Cognitive Disorders: Dementia and Major Neurocognitive Disorder

Biomedical Engineering - URJC

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Introduction

Overview

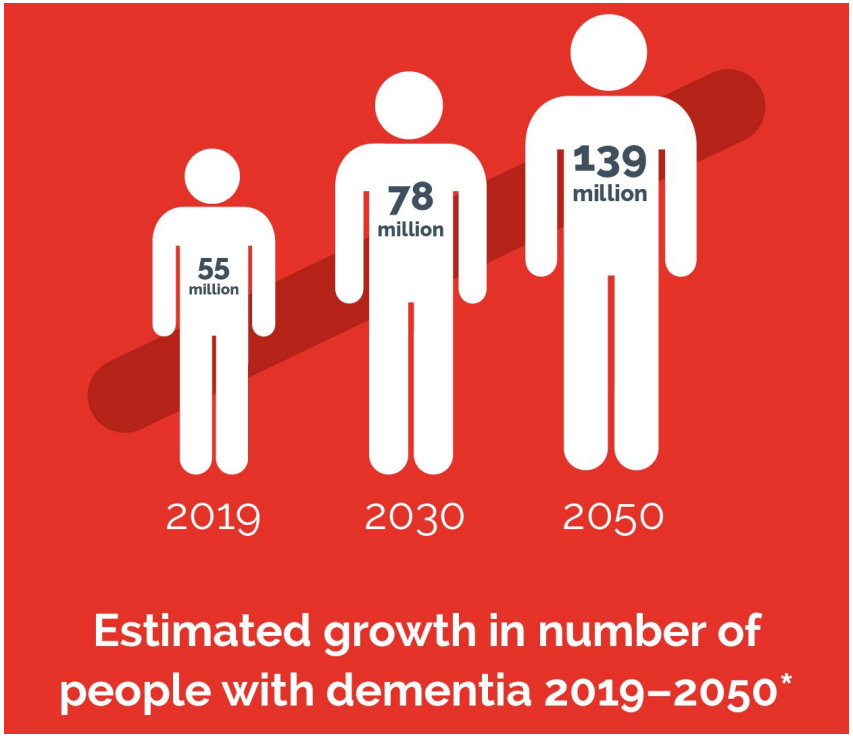
- **Dementia** is also called Major Neurocognitive Disorder (MND).
- MND involves a significant **decline in cognition**, affecting daily function.
- No cure exists; it's often **progressive**, impacting instrumental activities of daily living.
- Individuals often do not have insight into their deficits.

Introduction

Major neurocognitive disorder: characteristics

- A significant decline in: executive function, complex attention, language, learning, memory, perceptual-motor, or social cognition.
- The decline represents a change from a patient's prior level of cognitive ability.
- The decline is **persistent** and progressive over time (it is not *delirium*).
- There is a decline in the patient's ability to function and **perform everyday tasks**: Interference with independence in everyday activities.

Epidemiology



1. Increasing prevalence, particularly in aging populations.
2. Alzheimer's: 5th leading cause of death in the elderly.
3. Global impact and rising healthcare costs.

Etiology

Etiological sybtypes

It often takes time to distinguish the etiology. Many factor can help: imaging studies, lab studies, genetic markers, patient comorbidities, medical and family history, and clinical findings.

- Alzheimer disease
- Vascular disease
- Frontotemporal lobar degeneration
- Lewy body disease
- Parkinson disease
- HIV infection
- Huntington disease
- Prion disease
- Substance and or medication use
- Traumatic brain injury

Main subtypes of dementia

Alzheimer's disease

- Most common cause of dementia (70-80 % of all cases).
- It can occur sporadically or be familial.
- Progressive neurodegenerative disease caused by **neuronal cell death**.
- Risk factors: genetic component, **age**.
- The incidence of Alzheimer's disease doubles every 5 years, after the age of 65. Prevalence rates increase from 10 % after the age of 65 to 40 % after the age of 85.

Main subtypes of dementia

Vascular dementia

- Responsible of 15 % all cases.
- Its incidence increases with **age**.
- Risk factors for vascular dementia include hypercholesteremia, diabetes mellitus, hypertension, and smoking.
- Multiple and persistent micro-vascular injuries to the brain tissue over the years

Other subtypes

- Lewy body dementia: 5 % of dementia cases.
- Other: Parkinson disease dementia, Frontotemporal dementia, Creutzfeldt-Jakob disease.

Pathophysiology

- Diverse causes depdending on the subtype: degenerative, vascular, genetic, toxic.
- The most common cause: accumulation of native proteins in the brain
- For instance, in Alzheimer's there are cortex atrophy, amyloid plaques, neurofibrillary tangles.
- Vascular dementia: **ischemic brain injury**.

Pathophysiology

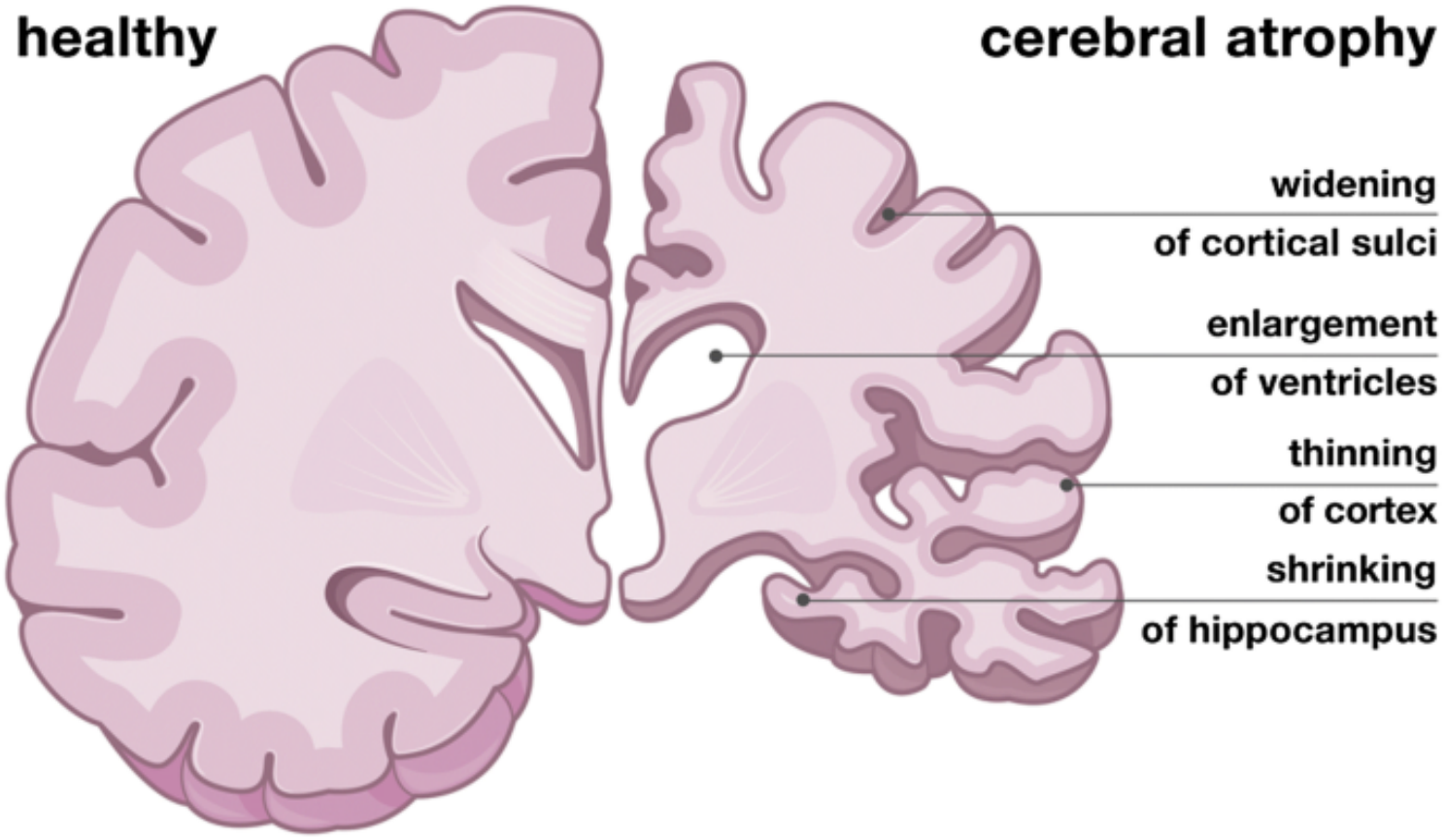
Alzheimer's disease

1. Atrophy of the cortex and deposition of **amyloid plaques**
2. **Neurofibrillary tangles** of hyperphosphorylated tau protein in neurons

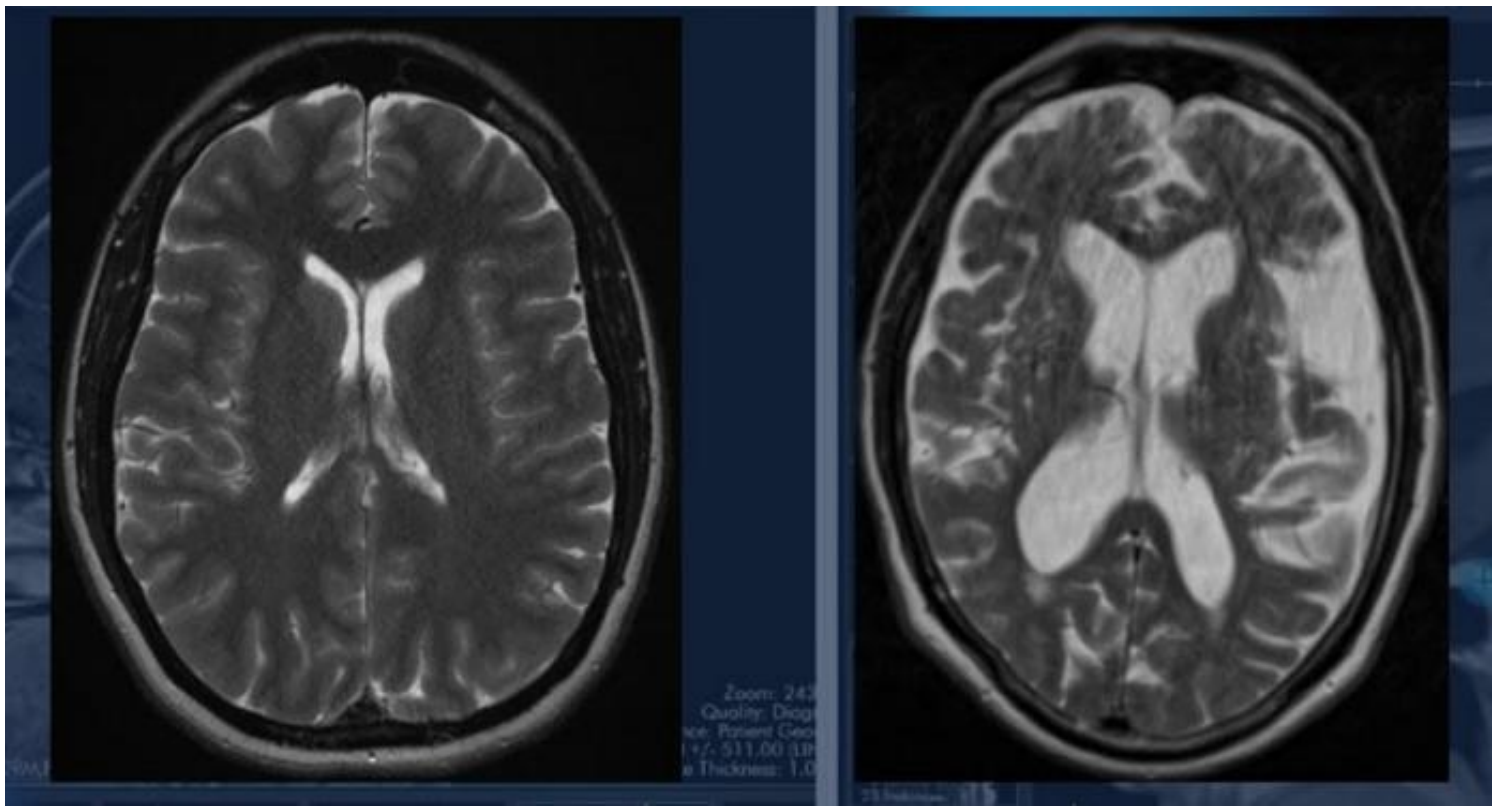
Lewy body dementia and Parkinson disease dementia

1. Intracellular accumulation of Lewy bodies
2. **Lewy bodies**: insoluble aggregates of alpha-synuclein protein in the brain.

Brain atrophy



Brain atrophy



Pathophysiology

Frontotemporal dementia

1. Deposition of hyperphosphorylated tau proteins in the frontal and temporal lobes.
2. Changes in early personality, behavioral changes, and aphasia.

Prion-related dementias

1. Creutzfeldt-Jakob disease, kuru, and so on.
2. Misfolded **prions**, which are proteinaceous particles that are infectious in nature and self-spreading.

Pathophysiology

HIV infection

1. Activation of macrophages and toxic inflammation leading to neurodegeneration in the brain.

Alcohol consumption

1. Multiple **cytotoxic** processes within the brain

Vascular dementia

1. **Ischemic injury** to the brain, leading to permanent neuronal death.
2. Stroke or multiple transient ischemic attacks
3. **Slow onset**

Clinical Presentation

- Patients with dementia do not present with a self-complaint of memory loss
- It is often a **relative** who brings the problem to the clinician's attention
- Informant-reported memory loss is a much better predictor of the disease
- Most important: cognitive impairment represents a change from baseline (the patient has stopped driving
- managing finances)

Clinical Presentation

Changes from baseline

- **Memory difficulty** is the most common chief complaint
- Retaining new information (eg, trouble remembering events)
- Handling complex tasks (eg, balancing a checkbook)
- Reasoning (eg, unable to cope with unexpected events)
- Spatial ability and orientation (eg, getting lost in familiar places)
- Language (eg, word finding)
- Behavior

Clinical Presentation: differential diagnosis

Cognitive impairment related to dementia must be distinguished from acute cerebrovascular disease (stroke or TIA), delirium and depression:

It is mandatory to differentiate some diagnoses that can mimic dementia:

1. Acute cerebrovascular disease
2. (Acute) delirium
3. Depression

Clinical Presentation: differential diagnosis

Dementia

1. Gradual onset of short-term memory loss (ie, loss of memory for recent events) and functional impairment in more than one domain:
2. Executive function (finances, shopping, cooking, laundry, transportation)
3. Basic activities of daily living (feeding, dressing, bathing, toileting, transfers)

Clinical Presentation: differential diagnosis

Cerebrovascular disease

1. **Sudden** deterioration in cognition
2. Episodes of confusion, aphasia, slurred speech, focal weakness

Clinical Presentation: differential diagnosis

Delirium

1. Acute cognitive impairment with clouded sensorium, difficulty with attention, and hypersomnolence.
2. Associated with prominent deficits in attention.
3. Patients have fluctuations in their level of consciousness and have difficulty maintaining concentration.

Clinical Presentation: differential diagnosis

Depression

1. Memory loss referred by patients themshelves, not relatives
2. Psychomotor slowing and poor effort on testing (*I just can't do this*)
3. **NOTE**: depression and dementia can occur in the same patient

Clinical Presentation

Medical history

- History must be obtained from the patient and their close friends, family members, or caregivers.
- Past medical, family, medication, and substance use history

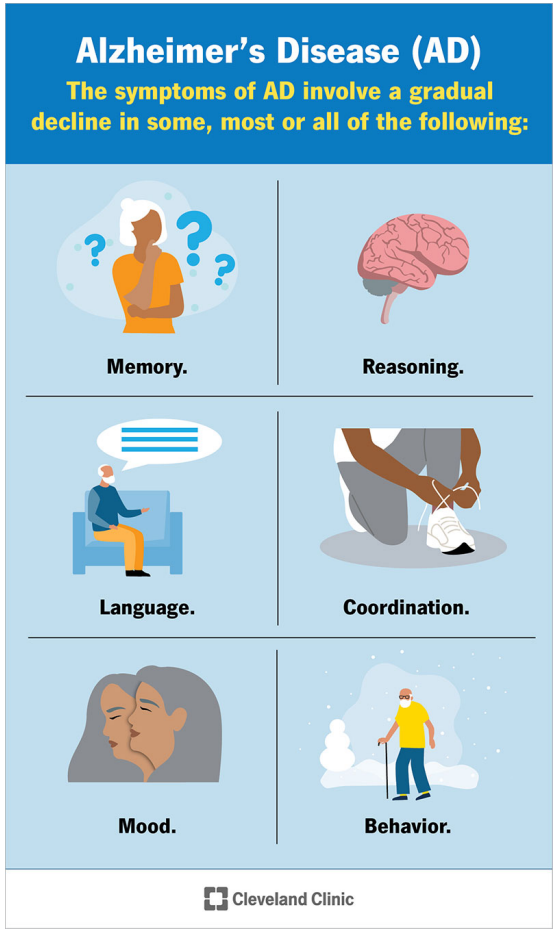
- Changes in behavior
- getting lost in familiar neighborhoods
- memory loss
- mood changes (aggressions)
- social withdrawal
- cognitive difficulty
- difficulty performing tasks
- difficulty in communication
- loss of independence

Clinical Presentation

Clinical Presentation

Evaluate their functional abilities or any changes in their ability:

- Ability to perform daily tasks
- Is the patient still driving?
- Have there been any episodes of wandering or getting lost?
- Can they handle money or go on shopping safely?



Clinical Presentation

Parkinson and Lewy body dementia

- Visual hallucinations
- Parkinsonian symptoms (bradykinesia, resting tremor, and muscle rigidity)

Ffrontotemporal dementia

- Behavior changes, including disinhibition and apathy

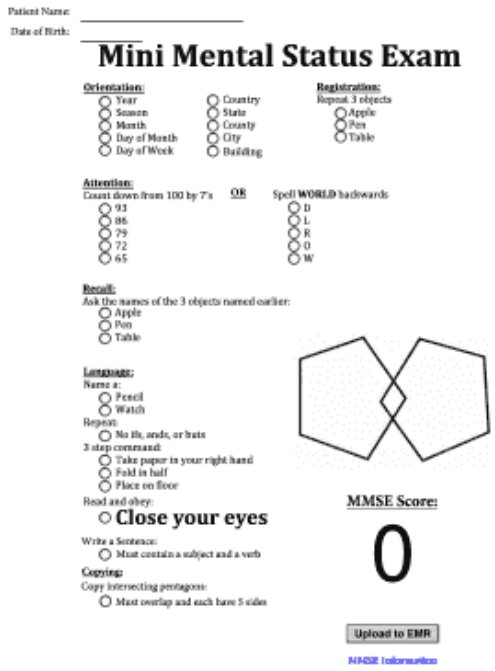
Creutzfeld-Jakob disease

- Myoclonus, ataxia, and memory and behavior changes

Clinical Presentation

Evaluate their functional abilities or any changes in their ability:

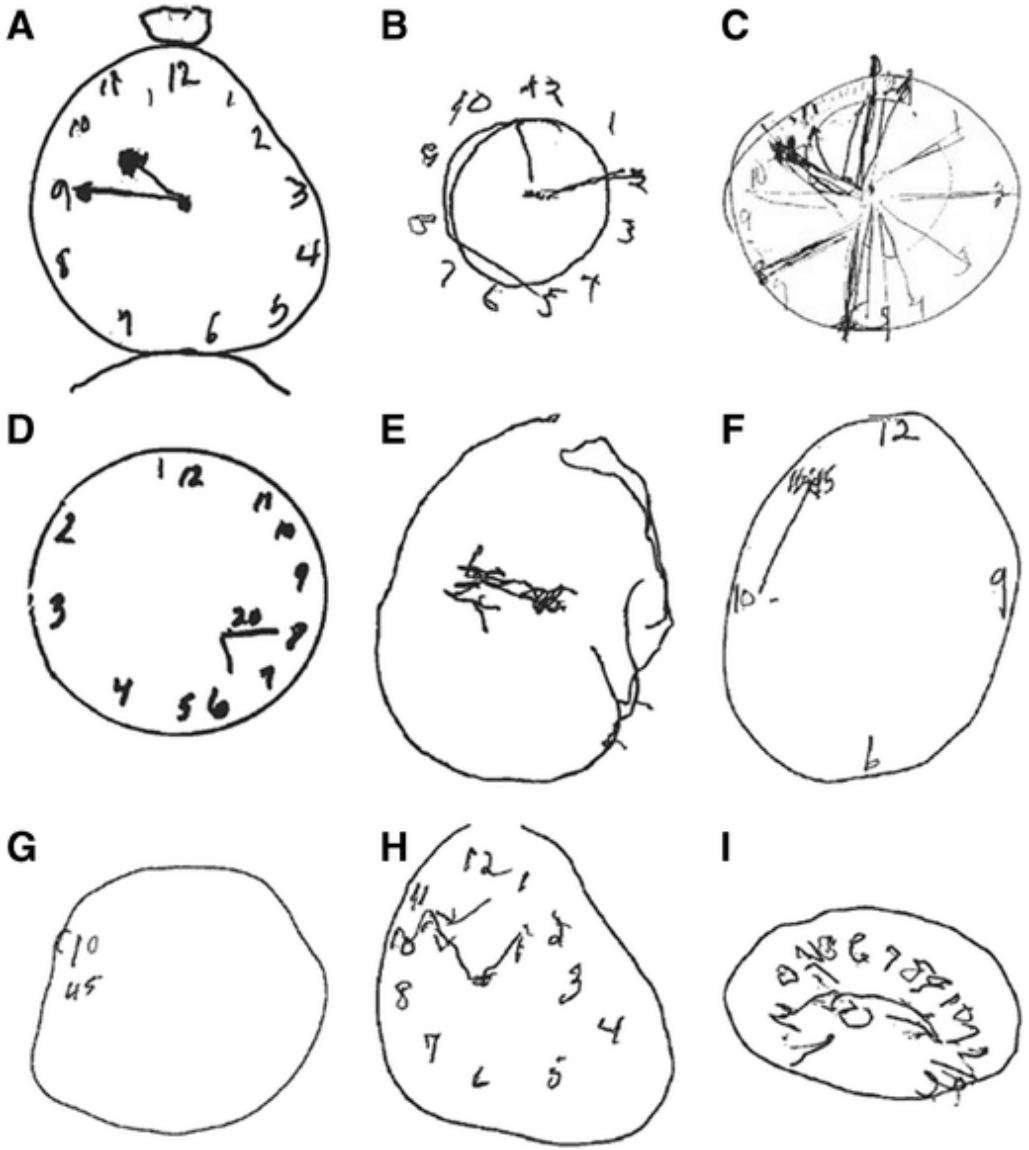
- Mini-mental status examination (MMSE)
- Montreal Cognitive Assessment (MoCA)
- Saint Louis University Mental Status (SLUMS)



Tests

These studies can be repeated over time to document the progression of decline. They can give an idea of the severity of the deficit along with specific cognitive domains that are affected.

Diagnosis



Diagnosis

Laboratory tests

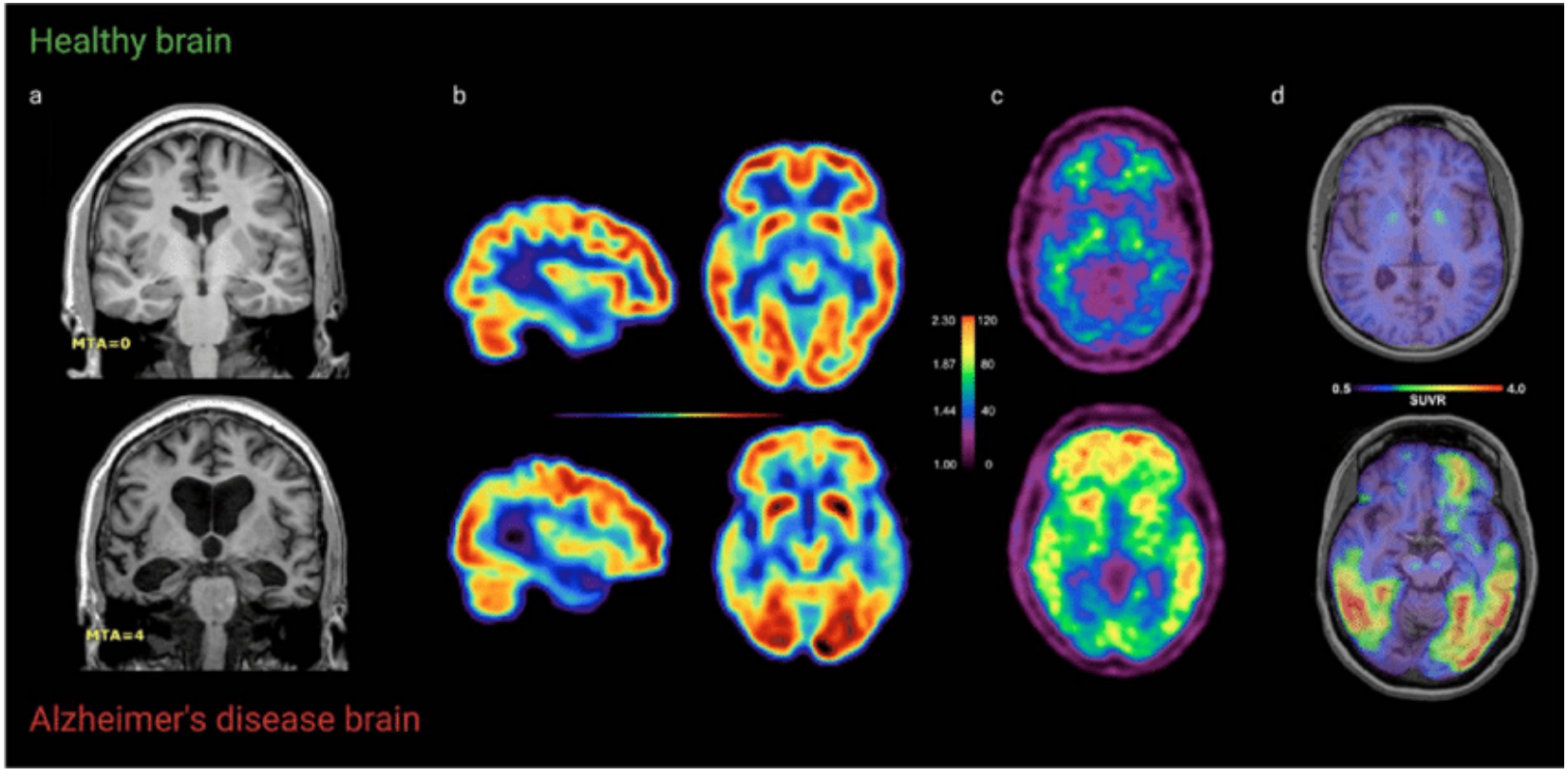
- Complete blood count, urinalysis, metabolic panel, vitamin B12, folic acid, thyroid function tests
- Serological tests for syphilis and HIV
- These test can rule out other causes of dementia, such as HIV-related dementia or vitamin B-12 deficit.

Diagnosis

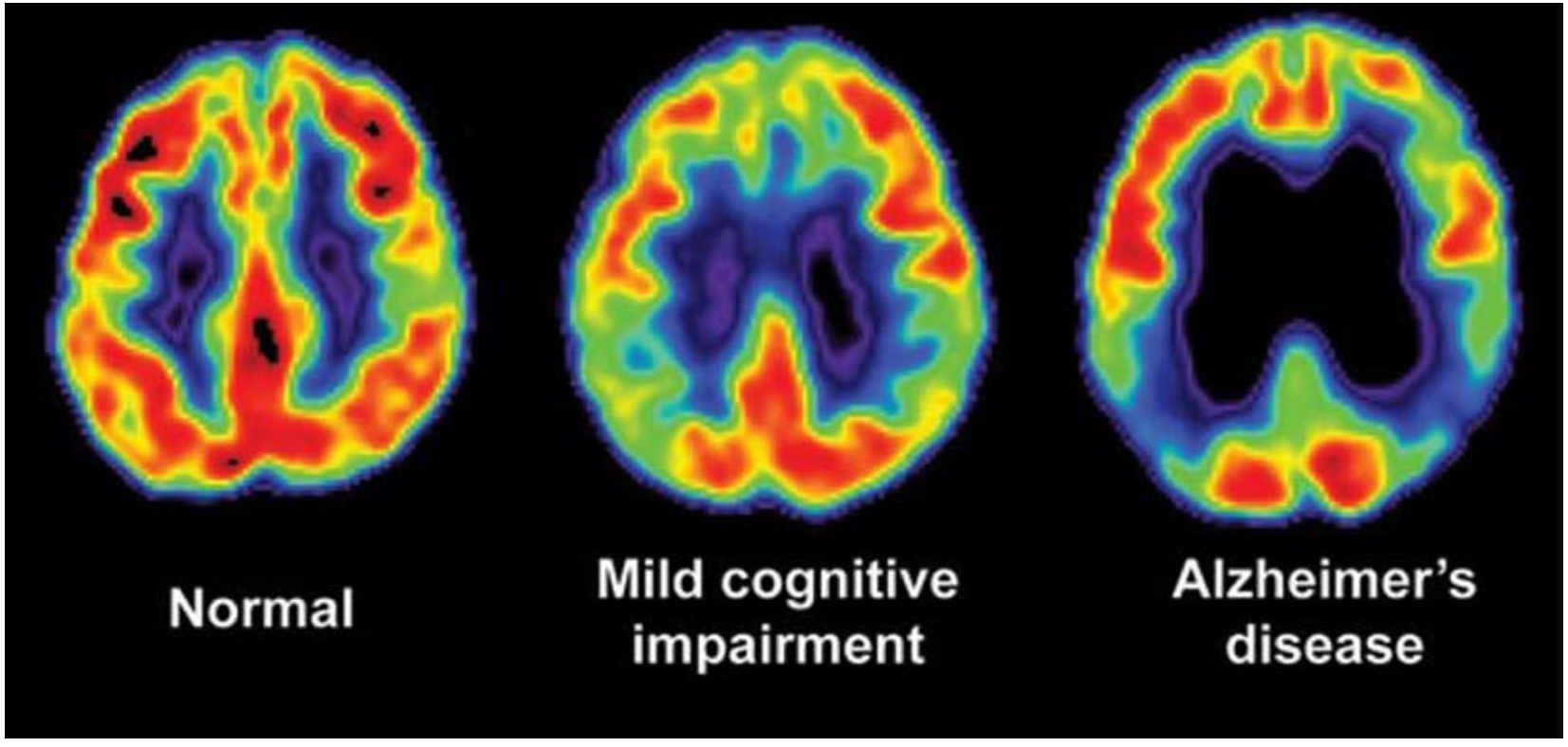
Neuroimaging

- Brain MRI (magnetic resonance imaging) is often the initial test ordered.
- Assessment of signs of vascular or ischemic disease
- Evaluation of regions or global atrophy
- DaTscan uses a radiotracer to highlight dopamine transporter proteins in a SPECT scan on the presynaptic dopaminergic neurons.
- Functional brain imaging techniques are PET, SPECT, and functional MRIm

Diagnosis


Healthy brain
a
b
c
d
MTA=0
MTA=4
2.30
1.87
1.44
1.00
120
80
40
0
0.5
4.0
SUVR
Alzheimer's disease brain

Diagnosis



Treatment

Medication

- Medications to improve cognitive function

- Cholinesterase inhibitors (**donepezil, galantamine, and rivastigmine**) and memantine.
- Cholinesterase inhibitors aim to slow or delay the worsening of symptoms.
- The benefits are **modest**, and ofthen in the **early stages** of the disease.
- Behavioral symptoms include irritability, anxiety, and depression.
- Antidepressants and sometimes antipsychotics can help.
- Non-drug approaches: supportive care, memory training, physical exercise programs, social stimulation.

Prognosis

Prognosis

- The prognosis of dementia is poor and some complication may arise

- Progressive condition with no cure or treatment.
- The 1-year mortality rate was 30 to 40 %
- 5-year mortality rate was 60 to 65 %.
- Men had a higher risk than women.

- Malnutrition
- Respiratory infections due to dysphagia
- Inability to perform self-care tasks
- Apathy
- Agitation, mood changes.