In the name of God

Cognition & Major Neurocognitive Disorders

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cognition

- The term cognition comes from the latin verb *cognosco* (“to know”)

- The word *cognition* dates back to the 15th century, when it meant "*thinking and awareness*.

- Attention to cognitive processes came about more than eighteen centuries earlier,however, beginning with Aristotle (384–322 BC) and his interest in the inner workings of the mind and how they affect the human experience

- Aristotle (384–322 BC) his interest in the inner workings of the mind and affect the human experience. Aristotle focused on cognitive areas pertaining to memory, perception, and mental imagery

- Hermann Ebbinghaus

- Wilhelm Wundt
- (1832–1920)

- William James
- (1842–1910)

- Jean Piaget :
- (1896 – 1980)

- Swiss psychologist

- Piaget's theory of cognitive development

- Jean Piaget was one of the most important and influential people in the field of Developmental Psychology. He believed that humans are unique in comparison to animals because we have the capacity to do "abstract symbolic reasoning

Piaget's Stages of Cognitive Development

Sensorimotor Stage

Birth to 2 yrs

Preoperational Stage

2 to 7 yrs

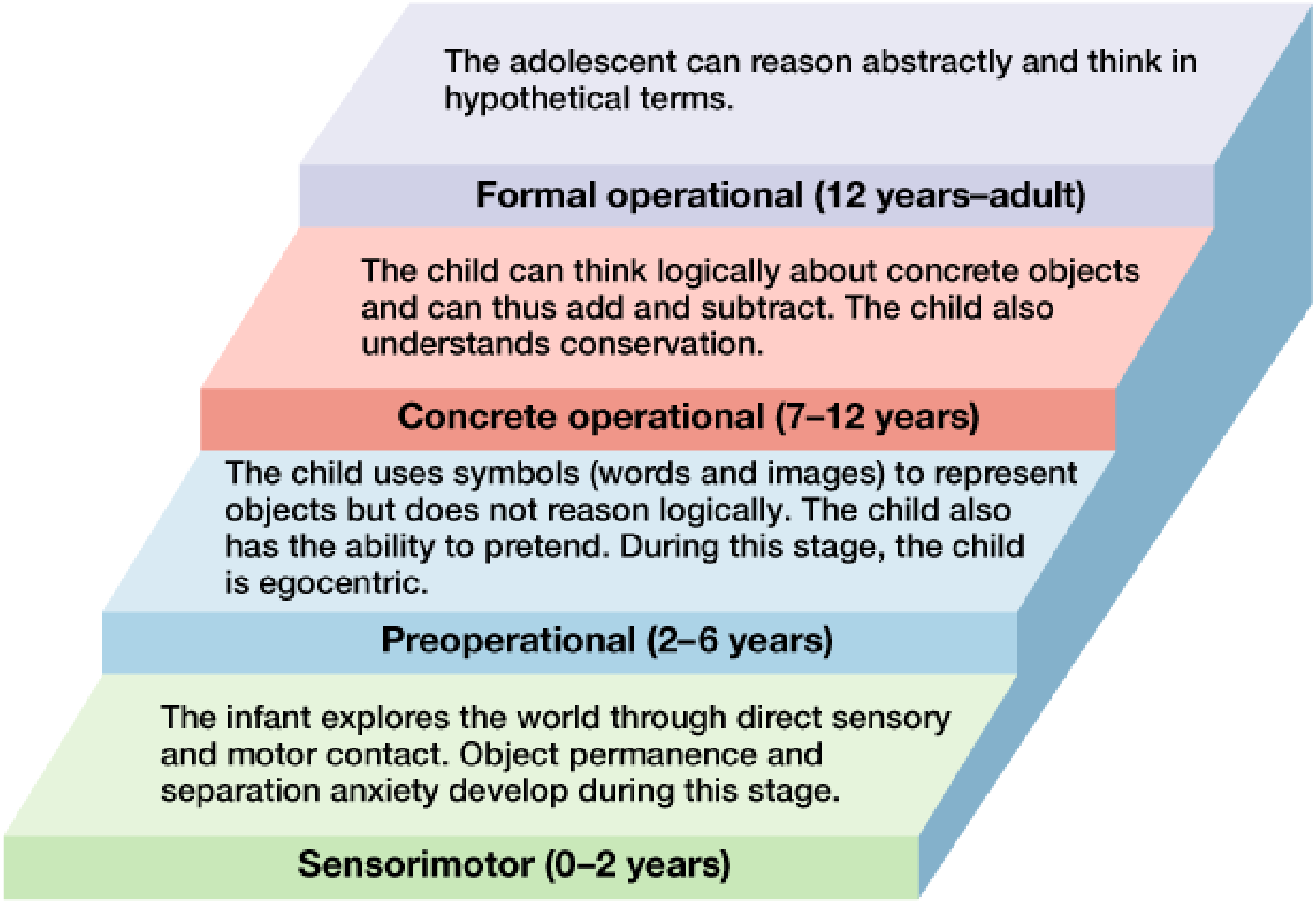
Concrete Operational Stage

7 to 11 yrs

Formal Operational Stage

12 and up

verywell


The adolescent can reason abstractly and think in hypothetical terms.
Formal operational (12 years–adult)
The child can think logically about concrete objects and can thus add and subtract. The child also understands conservation.
Concrete operational (7–12 years)
The child uses symbols (words and images) to represent objects but does not reason logically. The child also has the ability to pretend. During this stage, the child is egocentric.
Preoperational (2–6 years)
The infant explores the world through direct sensory and motor contact. Object permanence and separation anxiety develop during this stage.
Sensorimotor (0–2 years)

- What is the cognition?

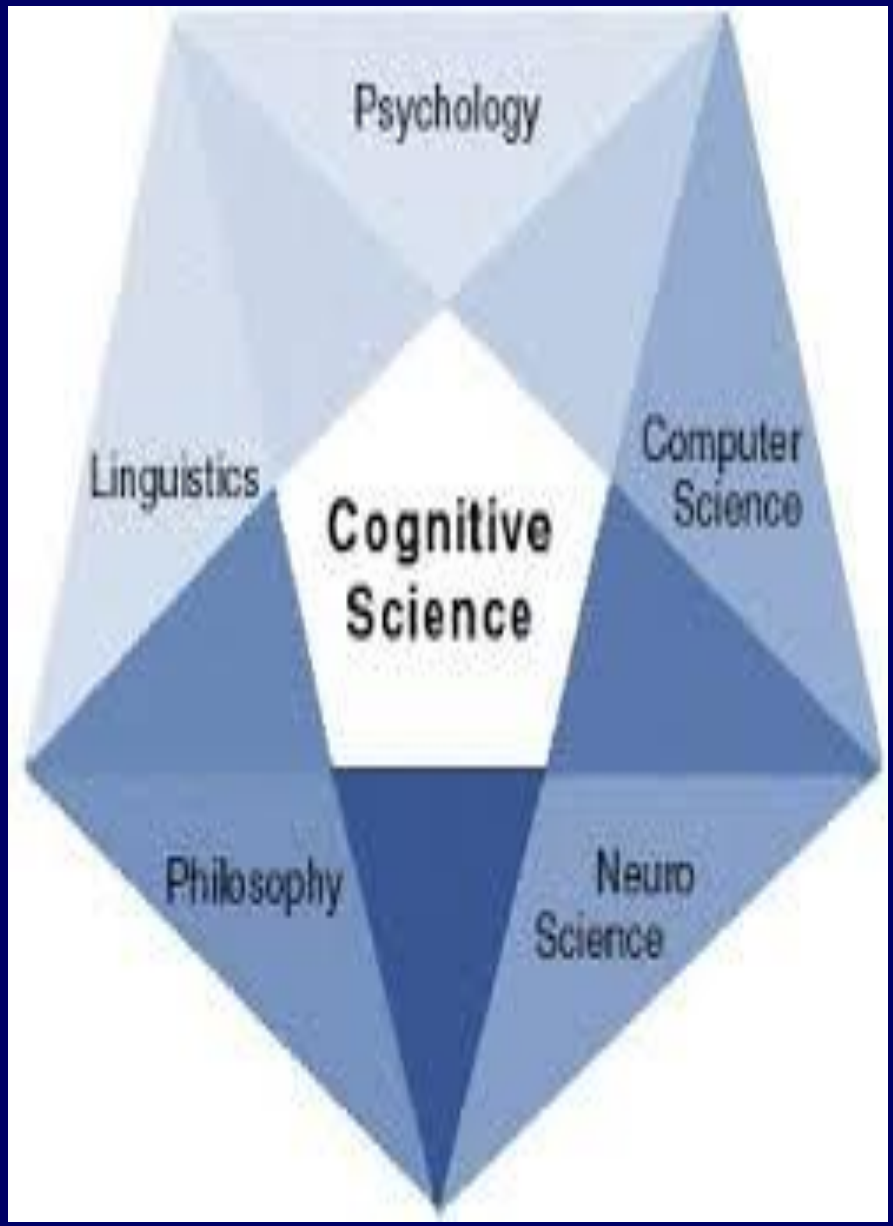
- the mental action or process of acquiring knowledge and understanding through thought, experience, and the senses.

- The cognition is used in several loosely-related ways to refer to a facility for the human like processing of information ;appling knowledge and changing preferences.

Cognitive science

- Study of the relationships among and integration of cognitve psychology, biology, neuroscience, anthropology, computer science, linguistics and philosophy.

Cognitive science: is the interdisciplinary, scientific study of the mind and its processes.

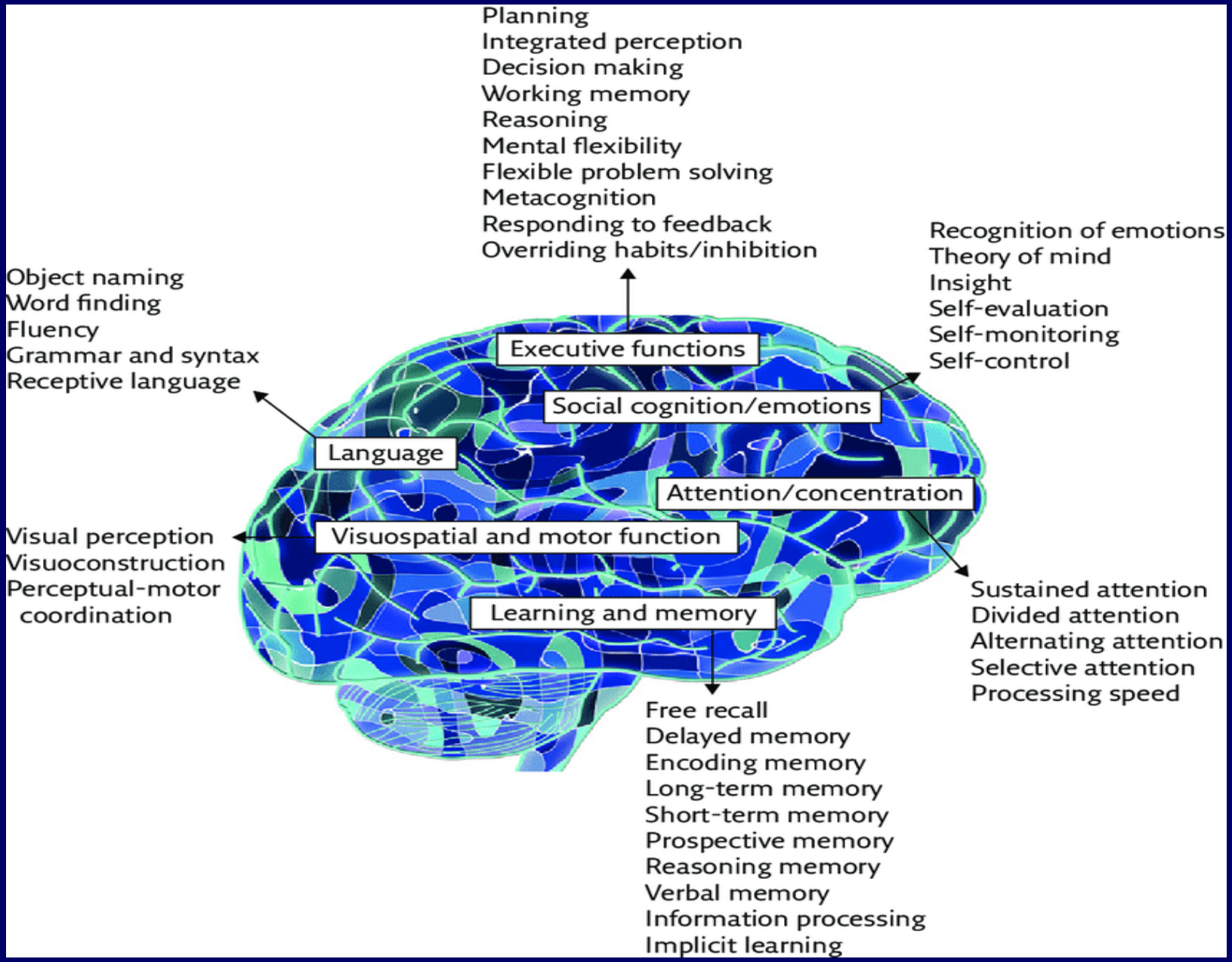


Cognitive psychology

- The scientific study of mental processes:
- intellectual functions such as
- attention, memory , working memory, judgment , evaluation, reasoning , , problem solving , decision making, comprehension ,Concept formation
- language.

Cognitive domains

- Intelligence
- Perception
- Attention
- Consciousness
- Thinking
- Memory
- Decision making
- Language
- Judgment
- Learning
- Problem solving
- planning


Planning
Integrated perception
Decision making
Working memory
Reasoning
Mental flexibility
Flexible problem solving
Metacognition
Responding to feedback
Overriding habits/inhibition
Executive functions
Recognition of emotions
Theory of mind
Insight
Self-evaluation
Self-monitoring
Self-control
Social cognition/emotions
Object naming
Word finding
Fluency
Grammar and syntax
Receptive language
Language
Attention/concentration
Visual perception
Visuoconstruction
Perceptual-motor coordination
Visuospatial and motor function
Sustained attention
Divided attention
Alternating attention
Selective attention
Processing speed
Learning and memory
Free recall
Delayed memory
Encoding memory
Long-term memory
Short-term memory
Prospective memory
Reasoning memory
Verbal memory
Information processing
Implicit learning

- Functions

- The frontal lobe is considered
- the *emotional control center*
- and the home of *our personality.*

- The frontal lobe *controls*
- *higher level thinking:*

- **Broca's area**
- Initiation
- Reasoning
- Planning
- Language
- Long term memory
- Impulse control
- Problem solving
- Judgment /abstract
- Motor function
- Social/sexual behavior
- Interpreting social cues
- Sequencing
- Mediating conflicting thoughts

- Executive function
- Attention
- consentration
- Memory(episodic m.)
- Working memory
- Motivation
- Decision making
- Mental flexibility
- Resilience
- Theory of mind
- Emotional processing
- (OFC)
- Task swithing

- Initiation : synonyms…beginning, starting
- problem solving :process of finding solutions to difficult or complex issues.
- Interpreting social cues:
- facial expression
- vocal tone
- body language
- body posture
- gestures

- **Task switching**: or
- *set-shifting*, is an executive function that involves the *ability to unconsciously shift attention between one **task** and another*. In contrast, cognitive shifting is a very similar executive function, but it involves conscious (not unconscious) change in attention.

- Decision making:is regarded as the cognitive process resulting in the selection of a belief or a course of action among several alternative possibilities. Every decision-making process produces a final choice, which may or may not prompt action

- Working memory:
- is a cognitive system with a *limited capacity* that is responsible for *temporarily holding information available* for processing.[1] Working memory is important for reasoning and the guidance of decision-making and behavior.[2][3] Working memory is often used *synonymously with short-term memory*

The executive functions all serve a "*command* and *control" function*; they can be viewed as the "*conductor*" of all cognitive skills. Executive functions help you *manage life tasks* of all types.

Major neurocognitive disorder (Dementia)

- Dementia also referred to as major neurocognitive disorder in the 5th eddition DSM , is marked by sever impairment in memory , Judgment , Orientation & Cognition .

Definition

- Progressive cognitive impairment in clear consciousness. Allertnes is intact.
- Impairment in intellectual function affecting more than one cognitive domains.
- Involved multiple domains.
- Interferes with social or occupational function
- Decline from a previous level
- Not explained by delirium or major psychiatric disease.
- 15%-----reversible illnesses

Definition of dementia

DSM-5 diagnostic criteria

Dementia = Major neurocognitive disorder

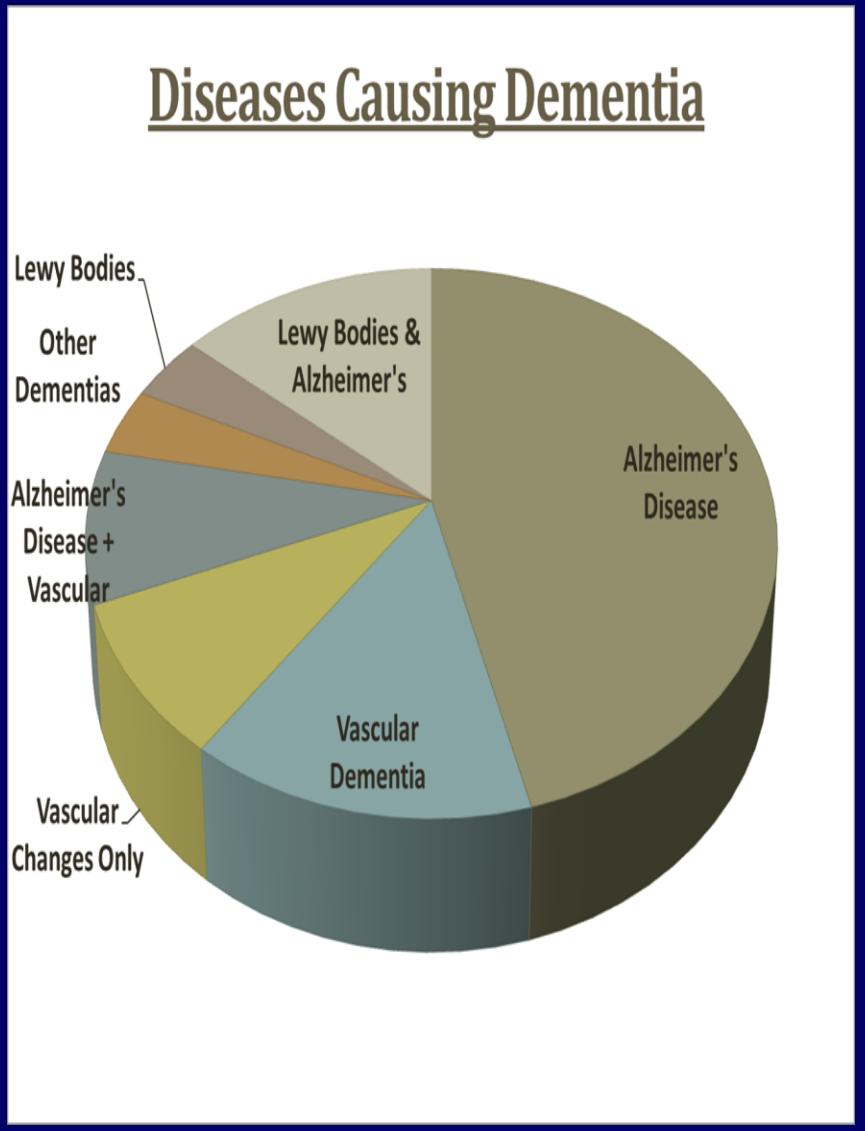
- Evidence of significant cognitive decline from a previous level of performance in **one or more cognitive domains**

&

- A **substantial impairment by standardized neuropsychological testing** (or if not available other quantified clinical assessment)

- The cognitive **deficits interfere with independence in everyday activities** (i.e., at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications)
- The cognitive deficits **do not occur exclusively in** the context of a **delirium**
- The cognitive deficits **not better explained by another mental disorder** (e.g., major depressive disorder, schizophrenia)

- AD : 50-60%
- VD : 15-30%
- AD & VD : 10-15%
- Other : 1-5%
  - DLB
  - FTD
  - TBI
  - HIV
  - Prion Disease
  - Parkinson Dis.
  - Huntington Dis.

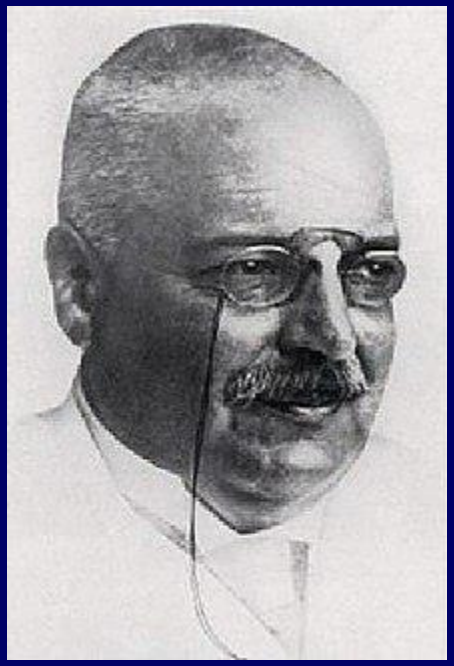


Differential diagnosis in dementia: Commone treatable causes

- Structural brain lesion (subdural bleed)
- Thyroid disease
- B12 deficiency
- Untreated sleep apnea
- Depression or anxiety
- Alcoholism
- NPH
- Meds: Benzos, opioids, anticholinergics (diphenhydramine, bladder drugs, tricyclics), neuroleptics, dopaminergics, other sedatives
- Substance induced , caused by toxin or medication .

Aloysius Alzheimer

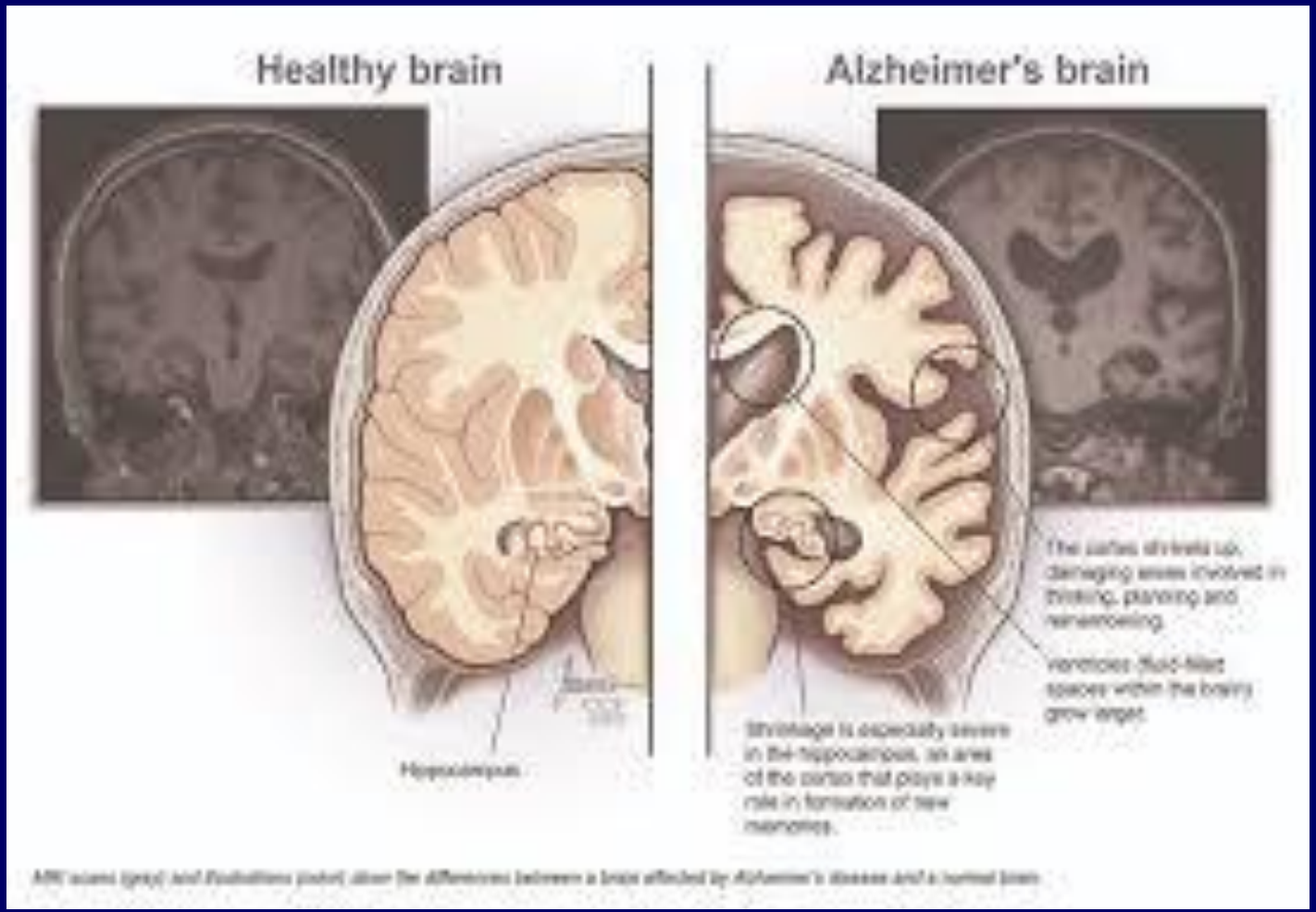
14 June 1864



Aloysius Alzheimer was a German psychiatrist and neuropathologist and a colleague of Emil Kraepelin.

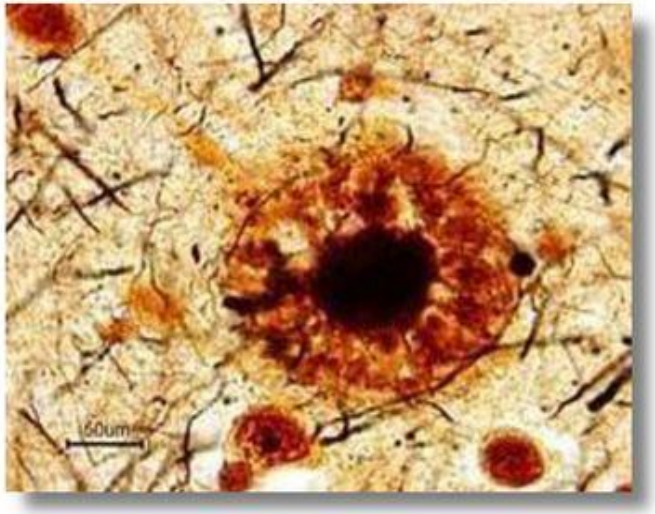
Alzheimer is credited with identifying the first published case of "presenile dementia", which Kraepelin would later identify as Alzheimer's disease

- Macroscopic finding:
- Diffuse atrophy with flatened cortical sulci &enlarged cerebral ventricles.
- Microscopic finding:
- Senile plaque(more strongly indicate AD)
- Neurofiblirary tangles(not unique to AD)
- Neuronal loss(cortex & hippocampus)
- Synaptic loss (as much as 50% in the cortex)
- Granulovascular degeneration of the neurons.


Healthy brain
Alzheimer's brain
Hippocampus
Shrinkage is especially severe in the hippocampus, an area of the cortex that plays a key role in formation of new memories.

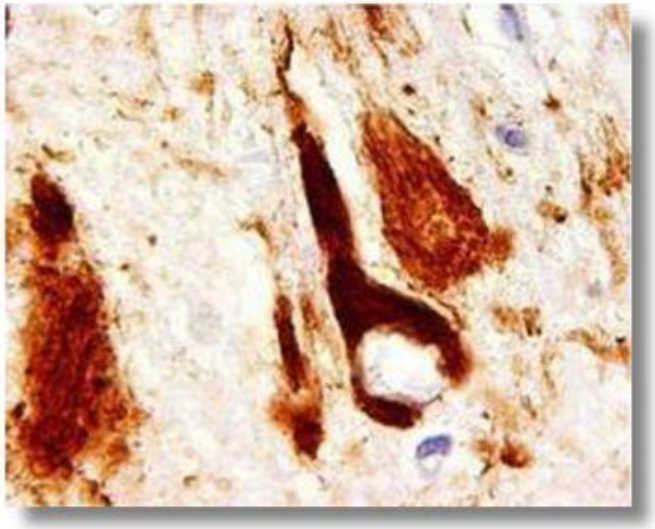
Neuropathology

Neuritic Plaques



Extracellular deposits of beta-amyloid

Neurofibrillary Tangles



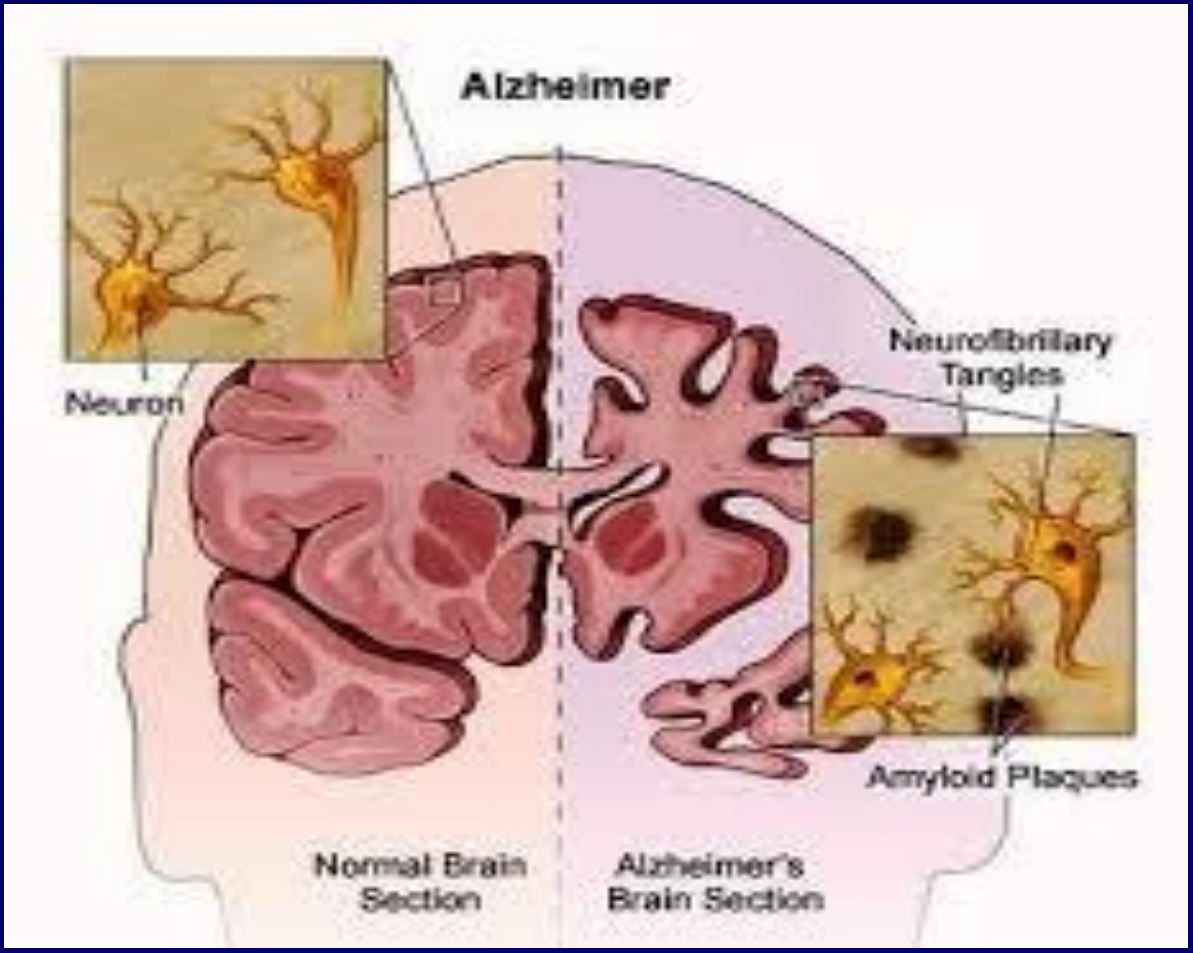
Intracellular deposits of hyperphosphorylated tau

Neurotransmiters:

ACH,NEP…….hypoactive

Degeneration of cholinergic neurons in the nucleus basalis of meynert in AD

Neuroactive peptides somatostatin & corticotropin decresed consentration.


Alzheimer
Neuron
Neurofibrillary Tangles
Amyloid Plaques
Normal Brain Section
Alzheimer's Brain Section

- Abnormality in the regulation of membrane phospholipid metabolism results in membranes that are less fluid &rigid.
- AL toxicity
- Excessive stimulation by the transmitter glutamate.

AD Risk Factors

- Age!!
- Mild cognitive impairment (MCI)
- ApoE-e4 positivity (3-8 times)
- Family hx in first degree relative (especially if younger onset)
- Vascular risk (diabetes, heart disease, etc.)
- Low education and physical/social activity
- Female sex

AD: Behavioral & Psych

- Depression, anxiety
- Irritability, hostility, apathy
- Delusions, hallucinations
- Sleep-wake changes
- Sundowning
- Agitation

Clinical presentation

- Gradual onset, slowly progressive
- Pronounced memory impairment

- Visuospatial impairment
- Executive Dysfunction
- Language impairment
- Apraxia
- Neuropsychiatric symptoms

- Most common form of dementia after age 65

Dementia with Lewy Bodies (DLB)

- Relatively earlier *occipital and basal ganglia* degeneration
- *Similar to Parkinson* disease dementia
- *α-synuclein* aggregates into Lewy bodies
- Concurrent AD pathology is common.
- People who have Lewy bodies in their brains often have the *plaques and tangles* associated with Alzheimer's disease.

DLB Clinical Features

Core features

- Parkinsonism
- Recurrent early visual hallucinations
- Fluctuations (clue: recurrent delirium evaluations)

- Suggestive features include REM sleep disorder (dream enactment) & neuroleptic sensitivity

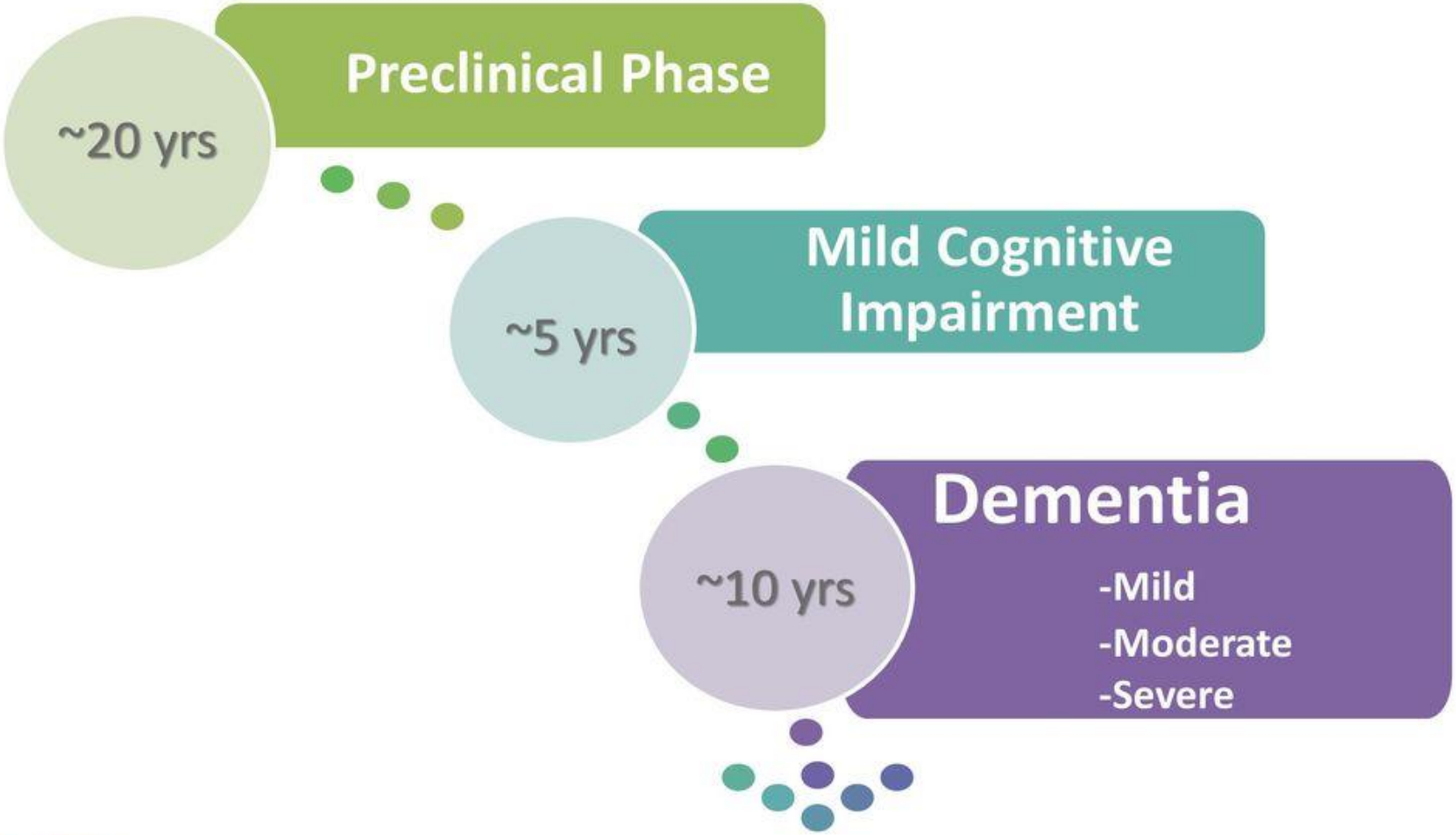
Frontotemporal Dementia (FTD)

- Average age of onset 58, rather than very old
- Often familial (30-50%)
- Behavior and personality change (may be initially misdiagnosed as a psychiatric disorder)
- Executive dysfunction
- Progressive non-fluent aphasia
- May see parkinsonism or muscle weakness

Vascular Dementia

- Suspect when
  - Abrupt onset and/or stepwise decline
  - Fluctuating course
  - H/o stroke
  - Focal neurologic symptoms or signs
- Usually see bilateral infarcts
- Often associated with executive dysfunction, gait disorder, apathy, incontinence

Spectrum of cognitive impairment



Mild Cognitive Impairment

- Cognitive decline *abnormal for age* and education but *does not interfere* with function and activities
- “At risk” state to develop a degenerative dementia
- When memory loss predominates, termed Amnestic MCI. This has ~*15% per year* of conversion to AD.

Mild cognitive impairment (MCI)

- Complaint (by patient or other informant)
- Testing indicates deficits in one or more areas of cognition 1.5 SD below age-adjusted norms
- ***Not impacting occupational or social functioning***
- MCI may represent "early dementia" and may progress with time
- Some patients with MCI remain MCI indefinitely or return to normal

- *Ask a close informant*
- Duration, rate, smoothness?
- Associated symptoms (headache, trouble with vision, speech, strength, coordination, gait)

- *What domains are affected?*

Repeats self? Forgets recent things? Appointments? Month & year?
Trouble with appliances? Trouble planning?
Change in personality, judgment, behavior?
Navigation problems? Hallucinations?
Word finding problems?

- *How is function affected?*

Finances, chores, hobbies, driving, occupation, social

- Medical problems and risk factors?
- Neurologic history (stroke, trauma, infection)?
- Educational background?
- Family history?
- Alcohol and drugs?
- Medications?

Remember, your first goal is to exclude readily treatable causes…

Diagnostic testing

- There is no “dementia test panel”
- For slowly progressive “typical” dementia in adults >65, most essential tests: **B_{12}, TSH, brain image (CT is ok)**
- Neuropsychology testing can help but not mandatory

- FDG- PET approved to differentiate AD from FTD
- Amyloid-PET has just been approved
- PET studies have little value in most cases and are expensive

- For younger patients, or rapid or atypical course, workup may be “tiered” to target range of diagnoses, emphasizing treatable causes

Examination

- General neurologic exam

Any focalities that suggest stroke?

Signs of parkinsonism or a gait disorder?

- *Cognitive screen*

Mini-mental (MMSE)

Montreal Cognitive Assessment (MoCA)

Drug treatment

- No current treatment slows down neuronal loss in the brain.

Cholinesterase inhibitors :

Donepezil(aricept) : daily, 5 & 10 mg ,tab

, rivastigmine(exelon) : BD , 1.5 , 3 , 4.5 , 6 mg , cap

, galantamine(reminyl) : BD , 4 , 8 , 16 mg , tab

Modest symptom improvement in AD

Sometimes marked improvements in PDD/ DLB

- Memantine(ebixa):NMDA inhibitore , 5 , 10 mg ,tab ,

Risk and Protective Factors

Etiologic Hypothesis	Risk and Protective Factors	Epidemiologic Evidence
Genetic Susceptibility	Deterministic (APP, PS1, PS2), Susceptibility (APOE) Family History	Strong
Psychosocial	High education, mentally stimulating activities, enriched social network, physical activity	Moderate
Vascular	Hypertension, obesity, diabetes, cerebrovascular disease, smoking Alcohol intake, antihypertensive therapy	Moderate
Nutritional and Dietary	Deficiency in folate, vitamin B12, antioxidants Omega-3-fatty acids, fruit, and vegetable intake	Limited or Mixed
Others	Head injury, occupational exposures Hormone therapy, anti-inflammatory drugs	Limited or Mixed

C Qiu et al. *Dialogues in Clin Neurosci*. 2009


Thank You!