Medicine TEAM 437

MED437 KING SAUD UNIVERSITY

Delirium, Dementia

Objectives :

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

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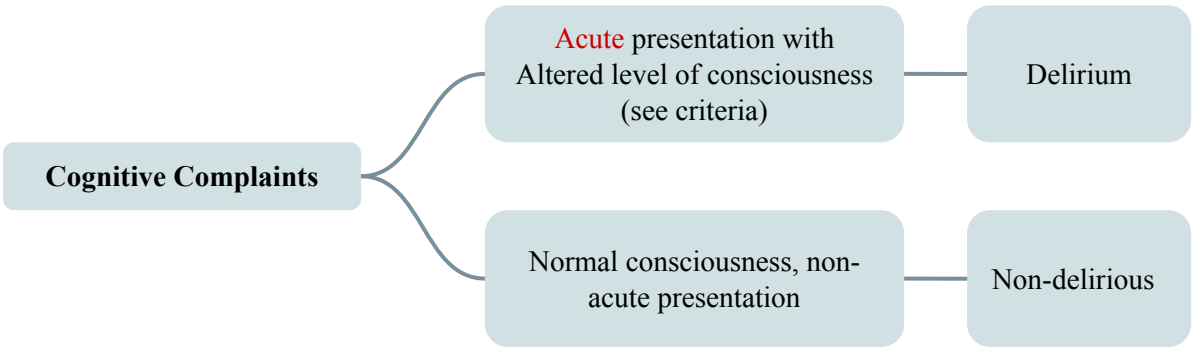
Delirium (هذيان)

- The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) diagnostic **criteria** for delirium is as follows:
  - **Disturbance in attention**
    - Reduced ability to direct, focus, sustain, and shift attention and awareness.
  - **Change in cognition**
    - Memory deficit, disorientation, language disturbance, perceptual disturbance and even a personality changes 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. While dementia is typically a **chronic slow progressive** condition.
  - 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. Usually dementia you may **not find a clear cause**, but in delirium you may find the patient has a **urinary tract infection** or **pneumonia**.
- Delirium, usually encompasses: "**Acute** confusional state" and "encephalopathy" These kind of interchangeably use, not exactly the same, but if you hear those you will think about delirium.

Dementia or 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 ≠ Being confused or mentally impaired ! There's some decline (slowing) of cognition and response speed with time. But once you have a deficit that particularly falling **behind everyone in the same age group**, that's a PROBLEM.

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.

  THIS IS A REALLY BIG CLUE. A person might look like he's just a **sleepy**! And the family will find excuses and say: "he's just tired". Why this changes? Because something **systematically** happened in the body.
- When the patient appears awake, assess level of attention.

  Give the patients a series of numbers like 5 numbers and see if they can repeat it to you, It's called a (digit span). You can give them something more challenging! let them repeat the numbers backwards.
- 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

- Alcohol or sedative.

  Super attentive but not really a productive type of attention. Like someone who took **heroin for a while** and suddenly stops.

Causes of Delirium

- **Metabolic**
  - E.g: Dehydration, hyponatremia, hypocalcemia, abnormal thyroid functions, liver and/or renal impairments, hypoglycemia.

Toxic

- Ethanol and drugs of abuse.

Infectious (anywhere in the body):

- UTI, pneumonia, or infections that result in systemic manifestations. Even dental problems untreated.

Side effects of drugs (directly) or the **abrupt discontinuation** of certain drugs like benzodiazepines (withdrawal).

Post surgery

- Anesthetics, pain.

Disorders of the central nervous system

- Large strokes, Post- seizures, infections.

What can look like delirium? Differential diagnosis

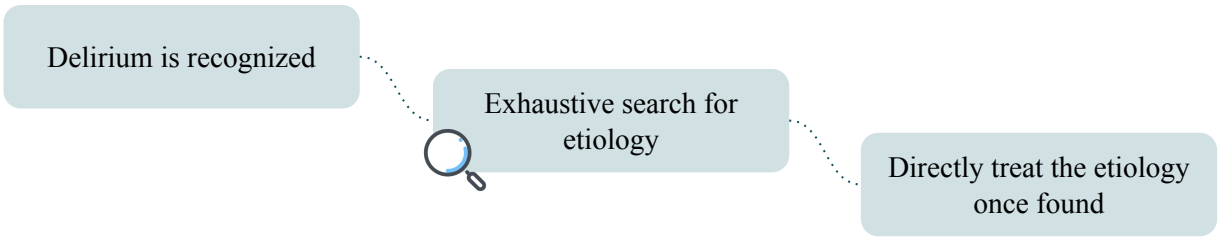
- Non-convulsive seizures

  Absence seizure it's kind of related to it, but not the same process. This is a scenario you can see it with somebody who comes in with static epileptics: This is seen when you *sedate* the patient with anesthetics and you kind of stopped their motor movements but the seizures still ongoing with alteration of consciousness
- **Sundowning behavior**

  Loss of circadian rhythm same as seen in jetlag, effects **older people** their **internal clock** doesn't sync well with the outside environment, they may sleep through the day and appear confused at night
- Dementia
- Psychiatric disorders
- Aphasias I see a patient coming with stroke and have an acute aphasia and people think it's an acute delirium!
- Transient Global Amnesia

  Important condition but not common. It's characterized by a confusion for a period not more than 24 hours after a trauma. Patient will have **severe memory impairment** "where am I? How do I get there?" 5 minutes later he will repeat the same questions.
  - Anterograde: Not remembering anything that happening **now**. From point now into the **future**.
  - Retrograde: The events the happened **before**. From 5 minutes before, todays before to years before.
  - The focus in Transient Global Amnesia is primarily in **anterograde** process, although there's a certain component of retrograde that might happen.

Delirium Management



- The choice of the investigations should be guided by your history and clinical examination findings.
- There are many causes of delirium, so an initial investigation may include (but not limited to) the following:
  - CBC, electrolytes, urea, creatinine, LFT, ESR, TSH +/- Autoimmune evaluation
  - Arterial blood gases
  - Urinalysis and toxicology screen
  - Chest X-ray, EKG
  - CT head, EEG, Lumbar Puncture

Mild Cognitive Impairment

- An intermediate phase it can only be a minor **memory impairment** but they still manage well alone.
- May or may not progress to dementia. But EVERY dementia patient must go through MCI first.
- Patients with MCI have a high risk of developing alzheimer.

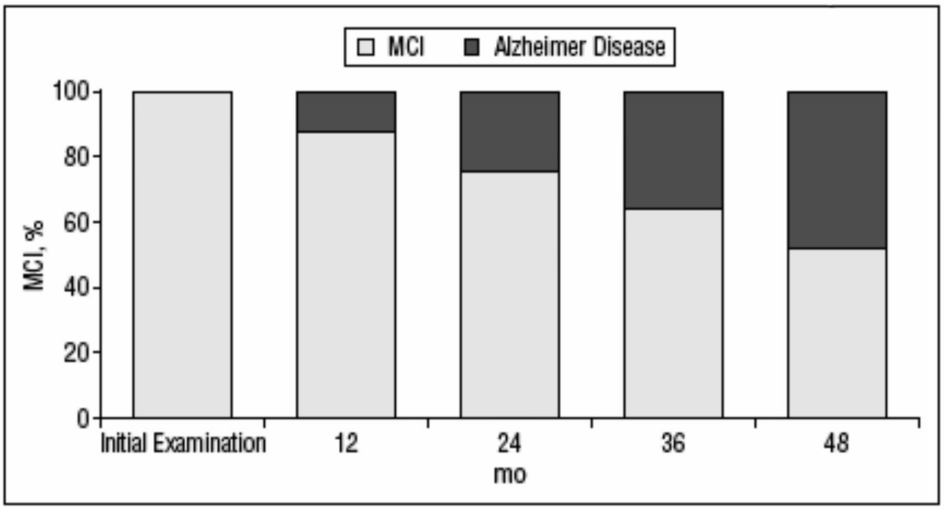
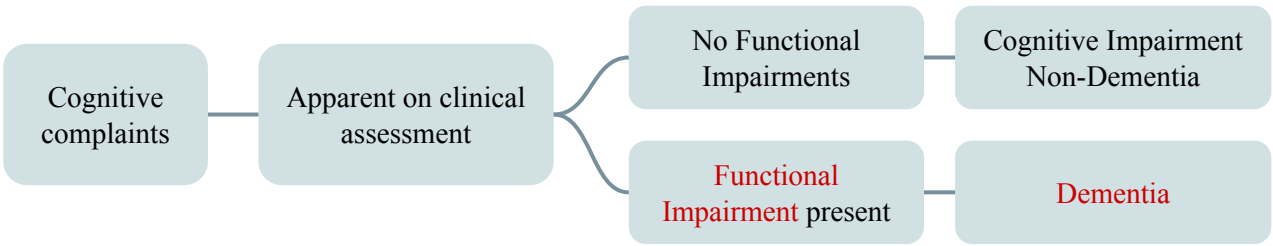


Figure 2. *Annual rates of conversion from mild cognitive impairment (MCI) to dementia over 48 months.*

Dementia or Cognitive Impairment?



- Functional impairment **interfere with patients independence of everyday activities** it means that a family member has to stay with them and do stuff for them, because they don't have the **mental capacity** to do things to themself, this does not mean somebody who need a wheelchair to get around.
- If there is no functional impairment it's not dementia

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** It's the ability to **plan** a task and **execute** it, **Act** upon that task, **follow** the steps of this task and **come to the result** that you're looking for. For example: if I want to travel to Jeddah, what I would do? I know how to open the computer, book a flight, get transportation.
  - **Complex attention** The ability to **monitor** yourself and task (make sure you're doing the right thing), and your ability to **switch** from task to another task.
  - **Perceptual-motor** How do you interact with the environment.
  - **Social cognition** Social impairment. For example: **not knowing the right things to say** in a right sitting or **behaving improperly** in certain situations.
- The cognitive deficits interfere with independence in everyday activities. Once it interferes with independence it becomes **Dementia** and it's no longer an MCI.
- 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). Unlike delirium

Major Dementias

Neurodegenerative	Other
Alzheimer's Disease	Vascular Dementia
Lewy Body Dementia	Normal Pressure Hydrocephalus
Parkinson's Disease Dementia	Creutzfeldt-Jakob Disease
Frontotemporal Dementia	Wernicke-Korsakoff
Huntington's Disease	Syndrome Secondary to infection or systemic illness

Alzheimer's Disease

Case:

- 73 year old male retired judge.
- Presents with 1 year history of cognitive concerns It's going on for a long time, doesn't sound like a delirium.
    - 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***. Seen even in people who have early dementia.
- His ability to use household appliances is also affected. Impaired executive function
- Tried putting on his shirt while still on the hanger*.

What cognitive domains are clearly affected in this case?

Memory and executive function*.

What likely this patient has? Dementia

What kind of dementia? Alzheimer's.

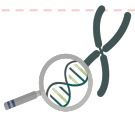
Eventually **all** dementia all domains are gonna be affected, but each one present differently! Alzheimer's present **memory** first.

General Characteristic:

- Uncommon under the age of 60.
- Decreased memory and new learning is the hallmark of the condition. Pathology starts at the **hippocampus** of temporal lobe (where **memories** are made).
- Language impairment: Word finding difficulties with circumlocution and anomia.
- Executive dysfunction.
- Apraxia, Unawareness of illness. Praxia is coming from **practice**, ability to do something, a particular **skill**. Apraxia the absent of this without any motor or sensory deficit.
- Visual-spatial impairments.
- Passivity, apathy > agitation. Apathy when you have NO **emotion** or any **connection** with the people.
- Delusions. **Unshakable Ideas** or **thoughts** about things that are **not true**. Unlike schizophrenia, in alzheimer's it's actually hard to see it as a delusion. They will start having suspicions about family members like "someone is stealing from me".
- Depression.
- Circadian rhythm disturbances (sundowning).
- Weight loss.

Risk Factors for AD

Major risk factors



- Increasing age.
- (**APOE ε4**) The E4 allele for Apolipoprotein E on chromosome 19. It's not a diagnostic tool. Only a risk factor
- Down Syndrome. Almost 100% chance of developing AD by the age of 40.
- Specific inherited types. They are less than 2% of all AD. much younger people 30/40.

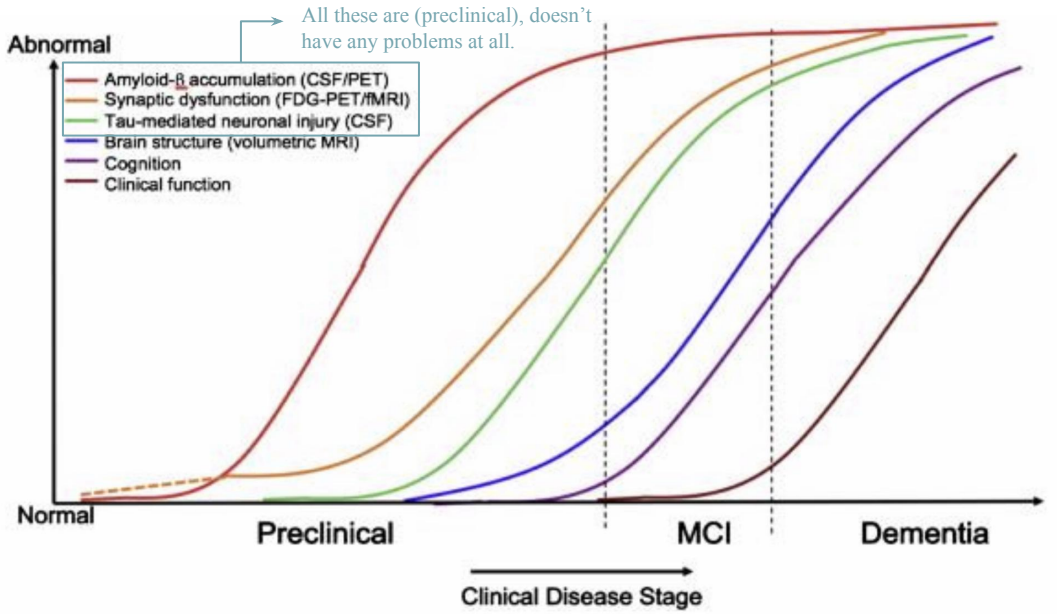
Mid-life vascular risk factors

- DM
- HTN
- Hyperlipidemia
- Lack of exercise

Brain Trauma

Pathophysiology.

- **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
- Whenever we learn something new (motor or cognitive skill), we create a new network and synapses. Neurons die from the time we're born, they just keep dying until we die. In AD there are an **accelerated** loss of synapses and neurons.
- The neuronal loss in the basal forebrain region is responsible for a **cholinergic deficit**. Treatment aims on reducing/replacing this acetylcholine loss.



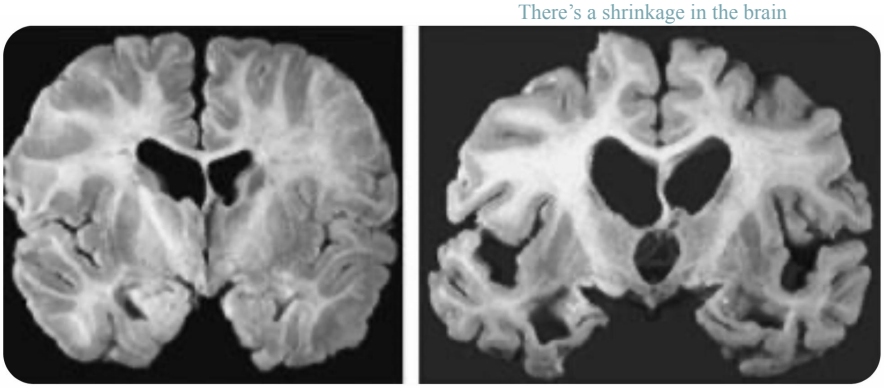
Diagnosis of Alzheimer's Disease

- 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).

Normal

Atrophic

There's a shrinkage in the brain



Shrunken cortex >

- Enlarged ventricles
- More **space** between the gyri.

Hippocampal atrophy: typical in alzheimer's

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**.
  - Hallucination: **seeing/hearing/smelling/feeling** something that is NOT there. Auditory hallucinations are more with **psychiatric** disorders while visual are more with **neurological** disorders.
  - Parkinsonism: **features** of **parkinson disease** (tremor, bradykinesia, rigidity, gait problems).
- Other symptoms include:
  - visual spatial impairment troubles with the directions > short term memory
  - sensitivity to neuroleptics
    - antipsychotic medications like **haloperidol**, they are dopamine blockers, so like parkinson disease there's dopamine deficiency already → they will get severe rigidity and bradykinesia
  - REM sleep behavior disorder
    - During rapid eye movement phase your brain paralyze you because if it didn't your body will be doing everything you're dreaming of.
    - Here normal paralytic mechanisms is **impaired**. Patient will be screaming, kicking during sleep.
    - Might be the only complain In some people.
  - Autonomic dysfunction
    - Postural hypotension, erectile dysfunction.

Lewy Body Dementia Cont.

- 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 in PD:
    - Clear history of PD tremor, rigidity, bradykinesia etc.. with NO cognitive impairment precedes the development of dementia by at least a year.
    - In LBD the cognitive feature must be **more prominent** than the parkinson features. They will have cognitive features starting **before** any parkinson features appear or around the same time.

Frontotemporal Dementia

- Mean age of onset is 58. Younger patients
- Preferentially involves the **frontal and temporal lobes**, symptoms depend on the region (lobe) involved, therefore there are variants:
    - **Behavioral Variant:**
        - 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). Frontal lobe control your behaviour and Disinhibition.

          Disinhibition: (keeping you from doing thing you should not be doing. Like saying a joke in a funeral.)
    - **Primary Progressive Aphasia** (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. Because of dementia that area is slowly degenerate.
    - **Semantic Dementia** (temporal variant of FTD)
        - Usually haven intact fluency, but comprehension is impaired and decreased naming ability Can't name things.
        - MRI may show focal left temporal atrophy.
- Common pathological inclusions include:
    - Hyperphosphorylated tau protein, TDP-43 protein, or FUS protein.

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** they share the same risk factors and both are so common.

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. Gait impairment is quite characteristic if it happened.
- Dementia is of a subcortical type
  - Executive dysfunction, and psychomotor slowing first. Other features of cognitive impairment develop later on. There're **enlargement** of ventricles with normal gyri and sulci. That means there's no degeneration happening like other dementia disorders.
- The typical gait has been described as "Magnetic"
  - The patient may **shuffle** drag **their feet on the ground** with a normal or wide base.
  - some may have some features of parkinsonism.
- It usually results from impaired CSF absorption at the level of the arachnoid villi.
- In Secondary NPH, there is usually a history of:
  - 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 before 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, than 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.
- A **prion** disorder and **can be transmitted** (transmissible spongiform encephalopathy).
- **Prions:**
  - Abnormally formed proteins that induce pathological transformations in other proteins.
  - Has been transmitted after the use of surgical equipment or growth hormones or blood transfusion.
- **Presentation:**
  - 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, hyperreflexia, and + Babinski.
- MRI
  - Abnormal signal intensity in the basal ganglia and cortical ribbon.
- EEG
  - 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). This type affects younger people.

Other Causes of Dementia

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

Drugs to Treat Cognitive Impairment

- Drugs such as (Cholinesterase Inhibitors) Donepezil, rivastigmine and galantamine which increase the presence of central nervous system acetylcholine help with cognitive and behavioral **symptoms** in Alzheimer's dementia. You can't give these drugs to myasthenic patient because it works centrally instead of peripherally.
- **Does not stop disease progression**, but may provide transient clinical stability.
- NMDA receptor antagonist, memantine, is helpful in moderate to advanced alzheimer's disease. NMDA if it overstimulate, it could lead to cell death sometimes.
- No pharmacological treatment available for MCI.
- Not a treatment, but education and physical activity protect from cognitive decline.

Summary

Delirium: Disturbance develops over a short period (usually hours to days) and tends to fluctuate during the course of the day. “Acute confusional state”

Presentation:

-Change in level of consciousness
-Change in cognition (eg:memory deficit, disorientation, language disturbance, perceptual disturbance)
-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.

Causes of Delirium:

- Metabolic, (dehydration, hyponatremia, hypocalcemia,liver and/or renal impairments, hypoglycemia)
-Toxic: ETOH (ethanol) and drugs of abuse or withdrawal effect
-Infectious (common): UTI, pneumonia, OR Post surgery (anesthetics, pain)
-Disorders of the central nervous system (large strokes, Post-seizures, infections)

Management: (it is a medical emergency)

ABCD, CBC, electrolytes, urea, creatinine, LFT, ESR, TSH +/- Autoimmune evaluation
● Arterial blood gases ● Urinalysis and toxicology screen ● Chest X-ray It could be an aspiration pneumonia you are not aware of, EKG
● CT head, EEG, Lumbar Puncture

Dementia: Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains develop within years.

Presentation:

● Learning and memory ● Language ● Executive function ● Complex attention
● Perceptual-motor ● Social cognition ● Normal consciousness

Causes: Neurodegenerative:
○ Alzheimer’s Disease ○ Lewy Body Dementia. ○ Parkinson’s Disease
○ Dementia○ Frontotemporal Dementia

Other:○ Vascular Dementia ○ Normal Pressure Hydrocephalus
○ Creutzfeldt-Jakob Disease ○ Wernicke-Korsakoff Syndrome

Management:

Depends on the cause, but remember it does not stop disease progression, but may provide transient clinical stability.

Summary

Disease	Clinical features	Pathophysiology	Risk factors	Management
Alzheimer's Disease	-Decreased memory and new learning -Language impairment -Apraxia -Unawareness of illness -Delusions	-Accumulation of amyloid beta and forming senile plaques ● Formation of neurofibrillary tangles	-Increasing age -APOE ε4 -Down Syndrome -DM, HTN, Hyperlipidemia, Lack of exercise	Diagnosis is clinical MRI: medial temporal atrophy bilaterally PET scans: decreased metabolism in temporal and parietal regions -NMDA receptor antagonist,memantine
LBD	-Visual hallucinations -Parkinsonism -Fluctuations in cognitive ability and level of consciousness. -REM sleep behavior disorder	Lewy Bodies present in neurons, which are the result of abnormal synuclein protein accumulation		Diagnosis is primarily clinical -PET scan: decreased occipital lobe metabolism -Abnormal myocardial scintigraphy
Vascular Dementia	Frequently coexists with Alzheimer's disease	Recurrent strokes in cognitive area	Hypertension Hyperlipidemia DM Smoking	
Frontotemporal Dementia	-Behavioral Variant -Primary Progressive Aphasia -Semantic Dementia	Inclusions of hyperphosphorylated Tau protein, TDP-43 protein, or FUS protein		MRI: focal left frontal atrophy
Normal Pressure Hydrocephalus	**Classically triad of:** **-Gait impairment (ataxia)** **-Dementia** **-Urinary incontinence**	Impaired CSF absorption at the level of the arachnoid villi		MRI: dilated ventricles (CSF pressure is normal) -Improvement after removal 30-50 cc of CSF

Questions

1- Which brain lobes are most commonly affected in Alzheimer's disease?

A. Occipital and temporal
B. Frontal and temporal
C. Parietal and temporal
D. Occipital and parietal

2- Compared with dementia, which of the following is a characteristic of delirium?

A. A fluctuating level of consciousness
B. Slow onset
C. Can be due to deficiencies of thiamine or cyanocobalamin
D. Decreased memory

3- Which of the following are commonly seen in brain imaging of patients with Alzheimer disease?

A. Enlarged cerebral ventricles and atrophic brain tissue
B. Normal cerebral ventricles and atrophic brain tissue
C. Enlarged cerebral ventricles and no atrophy of brain tissue
D. Normal cerebral ventricles and normal brain tissue, acetylcholine deficiency

4- A 70-year-old man with history of hypertension and diabetes presents with a stepwise loss of intellectual function. Prior episodes have been associated with unilateral weakness and difficulty swallowing. A unilateral Babinski sign is found on neurological examination, what is the most likely diagnosis?

A. Senile dementia of the Alzheimer type
B. Vascular (multi-infarct) dementia
C. Vitamin B12 deficiency
D. Dementia with Lewy bodies

5- Which brain lobes are mostly affected in frontotemporal Dementia?

A. Occipital and temporal
B. Frontal and temporal
C. Parietal and temporal
D. Occipital and parietal

Answers: 1-C, 2-A, 3-A, 4-B, 5-B