Neurocognitive/Neuropsychiatric Disorders

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SPECIAL TAHNKS TO:

1. Dr. Mohammed AlJaffer, MD, Assistant Professor and Consultant of Psychiatry, Forensic, and Nueropsychiatry, College of Medicine, King Saud University

2. Dr. Mohammed Al-Sughayir, MD, Professor and Consultant of Psychiatry, College of medicine, King Saud University

Objectives:

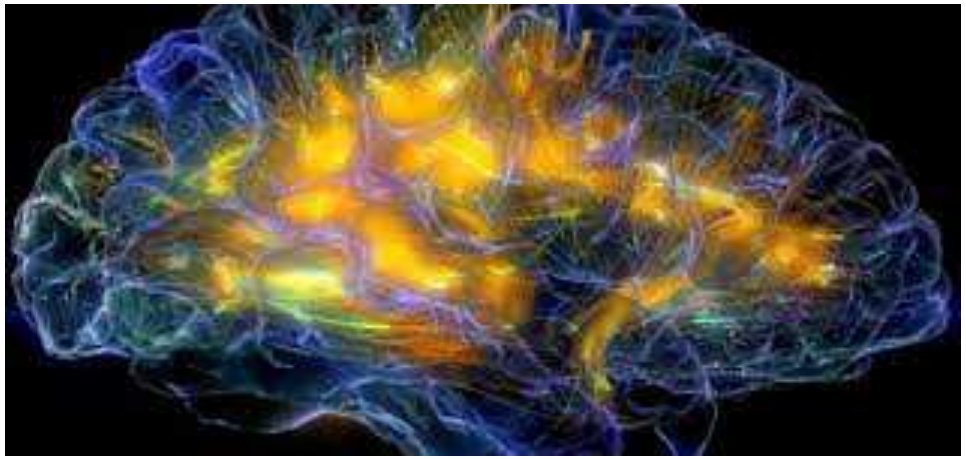
- ✓ Delirium
- ✓ Major Neurocognitive Disorders (MCD):
  - ✓ Dementia
  - ✓ Amnestic syndrome
- ✓ Traumatic Brain Injury (TBI)

Introduction:

- Cognition Functions Vs Cognitive Disorders

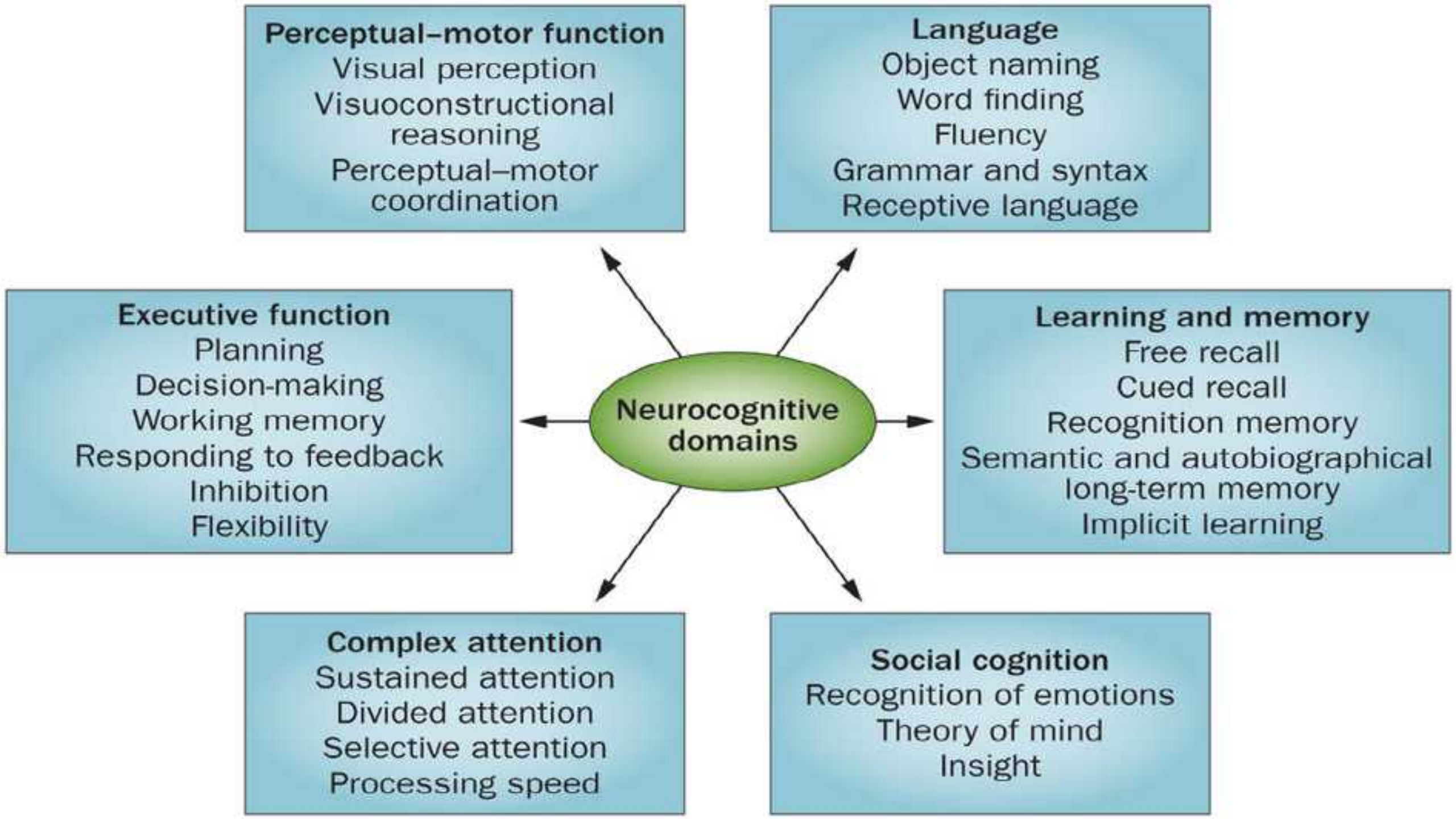
Cognitive functions Vs Cognitive disorders

- ***Cognitive functions:*** is the **mental action or process** of acquiring knowledge and understanding through thought, experience, and the senses



- It encompasses many aspects of intellectual functions and processes:
  - Attention
  - Concentration
  - Memory
  - Processing speed
  - Orientation
  - Impulse control
  - Language processing
  - Executive function

Wikipedia


Perceptual–motor function
Visual perception
Visuoconstructional reasoning
Perceptual–motor coordination
Language
Object naming
Word finding
Fluency
Grammar and syntax
Receptive language
Executive function
Planning
Decision-making
Working memory
Responding to feedback
Inhibition
Flexibility
Neurocognitive domains
Learning and memory
Free recall
Cued recall
Recognition memory
Semantic and autobiographical long-term memory
Implicit learning
Complex attention
Sustained attention
Divided attention
Selective attention
Processing speed
Social cognition
Recognition of emotions
Theory of mind
Insight

Cognitive functions Vs Cognitive disorders

Cognitive functions Vs Cognitive disorders

- ✓ Cognitive/Neurocognitive disorders characterized by:
  - ✓ Cognitive deficits:
    - ✓ That present in *many mental/neurological disorders*
    - ✓ *Not present from birth* or *very early in life*
    - ✓ Represent a *decline from a previously attained level of functioning*
  - ✓ Different than cognitive function/Processes:
    - ✓ (Our ways of thinking and conclusion formations)
  - ✓ Cognitive Therapy:
    - ✓ Type of psychotherapy that concerned with detection of:
      - ✓ Wrong thoughts and thinking process
      - ✓ **It is not treatment for cognitive disorders**

Cognitive functions vs Cognitive disorders

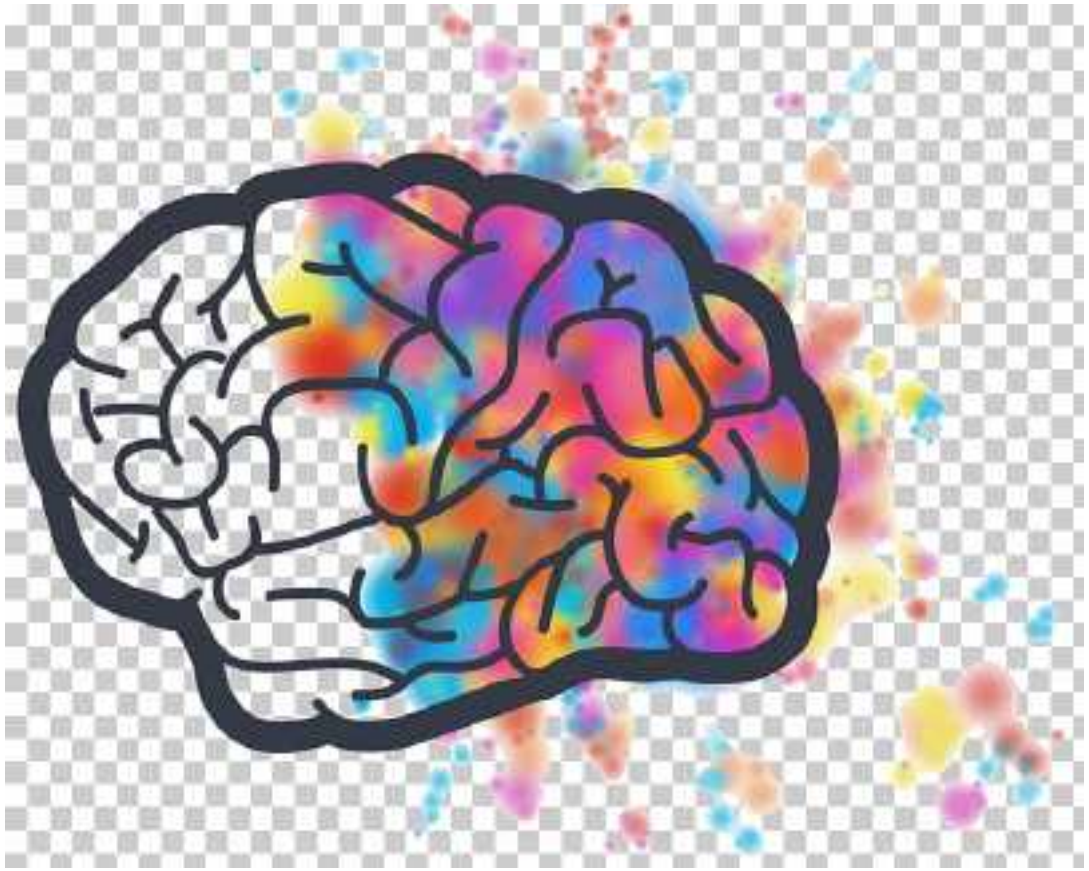
- ✓ ***In the Diagnostic and Statistical Manual of Mental Disorders, fifth edition DSM-5:***
  - ✓ **Neurocognitive disorders**:
    - ✓ ***Delirium***
    - ✓ ***Mild Neurocognitive Disorders***
    - ✓ ***Major Neurocognitive Disorder***
      - ✓ **Dementias**
      - ✓ **Amnestic syndromes**

Cognitive functions vs Cognitive disorders

- ✓ ***Delirium***:
  - ✓ *Short-term confusion* and *changes* in cognition
  - ✓ ***Acute global cognitive disorder WITH*** *disturbed consciousness*
- ✓ **Major Neurocognitive Disorder**:
  - ✓ **Dementias:**
    - ✓ *Severe impairments in memory, judgment, orientation, and cognition*
    - ✓ ***Chronic global cognitive decline WITHOUT*** *disturbed consciousness*
  - ✓ **Amnestic syndrome:**
    - ✓ Major neurocognitive disorder *caused by other medical condition*
    - ✓ Marked primarily by ***memory impairment*** or ***specific disorder of short-term memory*** *caused by:*
      - ✓ ***Medical condition***
      - ✓ ***Toxins or medications***
      - ✓ ***Unknown causes***

DSM V; Kaplan & Sadock (2014; 2009)

Delirium



Case number 1

- A 75-year-old male known to have a long-standing history of HTN, DM type 2, hypercholesterolemia, and BPH
- He was brought to the ER by his family with three days history of high-grade fever, lethargy, and dysuria
- He also started to have poor sleep for the last three days and therefore, his daughter gave him unknown medication that she bought from the pharmacy
- On the same day of ER presentation, he started to have a high-grade fever, and he started to be ***confused***
- His daughter stated that he was ***talking nonsense*** and it seems that he saw ***unobserved images on different occasions***. There was ***a history of fluctuating consciousness***, and he was ***disoriented to place, person, and time***

- There were periods where her father was ***less confused*** and ***less disoriented***. and it seems that he ***went back to his usual self***. And there were periods of ***complete confusion and disorientation***
- Past medical history: HTN, DH, Hypercholesterolemia, and BPH
- Personal/social history: smoke tobacco
- Patient was admitted to the hospital and diagnosed to have *UTI and mild urinary retention*
- Few hours later, after hospital admission:
  - ***He started to be aggressive and agitated***
  - ***He pulled out his IV lines***
  - ***Insisted to be discharged from hospital because he thought that nursing staff want to kill him***


Hallucination • Agitated • Distracted
Disoriented • Rambling • Withdrawn
Restless Delirium sense of place
Bewildered • Confused • Incoherent
Hallucination • Agitated • Distracted
Disoriented • Rambling • Withdrawn

Delirium (الهذيان):

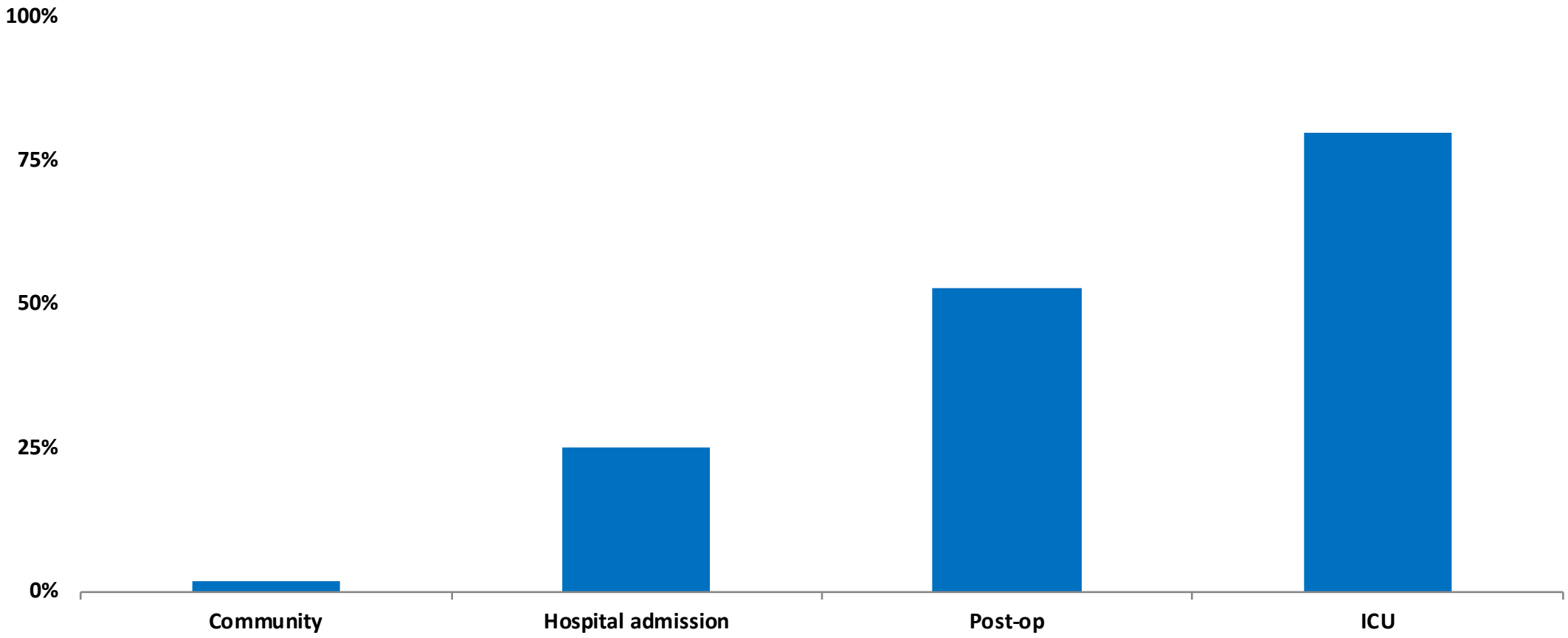
- ✓ Acute *transient reversible global cognitive impairment* with *impaired consciousness* due to a *medical problem*
- ✓ *Many terms are used to describe delirium:*
  - ✓ Acute confusional state
  - ✓ Acute organic syndrome
  - ✓ Acute brain failure
  - ✓ Acute brain syndrome
  - ✓ Acute cerebral insufficiency
  - ✓ Exogenous psychosis
  - ✓ Metabolic encephalopathy
  - ✓ ICU psychosis
  - ✓ Toxic encephalopathy

Epidemiology:

- ✓ It may occur at any age but more in elderly and children
- ✓ *Community Prevalence:* General: 1-2 % > 85years: ~ 14 %
- ✓ *10-30 % Medically* Ill Hospitalized patients
  - ✓ ~ 10 to > 50 % Post-Operative Patients
  - ✓ > 90 % Post-cardiotomy Patients
  - ✓ ~ 70-85 % ICU
- ✓ 60 % in nursing homes or post-acute care settings
  - ✓ ~ 80 % at end of life
- ✓ ***Underdiagnosed when patient is hypoactive and somnolent***
  - ✓ Such cases may be misdiagnosed as depression

DSM V; Kaplan & Sadock (2014; 2009)

Delirium complicates at least 25% of all hospitalizations in the elderly



Fong et al 2009

Delirium:

- ***Clinical features:***
  - Acute onset of mental status change with fluctuating course
  - Attention deficits
  - Confusion or disorganized thinking
  - Perceptual disturbances (e.g., visual hallucination)
  - Disturbed sleep/wake cycle (Sundowning phenomena)
  - Altered psychomotor activity
  - Disorientation and memory impairment
  - Behavioral and emotional abnormalities
  - Other cognitive deficits

(DSM-5) diagnostic criteria for delirium is as follows:

A) Disturbance in:

- ✓ ***Attention*** (Reduced ability to direct, focus, sustain, and shift attention)
- ✓ ***Awareness*** (Reduce orientation to the environment)

***B) The disturbance*:**

- ✓ Develops ***over a short period*** (usually hours to days)
- ✓ Represent a ***change in the baseline*** attention and awareness
- ✓ Tends to ***fluctuate in severity*** during the course of a day

C) An additional disturbance in cognition:

- ✓ Memory deficit, disorientation, language, perceptual disturbance

(DSM-5) diagnostic criteria for delirium is as follows:

D) Disturbance in criteria A and C:

- ✓ **Not** due to another preexisting, established, or evolving dementia
- ✓ Do not occur in the context of a severely reduced level of arousal (e.g. coma)

E) There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by a ***direct physiologic consequence*** of:

- ✓ General medical condition
- ✓ An intoxicating substance
- ✓ Medication use
- ✓ More than one cause

Diagnostic criteria (Simplified) (Reference)

A) Consciousness is disturbed (e.g. awareness of the environment is impaired but patient not in coma).

B) Cognitive functions are impaired +/- perceptual disturbance (illusions or hallucinations)

C) Acute onset with fluctuating symptoms (within hours during the day) & transient course (few days).

D) Caused by a physical problem (e.g. hypoxia, hypoglycemia, infection..etc.)

M. A. Al-Sughayir-Manual of basic Psychiatry September-2014/Neuro-cognitive D

Type of delirium (DSM-5 specifiers):

1) ***Hyperactive 30%*** (most clear and least controversial)
   - ✓ Hyperactive psychomotor activity
   - ✓ May have mood lability, agitation, refusal to cooperate with medical care

2) ***Hypoactive 24%*** (most difficult type to identify)
   - ✓ Hypoactive psychomotor activity
   - ✓ May be have sluggishness or lethargy that approaches stupor
   - ✓ Inappropriately diagnosed and treated as depression

3) ***Mixed level of activity 46%*** (Classic wax and waning pattern)
   - ✓ Normal psychomotor activity with disturbed attention and awareness
   - ✓ May have rapidly fluctuating activity level

DSM V (2013); Maldonado (2008)

Why it is important to discover delirium?

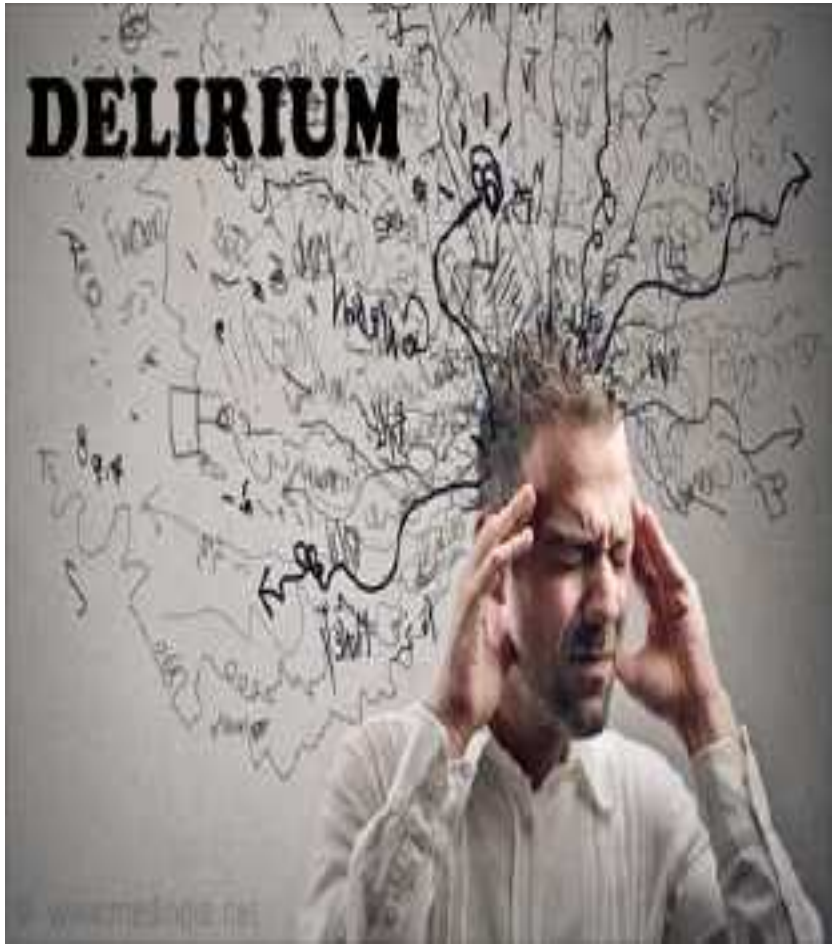
✓ It is a very ***serious medical and psychiatric condition*** and that due to high risk of:

1) Death *(due to associated serious medical condition)*
2) Violence toward medical staff
3) Self-harm or suicidal risk
4) Impaired judgment
5) Psychosis

Why it is important to discover delirium?

- ✓ Delirium is associated with:
  - ✓ ↑ morbidity and mortality
  - ✓ ↑ length of hospital stay
  - ✓ ↑ Rates of admission to long term care facilities
  - ✓ 20 % of patients discharged post hip # still had evidence of delirium

(Journal of American Geriatric Society 2001 May;49(5):678-9).



Why dose a delirious patient become suicidal or aggressive?

- ✓ Due to severe disturbance in the patient's perception, mood, judgment, thinking, and behavior

- ✓ Patient may act on hallucinations, illusions or delusional thoughts as *if they were genuine dangers* (e.g., blood extraction by a nurse might be perceived as an attack)

Delirium Risk factors/Predisposing Factors:

- ✓ ***> 60 years of age***
- ✓ Male sex
- ✓ Visual/hearing impairment
- ✓ Underlying brain pathology such as stroke, tumor, vasculitis, trauma, or dementia
- ✓ Major/ multiple medical illnesses
- ✓ Recent major surgery
- ✓ Depression (Mental illness)
- ✓ Functional dependence
- ✓ Dehydration
- ✓ Substance abuse/dependence
- ✓ Hip fx
- ✓ Metabolic abnormalities
- ✓ ***Polypharmacy***

Delirium Risk factors/Predisposing Factors:

Demographics General Medical Hx	Psychiatric Hx	Current Medical Problem	Medications	Current Status
✓ Male ✓ Age >75 ✓ Functional Impairment ✓ Immobility ✓ Low levels of activity ✓ Sensory Impairment ✓ Fall Hx	✓ Hx of Delirium ✓ Dementia ✓ Depression ✓ Bipolar ✓ Schizophrenia ✓ Drug/ETOH/ Toxins	✓ Severe Illness ✓ Multiple Illnesses ✓ Abn. Blood Work ✓ Metabolic D/O ✓ CNS pathology ✓ Trauma ✓ Burns ✓ Post-Op ✓ Poor O2 States	✓ > 3 drugs ✓ Psychoactive Meds ✓ Anticholinergic ✓ Meds 5HT Meds ✓ Examples: ✓ Opioids* Corticosteroids* Benzodiazepines* NSAIDS Chemo Meds	✓ Dehydration ✓ Malnutrition ✓ Sleep Deprivation ✓ Over Sedation ✓ Pain ✓ Abnormal VS ✓ Catheters IV ✓ Restraints

Maldonado (2008)

Etiology (Delirium Precipitating Factors):

I watch death

- ***I:*** Infections
- ***W:*** Withdrawal
- ***A:*** Acute metabolic
- ***T:*** Trauma
- ***C:*** CNS pathology
- ***H:*** Hypoxia
- ***D:*** Deficiencies
- ***E:*** Endocrinopathies
- ***A:*** Acute vascular
- ***T:*** Toxins
- ***H:*** Heavy metal

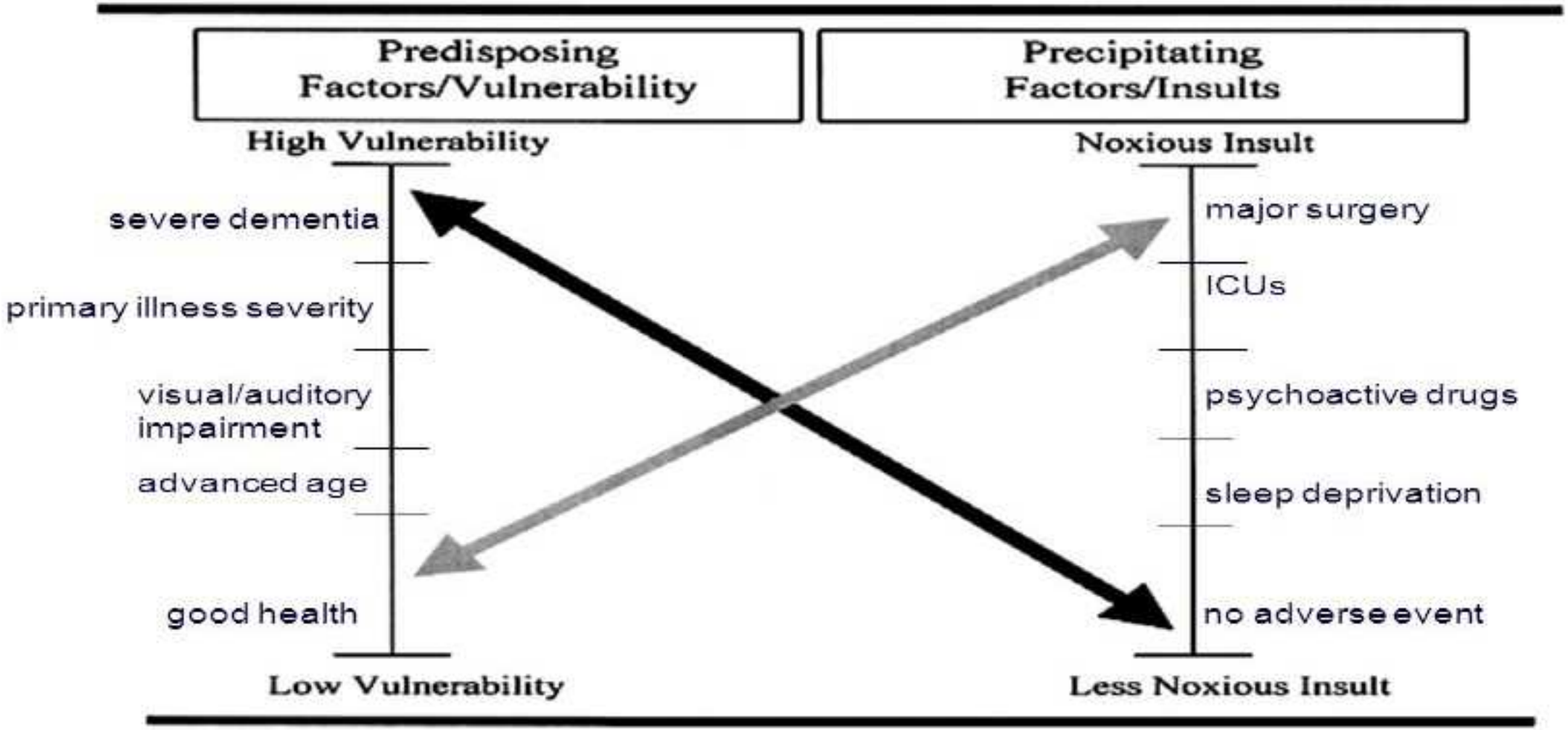
Etiology (Delirium Precipitating Factors): (Reference)

- ✓ Infections (encephalitis, meningitis, HIV, syphilis, sepsis, typhus, malaria)
- ✓ Withdrawal from substance of the abuse (alcohol, sedative-hypnotic, barbiturates)
- ✓ Acute metabolic (acidosis, alkalosis, liver/kidney failure)
- ✓ Trauma (closed head trauma, heatstroke, recent surgery, severe burns)
- ✓ CNS pathology (abscess, tumor, seizures, hydrocephalus)
- ✓ Hypoxia (anemia, hypoperfusion due to heart/lung failure, co poisoning)
- ✓ Deficiencies of vitamins (B12, folate, thiamine, niacin)
- ✓ Endocrinopathies (Hyper/Hypoglycemia, Hypo/Hyperadrenocorticism, Hyperparathyroidism)
- ✓ Acute vascular (hypertension, stroke, TIA, arrhythmia)
- ✓ Toxins (medications, illicit drugs, pesticides, solvents)
- ✓ Heavy metal (lead, manganese, mercury)

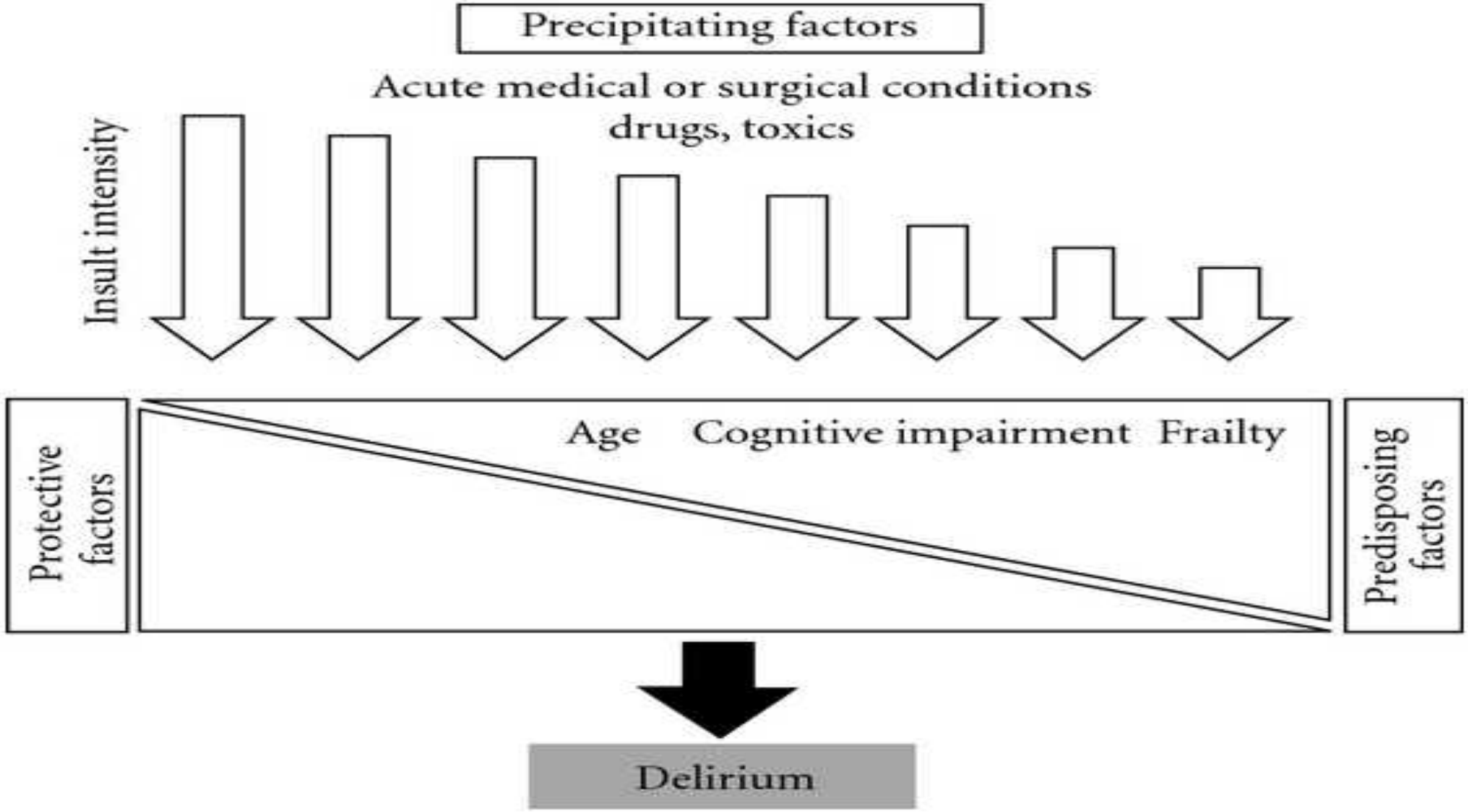
Life threatening causes of delirium:

1) ***Wernicke's encephalopathy***
2) ***Alcohol/Benzodiazepine withdrawal***
3) ***Hypoxia***
4) ***Hypoglycemia***
5) ***Hypertensive encephalopathy***
6) ***Intra-cerebral hemorrhage***
7) ***Meningitis/encephalitis***
8) ***Poisoning***

MULTIFACTORIAL MODEL OF DELIRIUM IN OLDER PERSONS

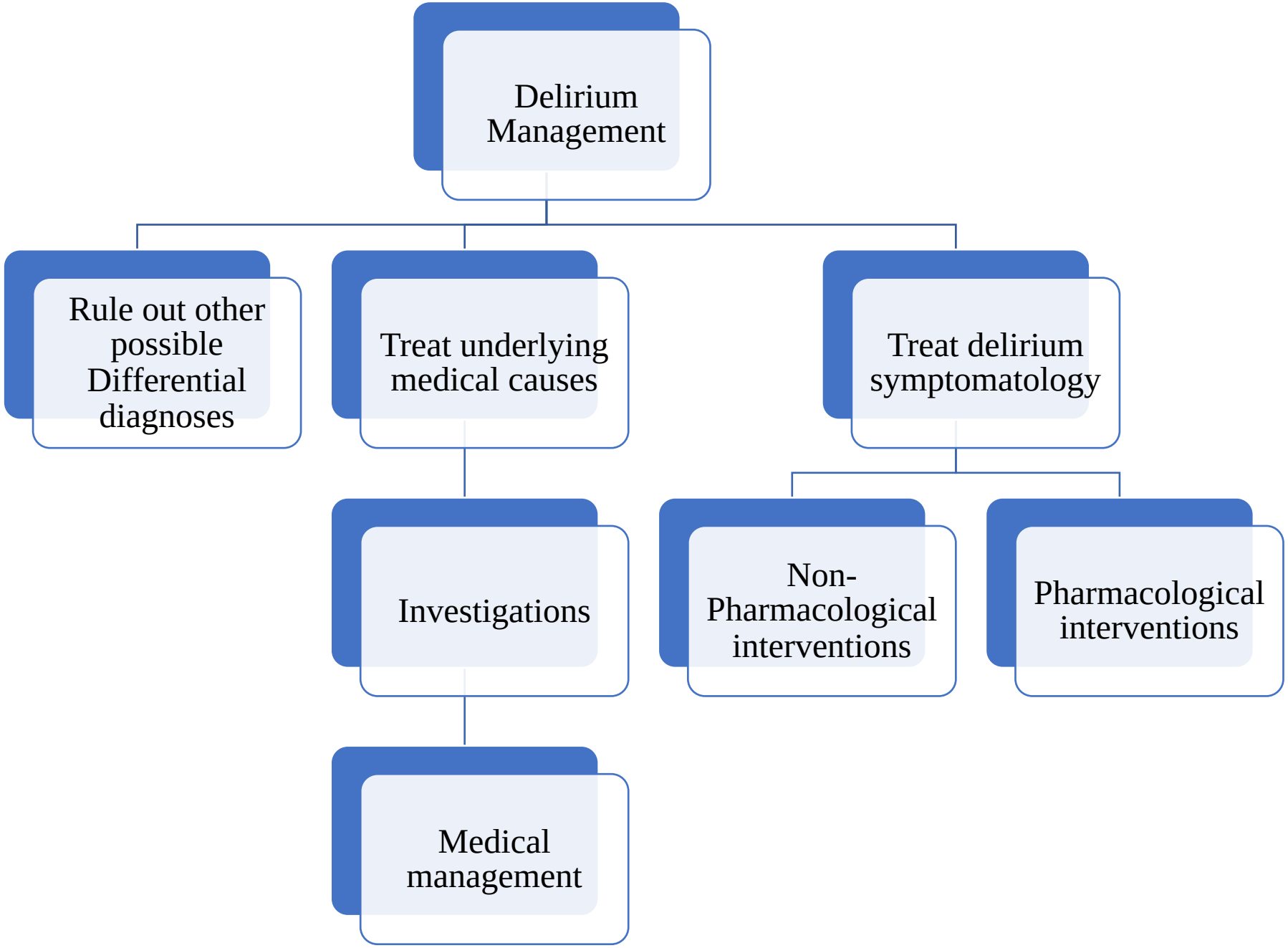


Ref: Inouye SK et al. JAMA 1996; 275:852-857


Precipitating factors
Acute medical or surgical conditions
drugs, toxics
Insult intensity
Protective factors
Age
Cognitive impairment
Frailty
Predisposing factors
Delirium

Delirium Management/Interventions:

Ensure patient / staff safety and than treatment of the underlying medical causes


Delirium Management
Rule out other possible Differential diagnoses
Treat underlying medical causes
Treat delirium symptomatology
Investigations
Non-Pharmacological interventions
Pharmacological interventions
Medical management

Delirium differential diagnoses

1) Dementia:
   - ✓ In many Occasions, delirium occurs in a patient with dementia, a condition known as beclouded dementia. However, a dual diagnosis (i.e., ***delirium in top of dementia***) can only be made when there is a definite history of pre-existing dementia
2) Substance abuse:
   - ✓ Alcohol, inhalants, sedatives, and opioids
3) Amnestic syndrome (see later)

Delirium differential diagnoses

4) Acute functional psychosis/ Major psychiatric illness (brief psychosis, mania, exacerbation of schizophrenia)

✓ Patients usually experience ***no change in their level of consciousness*** or their ***orientation***. The ***hallucination and delusions*** are more ***constant*** and ***better organized*** than those of patients with delirium

5) Severe depression:

✓ Patients with ***hypoactive symptoms of delirium*** may appear ***somewhat similar*** to severely depressed patients, but can be ***distinguished on the basis of EEG*** (normal in depression)

Delirium differential diagnoses

Proper assessment of mental functions

- ***Mini-Mental state exam (MMSE)***
  - Tests orientation, short-term memory, attention, concentration, constructional ability.
  - 30 points is perfect score
  - < 20 points suggestive of problem
  - Not helpful without knowing patient's baseline
- ***MoCA (Montreal Cognitive Assessment)***

Mini-Mental State Examination (MMSE)

Patient's Name:_____ Date:_____

Instructions: Ask the questions in the order listed.
Score one point for each correct response within each question or activity.

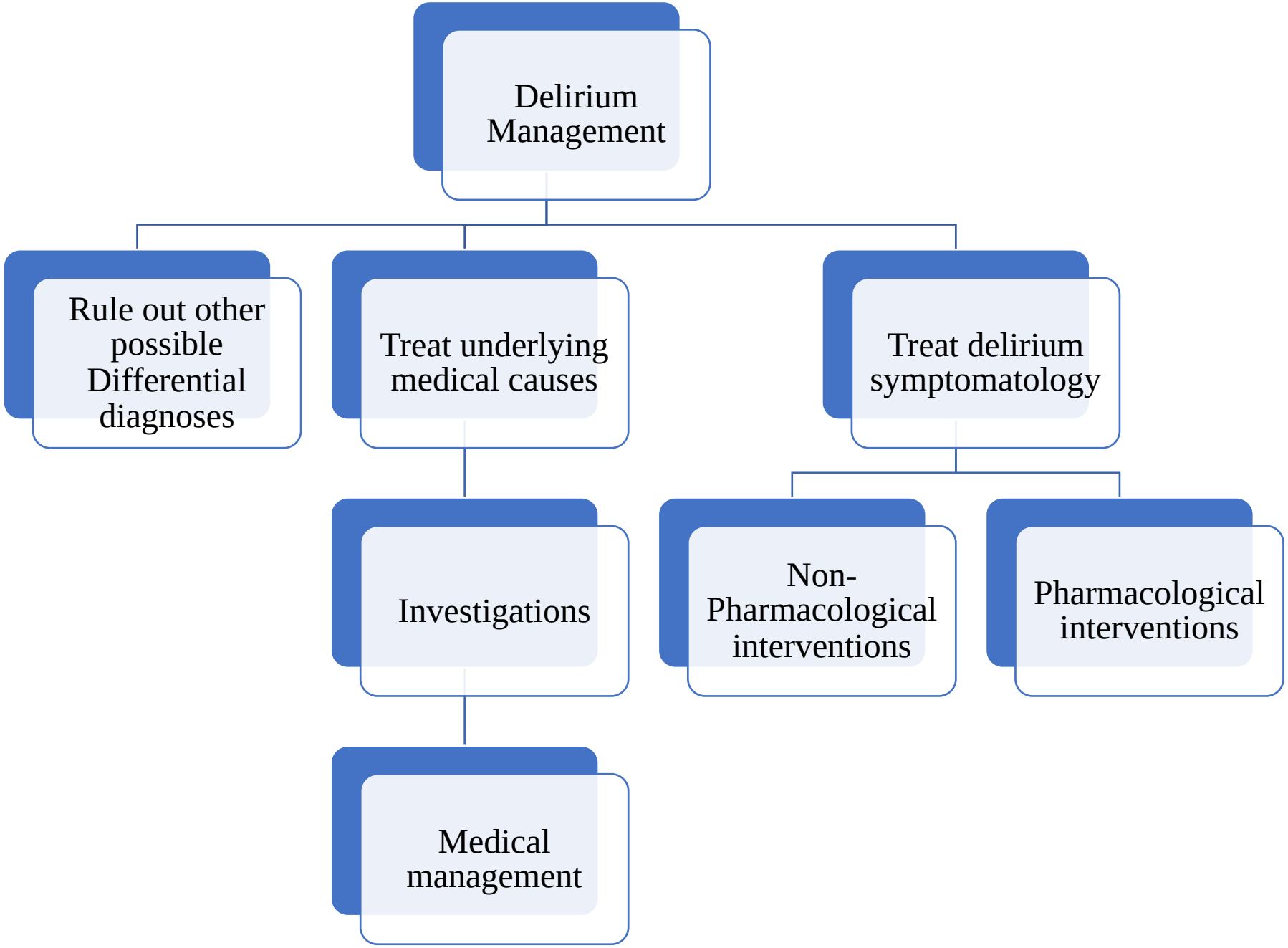
Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day of the week? Month?"
5		"Where are we now: State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient's response 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**

Treat underlying medical causes

- Investigation
- ***There is no specific diagnostic investigation for delirium***
  - ✓ **A) Good clinical skills are essential:**
    - ✓ *1) Careful History and physical examinations:*
      - ✓ Acute onset + review medical conditions/diseases + cognitive & consciousness disturbances
    - ✓ *2) Collateral history:*
      - ✓ Baseline cognition
      - ✓ Presence of sensory impairments
      - ✓ Exposure to risk factors
      - ✓ Review medications, procedures, tests,…etc

Treat underlying medical causes

- ***First line investigations:***
  - ✓ Complete blood count (CBC) with differentials WBCs
  - ✓ Electrolytes, Mg, Ca, and PO4 tests
  - ✓ Liver function tests
  - ✓ Renal function tests
  - ✓ Urinalysis + cultures & sensitivity
  - ✓ Blood cultures & sensitivity
  - ✓ Thyroid function test
  - ✓ Electrocardiogram (ECG)
  - ✓ Blood glucose
  - ✓ Chest x-rays
- ***Second line investigations:***
  - ✓ Drug screen
  - ✓ Cardiac enzymes
  - ✓ Blood gas (ABG)
  - ✓ Serum folate / B12
  - ✓ Electroencephalography (EEG)
  - ✓ Cerebrospinal fluid examinations.
  - ✓ Brain CT scan
  - ✓ Brain MRI


Delirium Management
Rule out other possible Differential diagnoses
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Investigations
Non-Pharmacological interventions
Pharmacological interventions
Medical management

Treatment of delirium symptomatology

1) ***Non-Pharmacological interventions***

- ✓ Symptomatic measures involving attention to *fluid and electrolyte balance, nutritional status, and early treatment of infections*
- ✓ ***Environmental interventions:***
  - ✓ Reduce *unfamiliarity* by providing a calendar, a clock, family pictures, and personal objects
  - ✓ Maintain a *moderate sensory balance* in the patient by avoiding sensory overstimulation or deprivation
  - ✓ *Minimize staff changes*, *limit noise* and the *number of visits*, a nightlight, and where necessary, *eyeglasses and hearing aids*
  - ✓ *Proper communication* and *support* are critical with these patients

Treatment of delirium symptomatology

2) ***Pharmacological interventions:***

- ✓ All the patient's medications should be reviewed, and any *unnecessary drugs should be discontinued (especially anticholinergic)*
- ✓ If ***some medication*** needed, the patient should receive the lowest possible dose
- ✓ Drugs such as *phenobarbital or benzodiazepine should be avioded*
  - ✓ *Their effects may increase disorientation, drowsiness, ataxia, and possible falls, head trauma and fractures*
- ✓ For agitation or aggressive behaviour: Haloperidol 5 mg oral/IV/IM or olanzapine 5 mg oral/IM (or other type of atypical antipsychotics)
  - ✓ Intramuscular administration may be preferable for some patients with delirium who are poorly compliant with oral medications or who are too sedated

Delirium course and Prognosis:

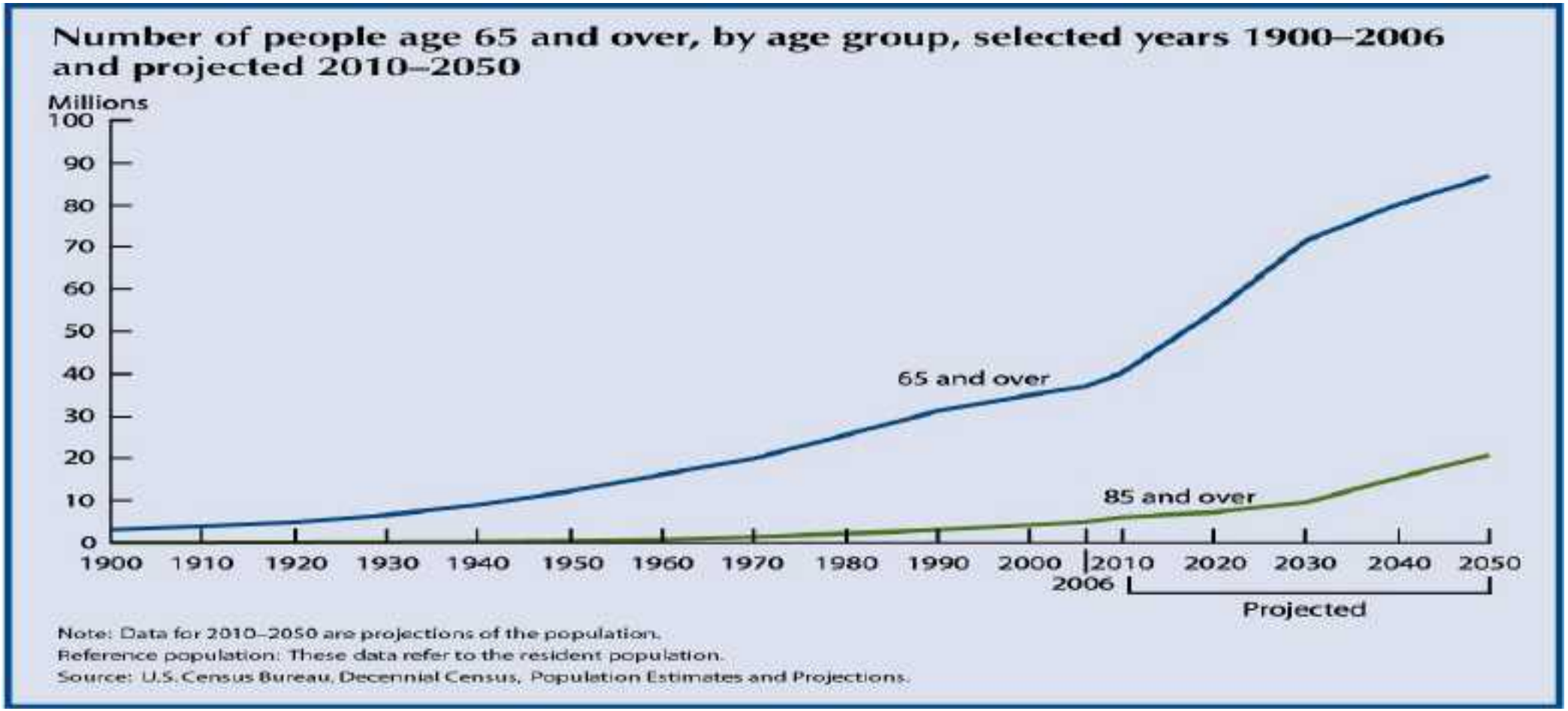
- ✓ The course usually short (7-10 days)
- ✓ Symptoms of delirium usually persist as long as the causally relevant factors are present
- ✓ The longer the patient has been delirious and the older the patient, The longer the delirium takes to resolve
- ✓ Delirium may spontaneously resolved or progress rapidly into death because of the serious nature of the associated medical conditions
- ✓ ***When underlying cause treated, it usually resolves rapidly***
  - ✓ ***Some residual deficit may persist***
- ✓Some patients may develop depression symptoms or Post Traumatic Stress Disorder (PTSD)

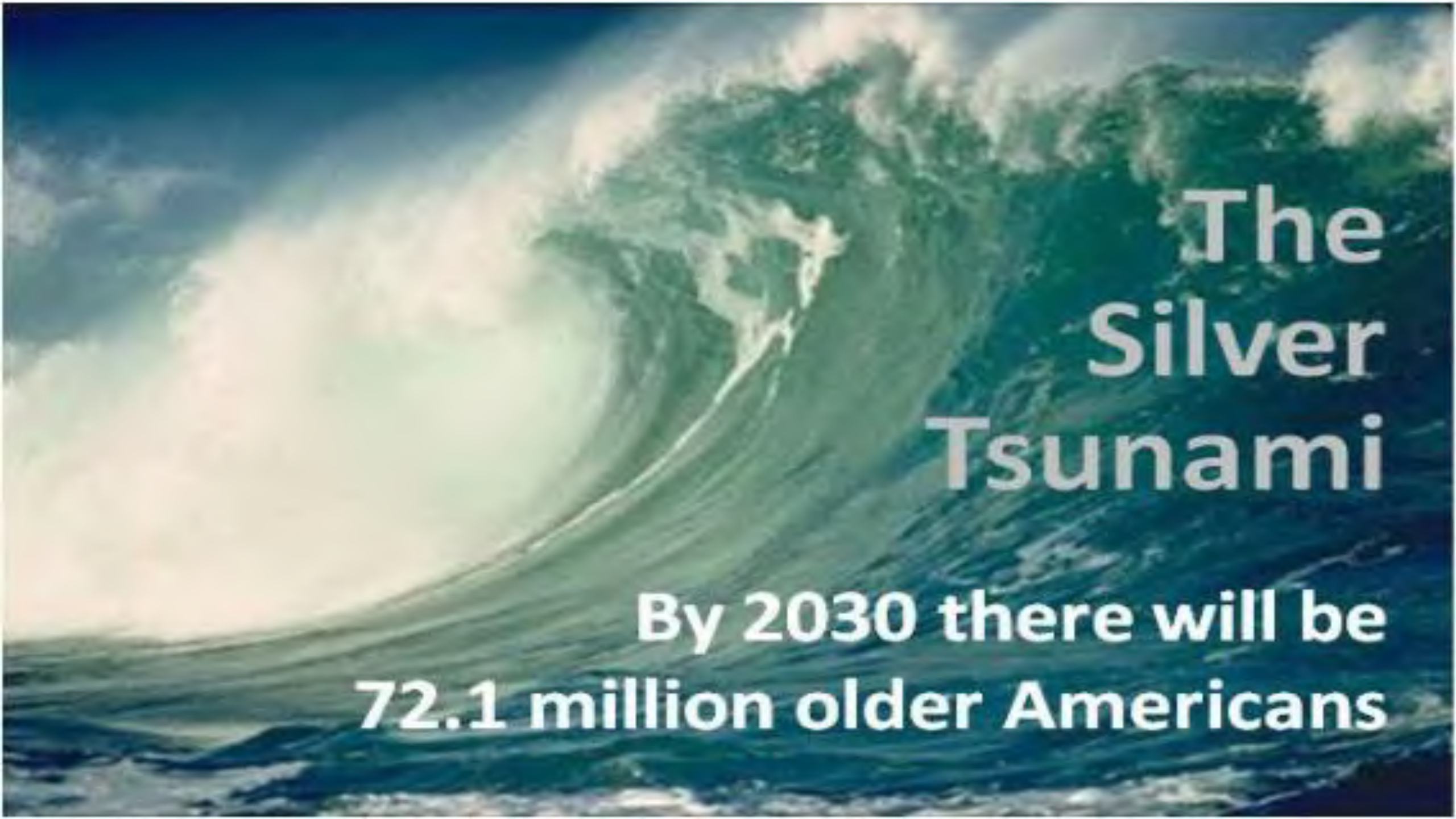
Major Neurocognitive Disorders

Introduction:

- ✓ Aging is a normal part of development
- ✓ Unlike childhood development, there are NO specific motor, speech or cognitive milestone for adults to meet as they enter old age
- ✓ Instead, aging is often accompanied by accumulating losses in functioning that gradually increase the risk of mortality
- ✓ Many of these changes (including some degree of memory loss) are considered to be completely within the realm of normalcy
- ✓ However, there are also a variety of conditions associated with old age that cause distress and dysfunction not only for the patient themselves but also for their family and caregivers

People > 65 make up one of the fastest growing segment of population



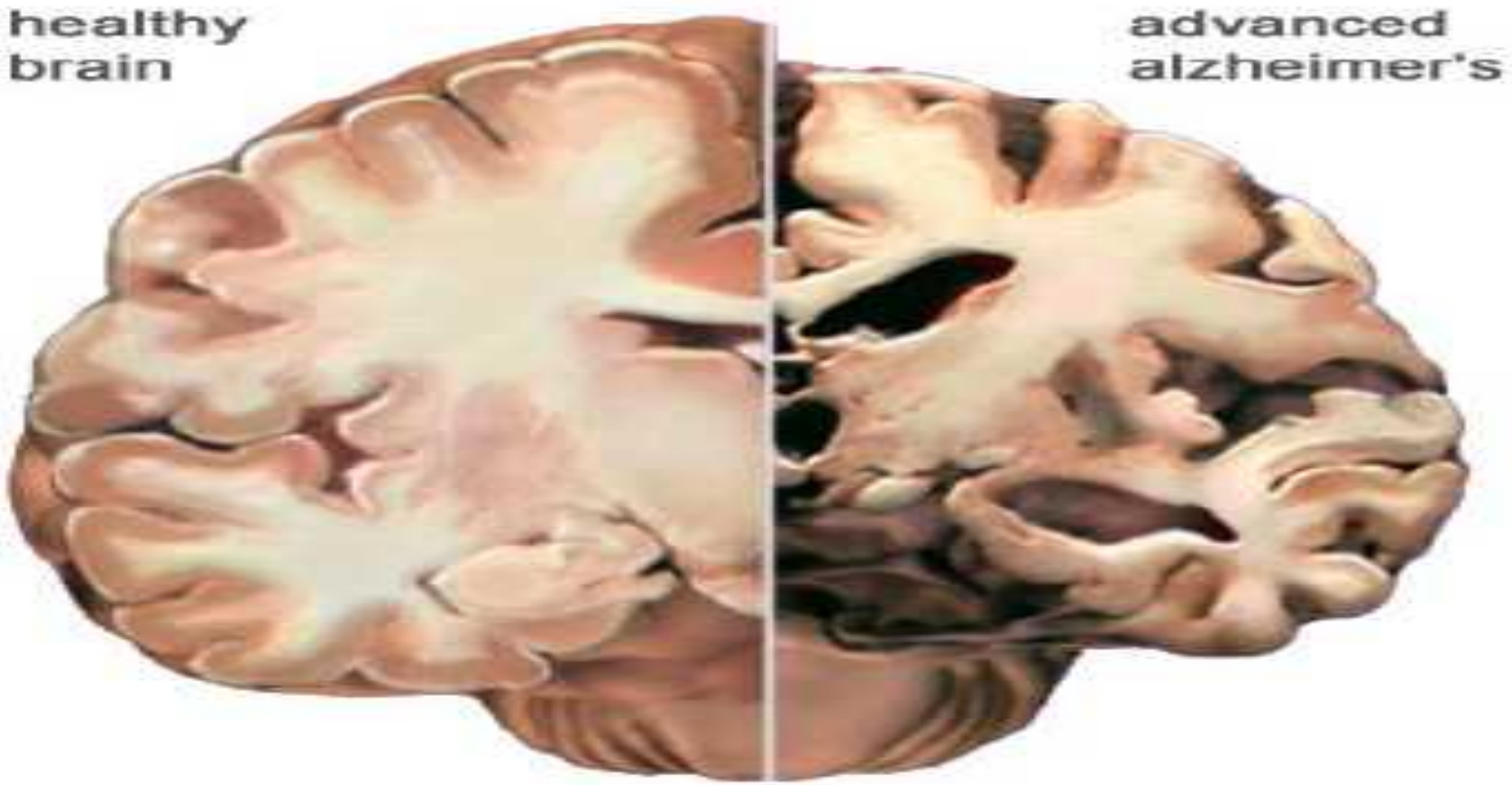

The
Silver
Tsunami
By 2030 there will be
72.1 million older Americans

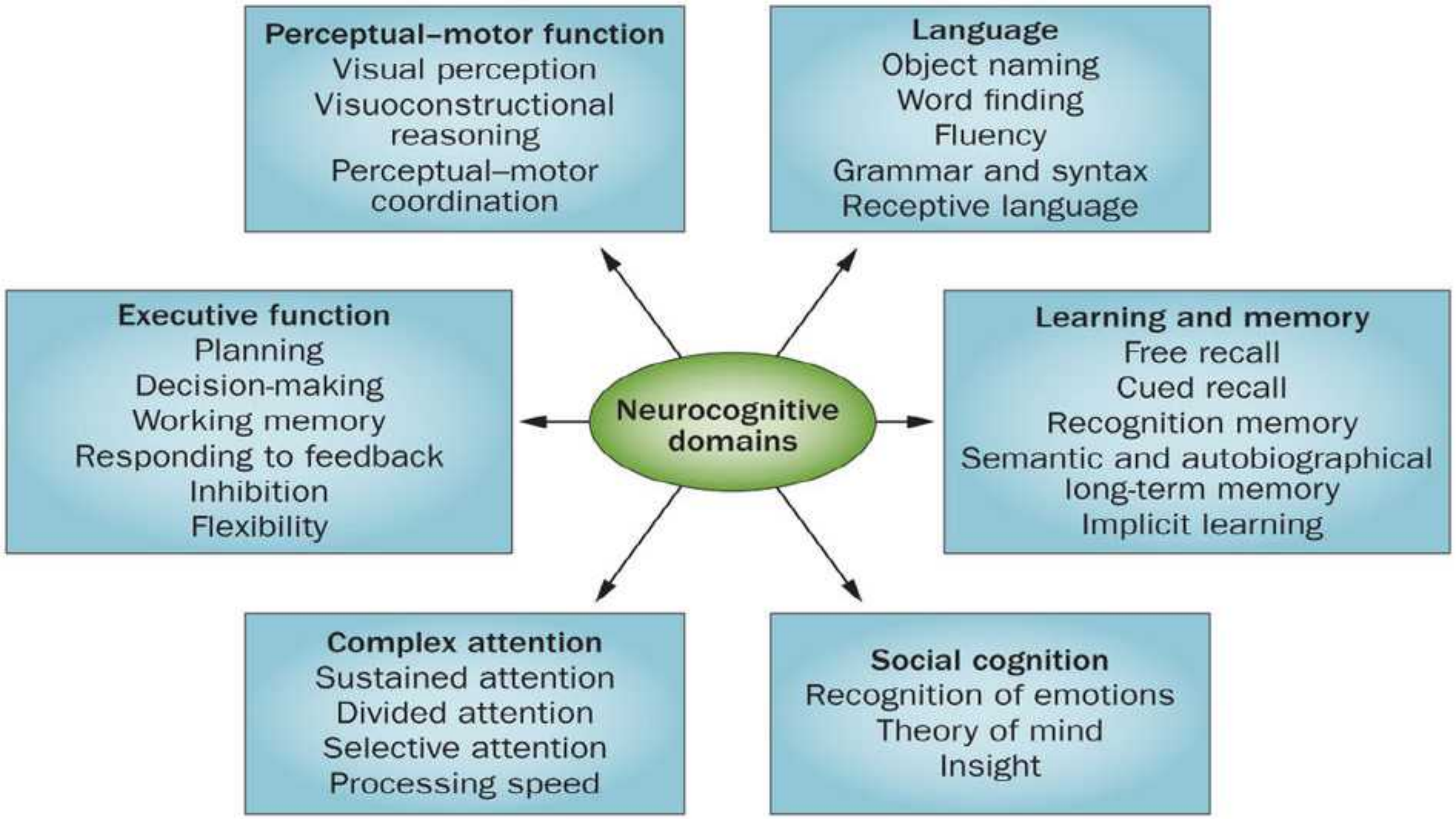
Case number 2

- 73 year-old-lady, she was diagnosed for many years to have DM, HTN, Hypercholesterolemia, and Osteoporosis
- Her family noticed in the **last year** that she start to be more **isolated and not socially engaged**
- She started to be more ***forgetful and repeating the same questions over and over***. More recently, she started to ***misplace things like her keys and her items***. Also, there were a few occasions where she left the refrigerator open

- More recently, the patient's family discovered that the patient is ***either not taking her oral medications or taking her medications wrongly***. In addition, she started to be more ***irritable and sometimes aggressive*** towards her family. She has ***poor insight into her current situation***
- Throughout the patient's history, there is ***no history of loss of consciousness***. And there is ***no motor abnormality***. There is no history of abnormal perception or unusual thinking; however, more recently, patient started to be ***more suspicious***

Dementia

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Semantic and autobiographical long-term memory
Implicit learning
Complex attention
Sustained attention
Divided attention
Selective attention
Processing speed
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Recognition of emotions
Theory of mind
Insight

Dementia

- ✓ Dementia refers to a disease process marked by:
  - ✓ Progressive cognitive impairment in clear consciousness
  - ✓ Does NOT refer to low intellectual functioning or mental retardation because these are developmental conditions
  - ✓ Cognitive deficits *represent a decline* from a previous level of functioning
  - ✓ Involves *multiple* neurocognitive domains
  - ✓ Cognitive deficits cause significant impairment in *social or occupational functioning or both*

The Dementia Syndrome (Reference)

A) Global deterioration of intellectual function (learning & memory, complex attention, language, executive function, perceptual-motor abilities, social cognition)

B) Clear consciousness (rule out delirium)

C) Impairment in performance of personal activities of *daily living and social or occupational activities* due to the decline in intellectual function

D) Noncognitive psychopathological symptoms and/or deterioration in emotional control, motivation, or personality frequently present but not necessary for diagnosis

E) Duration of at least 6 months

Lobo a: manual de psiquiatria general. Madrid, editorial panamericna s.a., 2013

Epidemiology:

- ✓ No gender difference
- ✓ Increasing *age* is the most important risk factor (It is primarily a disorder of the elderly)
- ✓ The prevalence of moderate to severe dementia:
  - ✓ In the general population is 5 % > 65 years
  - ✓ 20 - 40 % in > 85 years
  - ✓ 15 - 20 % In outpatient general medical practice
  - ✓ 50 % in chronic care facilities
- ✓ Affective symptoms, including depression and anxiety are seen in 40 to 50 % of demented patients
- ✓ Delusion and hallucination occur in 30 %

Dementia Presentation:

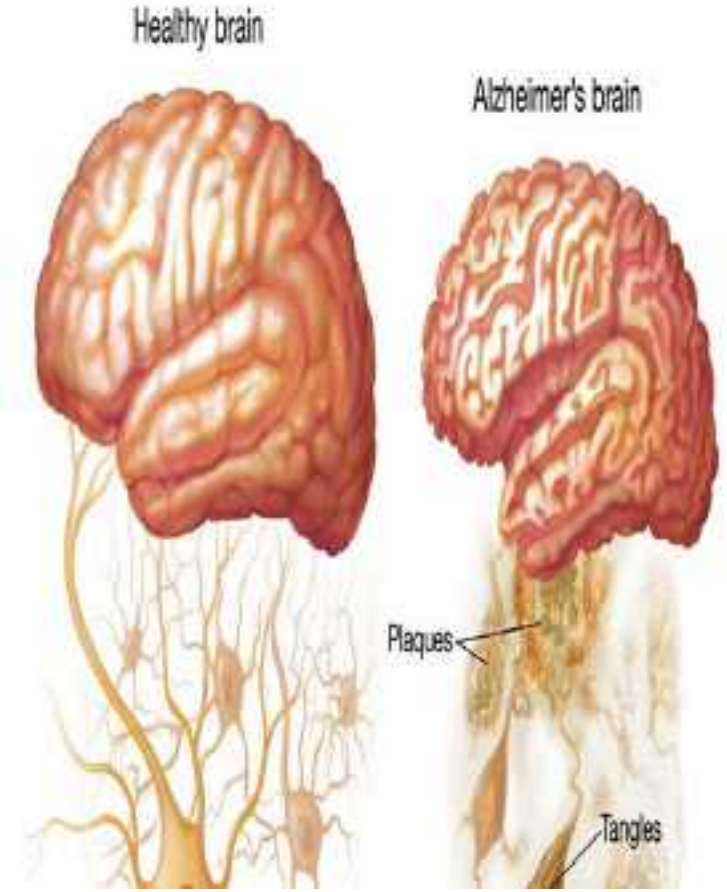
- ✓ In early stage cognitive impairment may not be apparent:
  - ✓ Gradual loss of social and intellectual skills (first noticed in work setting where high performance is required)
  - ✓ Mild memory impairment
  - ✓ Subtle changes in personality
  - ✓ Changes in affect (irritability, anger,…)
  - ✓ Multiple somatic complaints and vague psychiatric symptoms

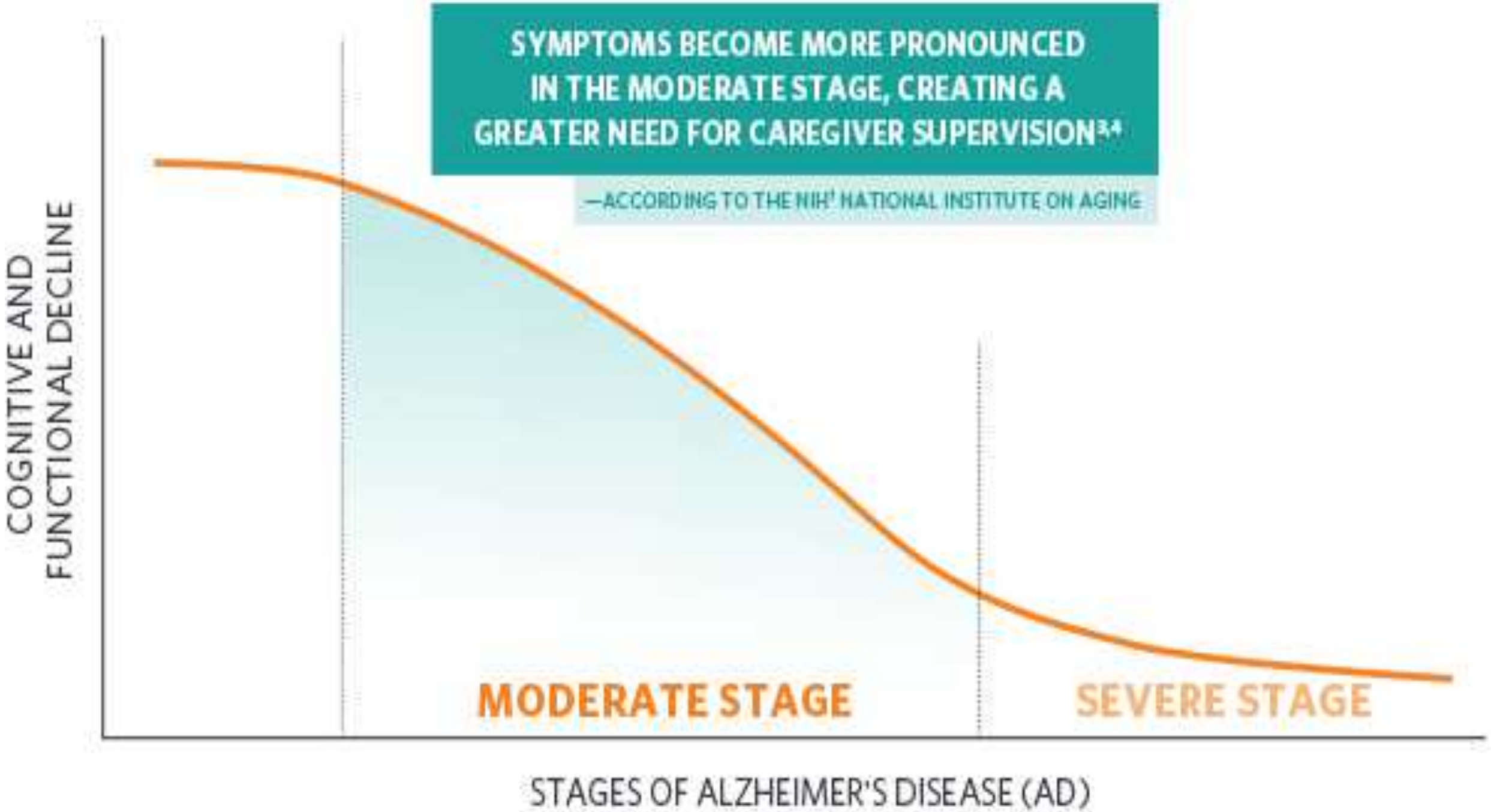
Dementia Presentation:

- ✓ In the late stages cognitive disturbances emerge:
  - ✓ Increasing memory impairment (esp. recent memory)
  - ✓ Attention impairment
  - ✓ Disorientation (particularly to time, and when severe to place and person)
  - ✓ Language: vague and imprecise speech with inappropriate repetition of the same thoughts (Perseveration)
  - ✓ Impaired judgment
  - ✓ Potential aggression (verbal & physical)
  - ✓ Psychotic features (hallucination &delusions)
  - ✓ Emotional lability
  - ✓ Catastrophic reaction (marked by agitation secondary to subjective awareness of intellectual deficits under stressful circumstances)

Causes of dementia:

1) Alzheimer's disease (AD) (50 - 60 %)
   - ✓ **Gradual onset and a continuous slow** but **steady decline** from a prior intellectual and functional capacities, especially memory
   - ✓ ***Age of onset:***
     - ✓ Before age 65 (5%)
     - ✓ After age 65 (95%)
   - ✓ Live an average of 10 years following diagnosis
   - ✓ ***Risk factors:***
     - ✓ *Old age, female, low education, first-degree relative with AD, cigarette smoking, depression, mild cognitive impairment, and social isolation*

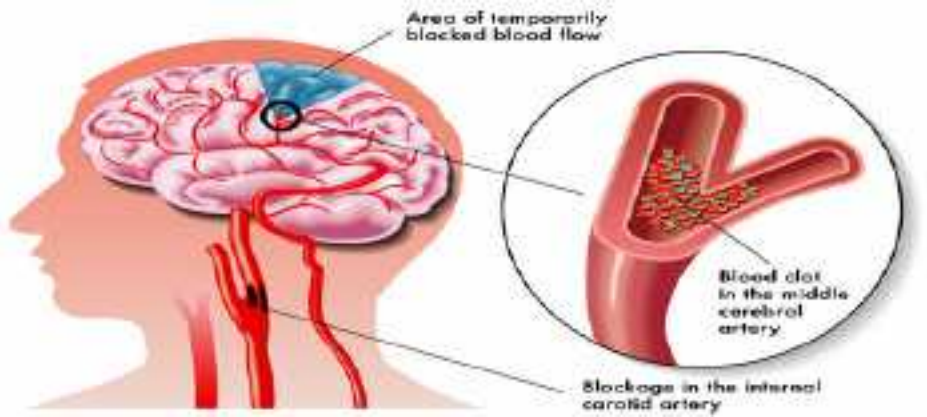


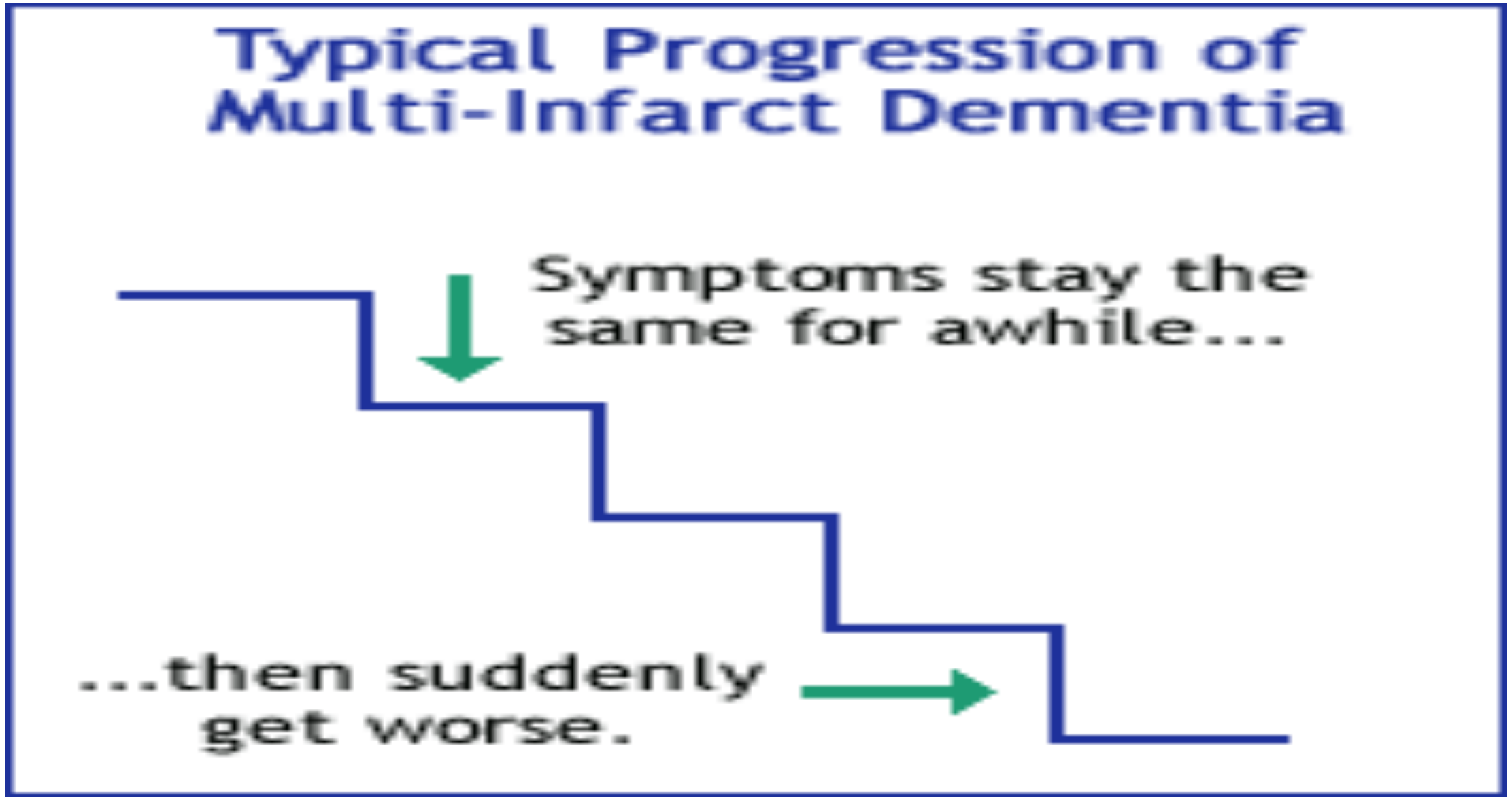

SYMPTOMS BECOME MORE PRONOUNCED IN THE MODERATE STAGE, CREATING A GREATER NEED FOR CAREGIVER SUPERVISION[3,4]
—ACCORDING TO THE NIH[1] NATIONAL INSTITUTE ON AGING
COGNITIVE AND FUNCTIONAL DECLINE
MODERATE STAGE
SEVERE STAGE
STAGES OF ALZHEIMER'S DISEASE (AD)

Causes of dementia:

2) Vascular (multi-Infarct) dementia (10 - 20 % of dementias):

- ✓ Declining **Stepwise deterioration** of intellectual functioning due to multiple infarcts of varying sizes or arteriosclerosis in the main intracranial vessels
- ✓ Risk factors for vascular dementia:
  - ✓ Age > 60
  - ✓ Male
  - ✓ Pervious stroke
  - ✓ Stroke risk factors: (*HTN, heart disease/atrial fibrillation, DM, Smoking, obesity, and hypercholesterolemia*)




Typical Progression of Multi-Infarct Dementia
Symptoms stay the same for awhile...
...then suddenly get worse.

Causes of dementia:

3) Medical conditions (reversible conditions; 15 % of dementias):

- ✓ A variety of **non-psychiatric**, **non-neurologic conditions** can **cause cognitive symptoms** which can strongly **resemble dementia**
- ✓ Referred as **reversible dementias**, as treating the underlying condition can *effectively restore cognitive function* back to its pervious state
- ✓ Common causes of reversible dementia:
  - ✓ Drugs (Benzodiazepines, anticonvulsants, anticholinergics…) , alcohol/substance abuse
  - ✓ Sensory impairments (Vision, hearing loss)
  - ✓ Metabolic abnormalities (Poorly treated DM)
  - ✓ ***Endocrinological problems (Hypothyroidism)***
  - ✓ ***Nutritional deficiency (Vitamin B12 deficiency)***
  - ✓ Infections (HIV, neurosyphilis)

Causes of dementia:

4) Lewy Body dementia: characterized by ***fluctuating in cognition, vivid visual hallucinations***, ***parkinsonian features*** (tremor, rigidity, gait problems/falls)

5) Frontotemporal dementia: degeneration of the frontal and temporal lobe and characterized by ***inappropriate behavior (hypersexuality), personality changes, and loss of impulse control***

6) Other type of dementia:

- ✓ Parkinson's disease (20 - 30 % of patients with Parkinson's disease have dementia)
- ✓ ***Normal-pressure hydrocephalus*** (Progressive memory impairment, slowness and marked unsteady gait (+ urine incontinence in the late stage)
- ✓ Huntington's disease (intellectual impairments with extrapyramidal features)
- ✓ Creutzfeldt-Jakob's disease (CJD)
- ✓ Traumatic Brain Injury (TBI)
- ✓ Prion disease

Dementias are classified as: (Reference)

- ✓ Cortical:
  - ✓Alzheimer’s disease
  - ✓Frontotemporal dementia
  - ✓Dementia with Lewy Body
- ✓ Subcortical:
  - ✓ Huntington’s disease
  - ✓ Parkinson’s disease
  - ✓ Normal-pressure hydrocephalus
  - ✓ ***Subcortical dementias are associated with psychomotor retardation, movement disorders, gait incoordination, apathy, and akinetic mutism***

Dementia workup:

1) Comprehensive history and physical examination

2) Investigations:

- ✓ Essential workup to detect treatable causes:
  - ✓ Blood work (CBC with differential, ***TSH***, blood glucose, electrolytes, Ca, Mg, ***vitamin B12***, folate, liver and renal function tests)
  - ✓ Other tests (serum HIV)
  - ✓ Neuropsychological testing (MoCA)
  - ✓ Neuroimaging (CT scan and MRI)

Dementia workup:

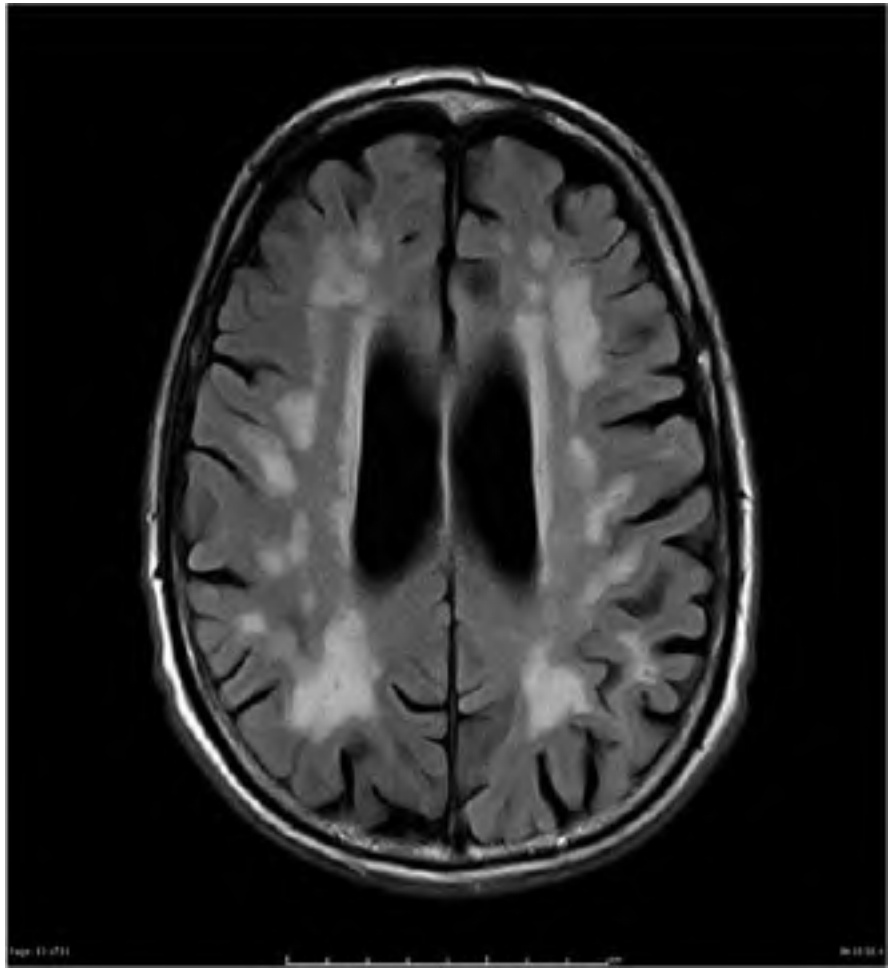
✓ ***Neuroimaging:***

✓Alzheimer’s dementia:

- ✓ Cortical atrophy
- ✓ Wide sulci & gyri
- ✓ Wide ventricles

Dementia workup:

- ✓ ***Neuroimaging:***
  - ✓ Vascular dementia:
    - ✓ Lesions and atrophy of cortical and/or subcortical structures corresponding to infarcts



Dementias Differential Diagnoses:

1) ***Normal aging***:

- ✓ Age-related cognitive decline (the course is not progressively deteriorating), NO loss of social or occupational functioning

2) ***Depression in the elderly (Pseudo-dementia):***

- ✓ Cognitive disturbance is relatively of rapid onset and preceded by ***depressive features***
- ✓ The differentiation is sometimes difficult as demented patients may also become depressed as they begin to comprehend their progressive cognitive impairment
- ✓ EEG and CT scan are normal in pseudo-dementia

3) ***Delirium:***

- ✓ The onset is rapid and consciousness is impaired
- ✓ Some demented patients may develop delirium
- ✓ Diagnosis of *dementia cannot be made* before delirium clears

Delirium Vs Dementia

Feature	Dementia	Delirium
onset	Slow/gradual (except for vascular dementia	Rapid
Duration to develop	months to years	hours to weeks
Attention	Preserved	Fluctuates
Awareness	Unchanged	Reduced
Consciousness	intact	impaired
Course	Chronic/deteriorating	transient/clears within 7-10 days

Delirium vs. Dementia vs. Depression

Features	Delirium	Dementia	Depression
Onset	Acute (hours to days)	Insidious (months to years)	Acute or Insidious (wks to months)
Course	Fluctuating	Progressive	May be chronic
Duration	Hours to weeks	Months to years	Months to years
Consciousness	Altered	Usually clear	Clear
Attention	Impaired	Normal except in severe dementia	May be decreased
Psychomotor changes	Increased or decreased	Often normal	May be slowed in severe cases
Reversibility	Usually	Irreversible	Usually

Dementias Treatment/Management:

1) ***Supportive measures:***
   a) Ensure patient safety
   b) Provide good meals & hygiene
   c) Encourage family's involvement
   d) Support
      ✓ ***Keep patient in familiar settings (if possible) to avoid accidents and possible agitation***

Dementia Friends
An Alzheimer's Society initiative

Dementias Treatment/Management:

2) ***Specific measures:***
   a) **Identify and correct any treatable or controllable condition**
      ✓ Hypothyroidism, Vitamin B12 deficiency, hypertension, diabetes

3) ***Symptomatic treatment:***
   a) **Agitation/aggression:** (small dose of antipsychotics (e.g. olanzapine 5mg, risperidone 2mg, or quetiapine 25mg)
   b) **Insomnia**
   c) **Depression**: (give a small dose of antidepressant (e.g. escitalopram 5 mg or sertraline 25mg)

   ✓ ***Be aware of possible side effects*** (***over-sedation, fall risk "head trauma/fractures", central anticholinergic activity that may cause delirium***)

Dementias Treatment/Management:

4) ***Cognitive-enhancing medications (mainly for Alzheimer's dementia):***

a) ***Cholinesterase inhibitors***:

- ✓ Donepezil (Aricept): *5 mg at night & can be increased gradually to 10 mg. It is well tolerated (S/E: diarrhea , weight loss ,bradycardia ,and syncope)*
- ✓ Rivastigmine (Exelon): *1.5 mg twice/day & can be increased gradually to maximum 6mg twice/day (S/E: anorexia , fatigue , somnolence, and dizziness)*
- ✓ Galantamine (Reminyl): *4mg twice/day & can be increased gradually to 12mg twice/day (S/E: similar to rivastigmine)*

Dementias Treatment/Management:

b) ***NMDA receptor antagonist:***

✓ Memantine (Epixa, Akatinol):

- an N-methyl-D-aspartate (NMDA) receptor antagonist , protects neurons from neurodegenerative process induced by glutamate excitotoxicity
- Memantine has been shown to have a modest effect in moderate to severe Alzheimer's disease and in dementia with Lewy body. In general, well tolerated
- Adverse drug reactions include confusion, dizziness, drowsiness, headache, insomnia, agitation, and/or hallucination. Less common adverse effects include vomiting, anxiety, hypertonia, cystitis, and increased libido

Course and prognosis:

- ✓ The course and prognosis depend on the cause
- ✓ Alzheimer's dementia:
  - ✓ Shows a ***progressive slow deterioration***.
  - ✓The patient may become incontinent of urine and/or stool
- ✓ Vascular dementia:
  - ✓ Shows ***stepwise deterioration***

Case number 3

- A 48-years-old male. Has a long-standing history of:
  - Hypertension
  - DM type 2
  - Hypercholesterolemia
- Presented with *significant cognitive and behavioural problems*
- He had difficulty with learning new information and making appropriate plans
- Personal/social history: smoke tobacco and consume alcohol on an almost daily basis for many years

Amnestic syndrome

- ✓ Definition:
  - ✓ **Impairment in short term memory** (retention of new information; temporal lobe function) due to a specific organic cause, in the ***absence of generalized intellectual impairment***
- ✓ Impairment in the ability to ***create new memories***
- ✓ It leads to social and occupational dysfunctioning
- ✓ The patient may show confabulation (filling memory gaps with incorrectly retrieved information)
- ✓ The insight is partially impaired
- ✓ In contrast to delirium, the ***immediate memory is usually intact***. (i.e. digit span test “frontal lobe function” is normal)
- ✓ In contrast to dementia, ***the remote memory is intact***

Etiology (major causes of amnestic disorders):

- ✓ ***Head injury lesions:***

  (Hippocampus, Posterior Hypothalamus and nearby midline structures)

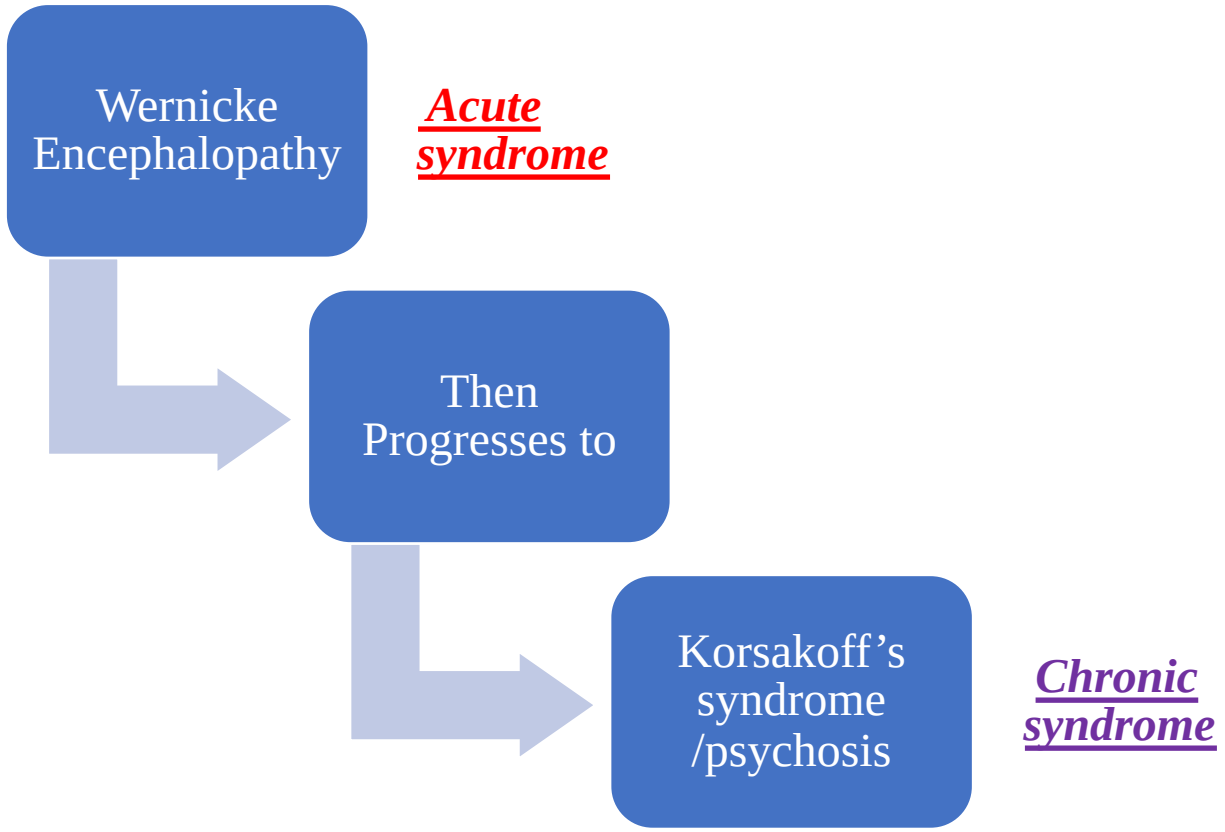
- ✓ ***Thiamine (B1) Deficiency***
  - ✓ Thiamine is essential for the enzyme transketolase, which essential for glucose metabolism
  - ✓ ***Associated with alcohol abuse***, ***poor nutrition*** (e.g., starvation), gastric carcinoma, persistent vomiting, hemodialysis

Major Causes of Amnestic Disorders

- **Systemic medical conditions**
  - Thiamine deficiency (Korsakoff's syndrome)
  - Hypoglycemia
  - Primary brain conditions
    - Seizures
    - Head trauma (closed and penetrating)
    - Cerebral tumors (especially thalamic and temporal lobe)
    - Cerebrovascular diseases (especially thalamic and temporal lobe)
    - Surgical procedures on the brain
    - Encephalitis due to herpes simplex
    - Hypoxia (including nonfatal hanging attempts and carbon monoxide poisoning)
    - Transient global amnesia
    - Electroconvulsive therapy
    - Multiple sclerosis
- **Substance-related causes**
  - Alcohol use disorders
  - Neurotoxins
  - *Benzodiazepines (and other sedative-hypnotics)
  - Many over-the-counter preparations

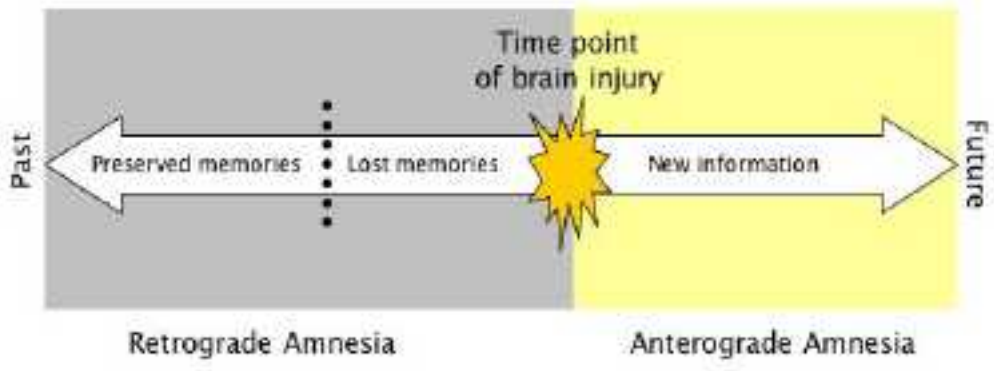
Wernicke-Korsakoff's syndrome

- ✓ Is an amnestic syndrome caused by thiamine deficiency
- ✓ Most commonly associated with poor nutritional habits of people with chronic alcohol use



- ✓ Wernicke encephalopathy
  - ✓ Acute syndrome
    - ✓ ***Impaired consciousness (confusion)***
    - ✓ ***Ophthalmoplegia***
    - ✓ ***Ataxia***
    - ✓ ***Memory impairment***

- ✓ Korsakoff's syndrome
  - ✓ Chronic syndrome
    - ✓ ***Peripheral neuropathy***
    - ✓ ***Irritability and personality changes***
    - ✓ ***Apathy***
    - ✓ ***Profound anterograde amnesia and inability to form a new memories.***
    - ✓ ***Confabulate or make up information when asked questions***



- ✓ Treatment:
  - ✓ Identify and reverse the cause if possible
  - ✓ Thiamine supply (if due to thiamine deficiency)
  - ✓ Supportive medical measures; fluids & nutrition

- ✓ Prognosis:
  - ✓ If it is due to thiamine deficiency and thiamine is provided promptly
    - ✓ ***Prognosis is good***
  - ✓ Otherwise, the course is usually chronic and may be progressive

Case number 4

- A 19-year-old male involved in a road traffic accident. He lost his consciousness for 5 days and remained 3 weeks in the hospital

- After discharge, his parents noticed that he become
  - **Impulsive**
  - **Disinhibited**
  - **Sometimes aggressive**
  - **More recently they noticed that he started to be more depressed and sometimes feeling so anxious**

Traumatic Brain Injury (TBI)

If the head hits a hard surface or if the person is severely shaken or jerked, the brain can strike the skull and become damaged.

Traumatic Brain Injury (TBI)

- ✓ **Definition:**
  - ✓ An ***insult to the brain from an external mechanical force***, possibly leading to ***permanent or temporary impairment*** of cognitive, physical, and psychosocial functions
  - ✓ Associated diminished or altered state of consciousness
- ✓ **Area of function affected:**
  1. Cognitive
  2. Sensory/perceptual
  3. Seizures
  4. Other physical changes
  5. Social-emotional

Traumatic Brain Injury (TBI)

- ✓ ***Acute consequences:***
  - ✓Impaired consciousness in varying duration (hours, days, weeks or months). ***long duration suggests poor prognosis***
  - ✓ Delirium (after severe head trauma)
  - ✓ Memory defects (on recovery of consciousness, defects of memory are usually present)
  - ✓ ***Anterograde (post-traumatic) amnesia***:
    - ✓Amnesia for events in the time between the trauma and the resumption of normal continuous memory
    - ✓ ***It is a good prognostic factor: probably full recovery when anterograde amnesia was less than 24 hours***
  - ✓ ***Retrograde amnesia:***
    - ✓ Amnesia for events in the time between the trauma and the last clearly recalled memory before the injury. ***It is not a good predictor of outcome***

Traumatic Brain Injury (TBI)

- ***Chronic Consequences:***
  - ***Lasting cognitive impairment:***
    - When the injury has caused a prolonged post traumatic amnesia (of more than 24 hours)
    - Parietal and temporal damage, especially on the left side
    - Recovery of function may be very slow and may continue over the years
  - ***Emotional disturbances:***
    - Depressive, anxiety and phobic features are common
    - Somatic complaints such as headache, fatigue and, dizziness
  - ***Personality changes:***
    - Irritability
    - Reduced control of aggressive impulses
    - Sexual disinhibition and some coarsening of behaviour (***particularly after frontal lobe injury***)
  - ***Psychotic features:***
    - Psychotic features related to depression (non-dominant frontal damage)
    - Paranoid psychosis (temporal lobe damage)

Traumatic Brain Injury (TBI)

- ✓ ***Social consequences:***
  - ✓ Many patients and their relatives experience severe distress of head injury, and have to make substantial changes in their way of life
- ✓ ***Medico-legal aspects:***
  - ✓ The compensation issue is more likely to contribute to disability if the patient feels someone else is at fault, financial compensation is possible, low social status and in industrial injury

Factors affecting the outcome of head trauma:

1) Duration of loss of consciousness
2) Duration of anterograde (Post-traumatic) amnesia
3) Amount and location of brain damage
4) Premorbid personality and past psychiatric history
5) Development of seizures
6) Medico-legal factors e.g. compensation

Treatment:

- ✓ A plan for ***long-term treatment*** should be made as early as possible after head trauma
- ✓ The treatment of the ***cognitive and behavioral disorders is similar to the treatment approaches used in other patients***
  - ✓ Head trauma patients may be particularly ***susceptible to the side effects associated with psychotropics/antipsychotics medications***
  - ✓ Drugs should be ***initiated in lower dosages*** than usual
  - ✓ Should be titrated ***upward more slowly*** than usual

Treatment:

- ✓ Aggression and impulsivity can be treated with antipsychotics or anticonvulsants
- ✓ Treatment should include physical and psychological rehabilitation
- ✓ Continuing psychosocial help should be provided to patients and caregiver by a special team

Capacity Vs. Competency (Reference)

- ✓ **Clinical** Vs. **Legal** term that denotes the ability to make rational and reasonably well informed decisions by a particular patient (vs. person) in their treatment and/ or life decision/s

- ✓ **Capacity:**
  - ✓ Is a ***clinical*** determination that addresses the integrity of ***mental functions***

- ✓ **Competency:**
  - ✓ Is a ***legal*** determination that addresses societal interest in restricting a person's right to make decisions or do acts because of incapacity

Valid Informed Consent (Reference)

- ✓ Permission voluntary given by a competent person without any elements of force, deceit, coercion after explanation and disclosure of:
  - ✓Purpose and details of procedure or treatment
  - ✓Risks, Benefits and available alternative treatment/s
  - ✓The right to withdrawal consent verbally or in written forms at anytime

Exceptions (Reference)

✓ Life threatening situation

✓ Patient who waive their rights to disclose and consent (do not want to be informed)

Rules of capacity (Reference)

- ✓ Being mentally ill doesn’t in itself imply a loss of capacity or competency

- ✓ Having Capacity or being Competent should be presumed until proven otherwise

Table 1. Legally Relevant Criteria for Decision-Making Capacity and Approaches to Assessment of the Patient.

Criterion	Patient's Task	Physician's Assessment Approach	Questions for Clinical Assessment*	Comments
Communicate a choice	Clearly indicate preferred treatment option	Ask patient to indicate a treatment choice	Have you decided whether to follow your doctor's [or my] recommendation for treatment? Can you tell me what that decision is? [If no decision] What is making it hard for you to decide?	Frequent reversals of choice because of psychiatric or neurologic conditions may indicate lack of capacity
Understand the relevant information	Grasp the fundamental meaning of information communicated by physician	Encourage patient to paraphrase disclosed information regarding medical condition and treatment	Please tell me in your own words what your doctor [or I] told you about: The problem with your health now The recommended treatment The possible benefits and risks (or discomforts) of the treatment Any alternative treatments and their risks and benefits The risks and benefits of no treatment	Information to be understood includes nature of patient's condition, nature and purpose of proposed treatment, possible benefits and risks of that treatment, and alternative approaches (including no treatment) and their benefits and risks
Appreciate the situation and its consequences	Acknowledge medical condition and likely consequences of treatment options	Ask patient to describe views of medical condition, proposed treatment, and likely outcomes	What do you believe is wrong with your health now? Do you believe that you need some kind of treatment? What is treatment likely to do for you? What makes you believe it will have that effect? What do you believe will happen if you are not treated? Why do you think your doctor has [or I have] recommended this treatment?	Courts have recognized that patients who do not acknowledge their illnesses (often referred to as "lack of insight") cannot make valid decisions about treatment Delusions or pathologic levels of distortion or denial are the most common causes of impairment
Reason about treatment options	Engage in a rational process of manipulating the relevant information	Ask patient to compare treatment options and consequences and to offer reasons for selection of option	How did you decide to accept or reject the recommended treatment? What makes [chosen option] better than [alternative option]?	This criterion focuses on the process by which a decision is reached, not the outcome of the patient's choice, since patients have the right to make "unreasonable" choices

* Questions are adapted from Grisso and Appelbaum.[31] Patients' responses to these questions need not be verbal.


thank
you