progressive Aphasia
- Semantic Dementia
- Common pathological inclusions include hyperphosphorylated tau protein, TDP-43 protein, or FUS protein

FUS: Fused in Sarcoma

TDP: 43 kD transactive response (TAR) DNA binding protein

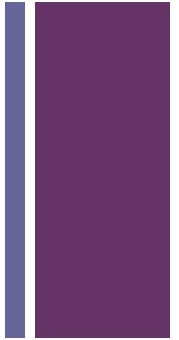
+ Frontotemporal Dementias



- Behavioral variant is associated with personality changes, inappropriate social behaviors (disinhibited), lack of insight, Binging on certain foods, emotional blunting, rigid and cannot adopt to new situations, along with decreased attention modulation. MRI shows atrophy in the frontal lobes (may be asymmetric)
- Progressive non-fluent aphasia: Patients present first with a non-fluent type of aphasia (similar to a Broca's lesion). MRI may show focal left frontal atrophy.
- Semantic dementia (temporal variant of FTD): Usually have intact fluency, but comprehension is impaired and decreased naming ability. MRI may show focal left temporal atrophy.



Normal Pressure Hydrocephalus

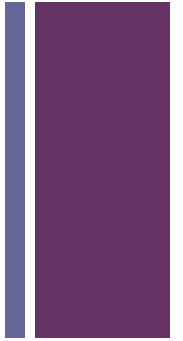


- A rare disorder
- It classically presents with gait impairment, urinary incontinence along with the dementia. However these features are not unique to NPH.
- Dementia is of a subcortical type, where there is executive dysfunction, and psychomotor slowing first. Other features of cognitive impairment develop later on.
- The typical gait has been described as “magnetic”, the patient may shuffle their feet on the ground with a normal or wide base, some may have some features of parkinsonism.

+ NPH

- It usually results from impaired CSF absorption at the level of the arachnoid villi.
- In Secondary NPH, there is usually a history of a previous meningitis, inflammatory disorder, or subarachnoid hemorrhage. Idiopathic NPH is when there is no preceding explanation for the condition.
- Patients who present with gait impairment > cognitive impairments have better prognosis if identified early.
- Some patients will improve after a lumbar puncture that removes 30-50 cc of CSF. If this test is positive, then a CSF shunting procedure is performed.
- The MRI brain may also show dilated ventricles (however CSF pressure is normal).

+ Creutzfeldt-Jakob Disease



- Rare, 1 in a million
- It is a prion disorder and can be transmitted (transmissible spongiform encephalopathy)
- Prions are abnormally formed proteins that induce pathological transformations in other proteins.
- It has been transmitted after the use of surgical equipment or growth hormones

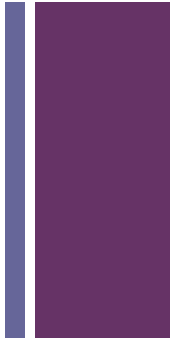
+ CJD

- CJD presents as a rapidly progressing dementia, disease duration usually 6 months. Myoclonic jerks may occur.
- Any picture of cognitive impairment may occur, as may other neurological symptoms like parkinsonism, ataxia, field defects, spasticity, hyper-reflexia, and + Babinski.
- MRI may show abnormal signal intensity in the basal ganglia and cortical ribbon
- EEG shows characteristic periodic sharp wave complexes
- No treatment, patients die within a year.
- The bovine variant CJD has been linked to consumption of beef (UK outbreak in the 90s)



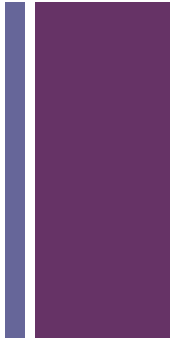
+ Other causes of dementia

- HIV Associated neurocognitive disorder
- Syphilis
- Vitamin B12 deficiency
- Autoimmune disorders (eg: SLE)
- Alcohol leading to wernicke-Korsakoff's syndrom, characterized by confabulations to compensate for amnesia



+ Drugs to treat cognitive impairment

- Drugs such as Donepezil, rivastigmine and galantamine which increase the presence of central nervous system acetylcholine help with cognitive and behavioral symptoms in Alzheimer's dementia
- Does not stop disease progression, but may provide transient clinical stability
- NMDA receptor antagonist, memantine, is helpful in moderate to advanced alzheimer's disease
- No pharmacological treatment available for MCI
- Not a treatment, but education and physical activity protect from cognitive decline



+ Questions

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