Psychiatry 5th year

Chapter 8: Neurocognitive Disorders

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Definition:

- The neurocognitive disorders (NCDs) comprise a group of conditions defined by a decline in the level of cognitive functioning, which composed into six domains that may be affected, include:

1. **Attention** .
2. **Function.**
3. **Learning and memory.**
4. **Language.**
5. **Perceptual-motor skills.**
6. **Social interaction**.

- The DSM-5 divides the NCDs into three main categories:

1. Delirium,
2. Mild NCDs.
3. Major NCDs (dementias).


DELIRIUM

Delirium

- **Delirium**: Acute state of confusion characterized by fluctuations in awareness, cognition, and attention.
- It is a **medical emergency,** associated with **high mortality!**
- Potentially reversible, Can advance to coma, seizures, or death.
- Consider delirium as acute brain failure!

- **EPIDEMIOLOGY**
  - Up to one-half of hospitalized elderly patients develop delirium.
  - Delirium often goes unrecognized (65–88% of the time).

    As many as 90% of patients with a preexisting NCD (dementia) will experience a superimposed delirium when admitted to the hospital.
- **ETIOLOGY:**
  - Almost any medical condition can cause delirium, ex: pneumonia, Meningitis, hypoglycemia...etc.

  - Substance intoxication delirium.
  - Substance withdrawal delirium.
  - Medication-induced delirium.
  - Delirium due to another medical condition.

  But the exact mechanism is unknown

- **RISK FACTORS**
  - Age > 65 years
  - Hearing or vision impairment.
  - Preexisting cognitive impairment
  - Prior history of delirium.
  - Severe or terminal illness
  - Multiple medical comorbidities.

- **PRECIPITATING FACTORS:**
  - Polypharmacy, including the use of psychotropic medications
  - Infection.
  - Dehydration.
  - Organ failure.
  - Alcohol use or withdrawal.
  - **Pain.**
  - **Malnutrition.**
  - **Impaired mobility.**
  - **Sleep deprivation.**
  - **Mechanical ventilation.**

WARDS TIP

Common causes of medication-induced delirium:

- Anticholinergics
- Benzodiazepines
- Nonbenzodiazepine hypnotics ("Z-drugs")
- Opioids (especially meperidine)
- Corticosteroids
- Tricyclic antidepressants
- H2 blockers

TABLE 8-1. Clinical Scenarios of Delirium on Exam		
Scenario	**Likely Diagnosis**	**Diagnostic Testing**
Delirium + fever + cough + rales	Pneumonia	Chest x-ray
Delirium + dysuria + suprapubic tenderness	Urinary tract infection	Urinalysis and urine culture
Delirium + constricted pupils (miosis) + bradypnea	Opioid intoxication	Urine toxicology screen
Delirium + fever + nuchal rigidity + photophobia	Meningitis	Lumbar puncture
Delirium + tachycardia + tremor + thyromegaly	Thyrotoxicosis	TSH, free T_4, T_3
Delirium + insulin use	Hypoglycemia	Blood glucose

- **CLINICAL MANIFESTATIONS**
  - Primarily a disorder of **attention** and **awareness**
  - Cognitive deficits **develop acutely** over hours to days.
  - deficits in **recent memory,** language, or perceptual disturbances (hallucinations).
  - Symptoms **fluctuate** throughout the day, typically worsening at night.

  ■ **Circadian rhythm disruption and emotional symptoms are common.**

- There are three types of delirium based on psychomotor activity.

1. **Mixed type (most common)**: psychomotor activity may remain stable and may fluctuate rapidly between hyperactivity and hypoactivity.

More common in the elderly.

2. **Hypoactive** ("quiet") type: Decreased psychomotor activity, **More likely to go undetected.**
3. **Hyperactive type** ("ICU psychosis"): Manifests with agitation and uncooperativeness. More common in **drug withdrawal or toxicity**. More easily identified due to its disruptiveness.

■ **Hospitalized patients usually recover within 1 week, although some degree of cognitive deficits can persist for months or even indefinitely.**

Diagnosis

- A useful clinical tool for evaluation of a patient with suspected delirium is the **Confusion Assessment Method** (CAM). This method takes 5 minutes to perform and has a high sensitivity and specificity.

- Feature 1: Acute onset in a fluctuating course.
- Feature 2: Inattention.
- Feature 3: Altered consciousness.
- Feature 4: Disorganized thinking.

- Delirium is diagnosed in a patient with **inattention** of **acute onset** and/or **fluctuating course** along with either **disorganized thinking** or **altered consciousness**.
- Once delirium has been diagnosed, the cause(s) should be sought.

Diagnosis

TABLE 8-2. *DSM-5* Criteria for Delirium
■ Disturbance in **attention** and **awareness**.
■ Disturbance in **an additional cognitive domain**.
■ Develops **acutely** over hours to days, represents a **change** from baseline, and tends to **fluctuate**.
■ **Not** better accounted for by **another neurocognitive disorder**.
■ **Not** occurring during a **coma**.
■ Evidence from history, physical, or labs that the disturbance is a **direct consequence** of **another medical condition**, **substance intoxication/withdrawal**, exposure to **toxin**, or due to multiple etiologies.

Diagnosis

- Once delirium has been diagnosed, the cause(s) should be sought.
  - Finger-stick blood glucose, pulse-oximetry, arterial blood gases, and electrocardiography can quickly provide useful data at bedside.
  - Labs typically obtained in a delirium workup include a basic metabolic panel, serum magnesium, complete blood count with differential, urinalysis, and urine culture.
  - Urine and blood drug screen, blood alcohol level, therapeutic drug levels (e.g., antiepileptics, digoxin, lithium), hepatic panel, thyroid hormone levels, inflammatory markers (e.g., C-reactive protein, erythrocyte sedimentation rate), vitamin B12 level, or chest x-ray may also be warranted depending on the clinical presentation.
  - Head imaging (head CT or brain MRI), EEG, and lumbar puncture should be performed if focal neurological deficits are present or a cause of delirium cannot be identified with the initial workup.

TREATMENT

- **Treat the underlying cause(s)**

  Address potential exacerbating factors: Mobility limitations, sensory deficits, sleep cycle disruption, constipation, urinary retention, dehydration, electrolyte abnormalities, uncontrolled pain, and medications.

- Supportive care

  - Encourage a family member to stay at the bedside to help with supervision and orientation.
  - Utilize a one-to-one sitter if needed.
  - Reorient the patient on a regular basis regarding time, place, and situation. Open window shades during the day and place whiteboards, calendars, and clocks in plain sight.

- **Haloperidol** is the preferred agent and can be administered orally, intramuscularly, or intravenously.

  D2 antagonists exacerbate extrapyramidal symptoms; use with caution in patients with Parkinsonism.

- Prevention of complications

  - Avoid benzodiazepines (except in alcohol or benzodiazepine withdrawal) as they may worsen the delirium by causing paradoxical disinhibition or over-sedation.
  - Avoid the use of restraints. They can worsen agitation and cause injury. When restraints are necessary, reassess often and remove as soon as possible. Use the least restrictive means appropriate for the situation.

An 83-year-old female is admitted to the hospital after presenting with a fever and altered mental status. Her home nurse aide reports that the patient was in her usual state of health until 24 hours prior to admission when she became confused and seemed to be talking to herself. In a few hours, her mental status improved then deteriorated again. After the patient dialed 911 to report that she was being held hostage by terrorists, her nurse aid called an ambulance on her behalf.

On examination, the patient is somnolent and has difficulty responding to questions appropriately. She is disoriented to place and time.

When the daughter calls to check in, she shares that her mother has had progressive memory deficits over the past several years. The patient can no longer drive and requires assistance with finances and meal preparation.

What is the most likely acute diagnosis?

The patient most likely has delirium. She presents with a sudden change in cognition as manifested by confusion, disorientation, and hallucinations. She has had an acute change from her baseline behavior. Her symptoms wax and wane throughout the day, representing the typical fluctuation found in delirium. She presents with a fever, likely secondary to an infection. If confirmed, her diagnosis would be delirium due to the specific infectious etiology.

Collateral information points to a prior diagnosis of major neurocognitive disorder (dementia). She has a history of memory impairment that began gradually and has progressively worsened. There is also history of impairment in executive functioning, and she can no longer care for herself. The existence of a major neurocognitive disorder is a risk factor for the development of a superimposed delirium.

Mild and Major Neurocognitive Disorders

Mild and Major Neurocognitive Disorders

- The non-delirium NCDs are characterized by a chronic cognitive decline that impacts functioning in daily activities.

- Major Neurocognitive Disorders:

1. Significant cognitive decline
2. Interferes with independence in daily living activities (IADLs), ex: shopping, paying bills.
   - Overtime can lead to total dependence

- Mild neurocognitive disorders:

1. Moderate cognitive decline (MCI) or cognitive impairment, no dementia [CIND]
2. DOES NOT interfere with independence in daily living activities

Clinical scenario of Mild & Major NCDs

Scenario	Likely diagnosis
cognitive impairment + cogwheel rigidity + resting tremor	Lewy body disease Parkinson disease
cognitive impairment + fatigue + cold intolerance	hypothyroidism
cognitive impairment + vegan diet + paresthesias + diminished position and vibration sensation	Vitamin B12 deficiency
cognitive impairment + tremor + Kayser– Fleischer rings	Wilson disease

Diagnosis

- **Mini Mental State Exam (MMSE)**
  - is a screening test used due to its speed and ease of administration.
  - 5-15 minutes
  - Assesses orientation, attention/concentration, language, constructional ability, and immediate and delayed recall.
  - Perfect score: 30. Dysfunction <25

- Not as sensitive for mild NCDs and early major NCDs.
- Lacks specificity.
- Norm tables are available to adjust for age and education.

- **Mini-Cog**
  - Consists of three-item recall and clock-drawing tasks.

Positive screening	Negative screening
1. No items recalled after 3 minutes. 2. Only one to two items recalled with abnormal clock drawing.	1. All three items repeated correctly after 3 minutes. 2. One to two items recalled with normal clock drawing.

Diagnosis

■ **Other commonly used screening tools include:**

- Blessed Orientation-Memory-Concentration (BOMC).
- Montreal Cognitive Assessment (MoCA).
- Frontal Assessment Battery (FAB).

■ **An abnormal screening test indicates the need for further testing, preferably formal neuropsychological testing.**

TABLE 8-3. *DSM-5* Criteria for Mild and Major NCDs

Criterion	Mild NCDs	Major NCDs
Functional decline in at least one cognitive domain relative to baseline as evidenced by		
Concern (expressed by the patient or caretaker)	Mild decline	Significant decline
Objective findings on cognitive testing (preferably standardized neuropsychological testing)	Modest impairment	Substantial impairment
Effect on functioning in daily life.	Ability to perform IADLs preserved	Impaired performance of IADLs/ADLs
Deficits do not occur exclusively in the context of a delirium		
Deficits are not better explained by another mental disorder.		

ADLs, basic activities of daily living; IADLs, independent activities of daily living.

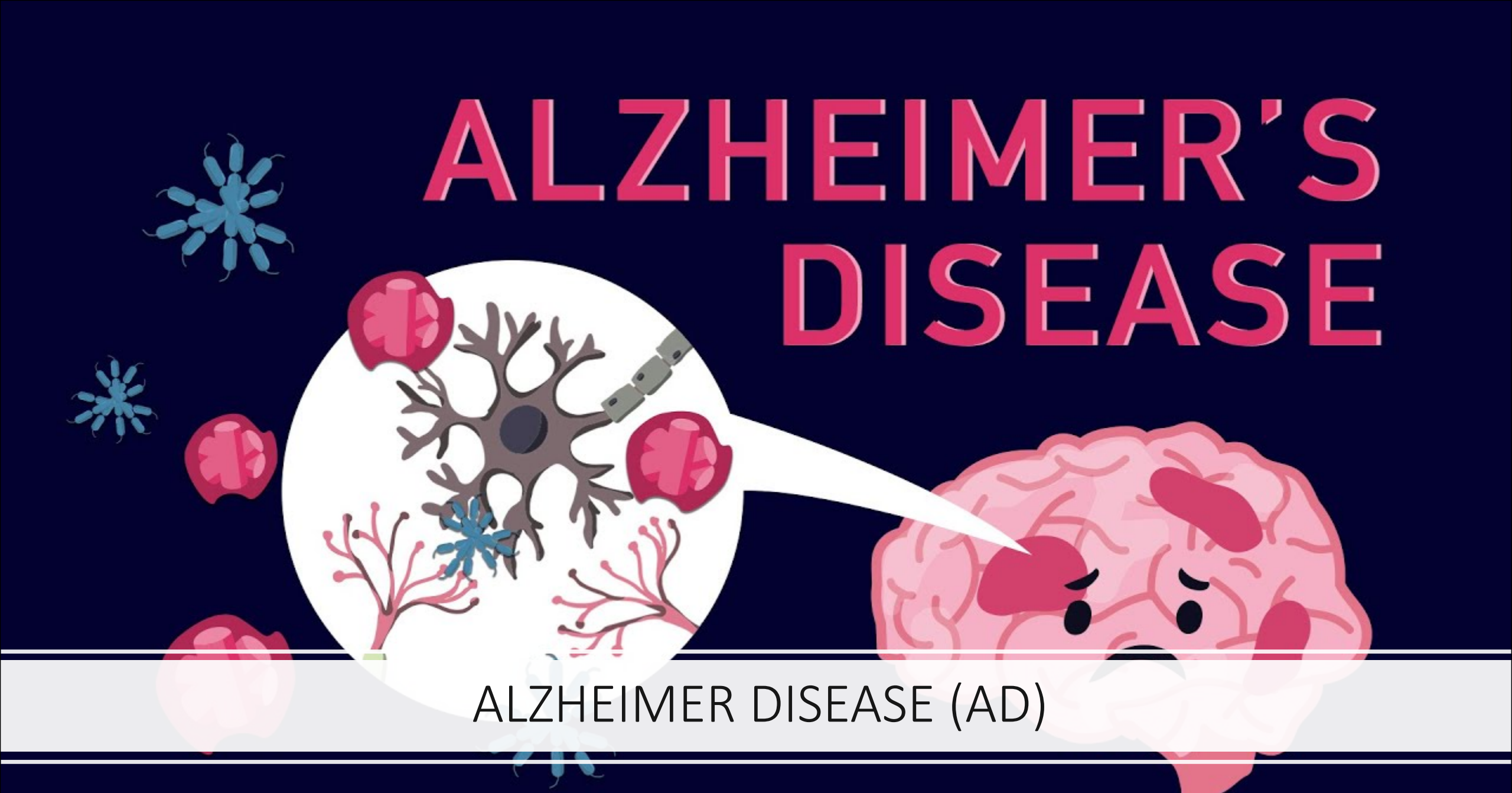
Diagnosis

TABLE 8-4. Clinical Scenarios of Neurocognitive Disorders on Exam	
Scenario	**Likely Diagnosis**
>65-year-old patient with memory impairment + executive dysfunction + poor insight progressing later to psychiatric/behavioral disturbances + insomnia + apraxia.	Alzheimer disease
>65-year-old patient with executive dysfunction + cognitive slowing + **stepwise** progression ± focal neurologic abnormalities ± history of known **stroke**.	Vascular NCD
>60-year-old patient with **gait apraxia** + **urinary urgency** → **incontinence** + executive dysfunction + apathy.	Normal pressure hydrocephalus
>50-year-old patient with **parkinsonism preceding cognitive decline** by several years.	Parkinson disease
>50-year-old patient with **concomitant development** of cognitive impairment (**visuospatial dysfunction**) + parkinsonism, as well as **REM sleep behaviors** + fluctuating alertness level + visual hallucinations.	NCD with Lewy bodies
Patient of any age with cognitive slowing + short-term memory impairment + **fatigue** + **cold intolerance**.	Hypothyroidism
Patient of any age with cognitive slowing + depression + **vegan diet** + paresthesias/numbness + ataxia.	Vitamin B12 deficiency

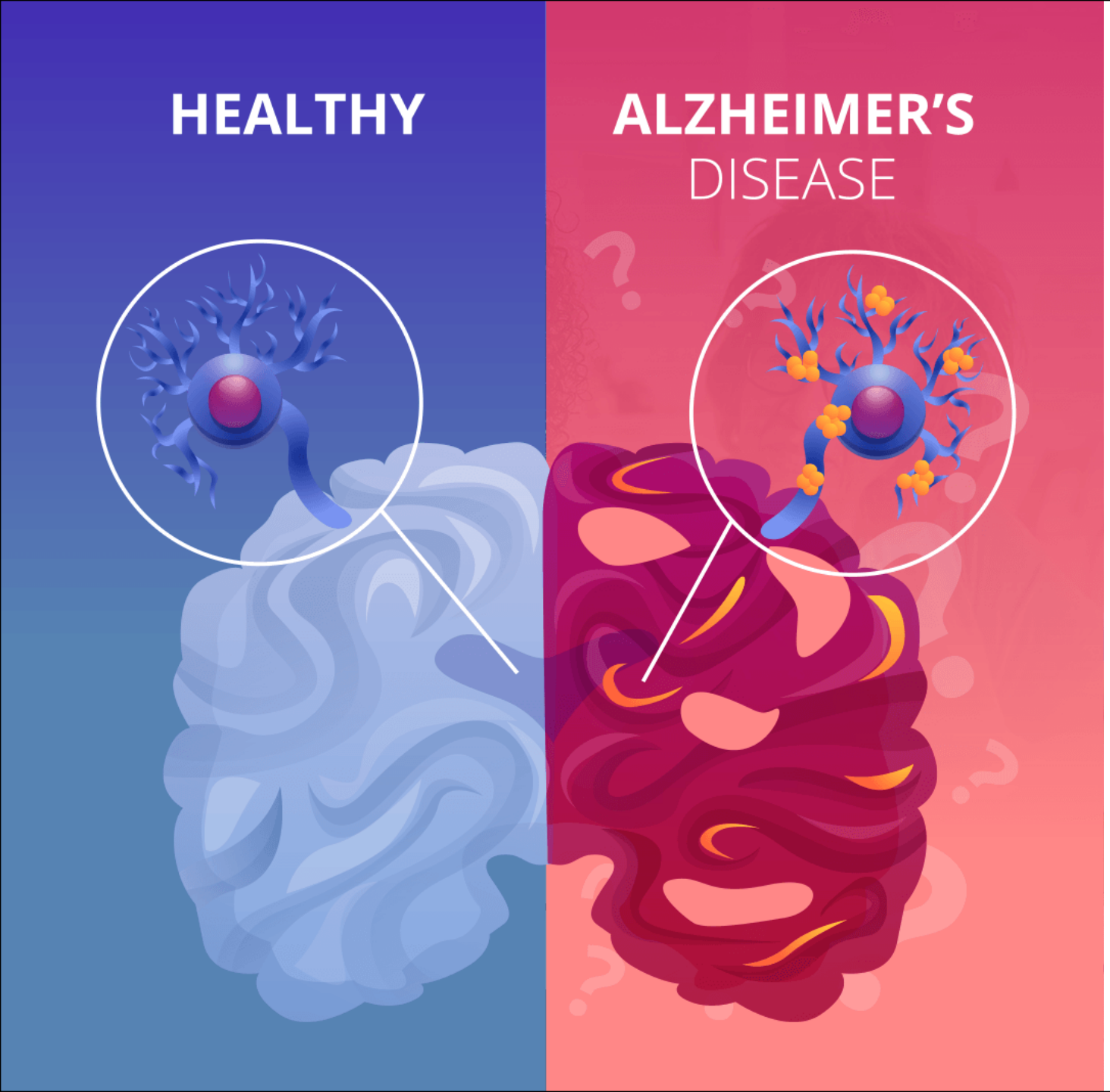
Major neurocognitive disorder

ACQUIRED DISORDER OF COGNITIVE FUNCTION THAT IS COMMONLY CHARACTERIZED BY **IMPAIRMENTS IN THE MEMORY, LANGUAGE, ATTENTION EXECUTIVE FUNCTION, SOCIAL COGNITION, AND/OR PERCEPTUAL MOTOR DOMAINS**.

MOST FORMS ARE ASSOCIATED WITH OLDER AGE.



ALZHEIMER DISEASE (AD)



Alzheimer disease

- Alzheimer disease is a progressive NCD and it is the **most common** underlying etiology of major NCDs (dementias).

- **Epidemiology:**
  - AD is the leading cause of dementia and the sixth most common cause of death in the US.
  - AD pathology is estimated to play a role in 60–90% of major NCDs.
  - Two-thirds of patients diagnosed with AD are women

Diagnosis is made after the age of 65 in the vast majority of individuals.

- **Etiology:**
  - **Accumulation** of extra-neuronal ***beta*-amyloid plaques** and intraneuronal *tau* protein tangles is associated with progressive brain atrophy.
  - Approximately 1% of AD results from an autosomal dominant single-gene mutation (amyloid precursor protein, presenilin 1, or presenilin 2), which is associated with an early onset of symptoms.

    The epsilon-4 variant of the apolipoprotein gene is a risk factor for developing early-onset AD.

- **Other risk factors:**
  - Age (strongest predisposing factor for regular AD)
  - Family history of dementia (strongest predisposing factor for early-onset AD)

Clinical Manifestations

The most common initial presentation is **short-term memory loss**, which insidiously progresses to dementia with deficits in other cognitive domains

- **Death often occurs within 10 years of diagnosis.**

1. Gradual progressive decline in **cognitive functions:**
    1. Short term memory
    2. Language impairment
    3. Temporal and spatial disorientation

2. Non-cognitive Sx:
    1. Behavioral, ex: apathy, agitation
    2. Mood disorders
    3. Paranoia

Diagnosis

- Perform a comprehensive clinical evaluation
- A diagnosis of possible NCD due to AD is made based on the presence of characteristic clinical findings:
  - Insidious onset.
  - Gradual progression.
  - Impairment in one (mild NCD) or more (major NCD) cognitive
  - domains.
- Assess for reversible causes of cognitive impairment
- Obtain laboratory tests (for Vit B12, TSH) and neuroimaging (brain MRI) to assess for underlying causes of major neurocognitive disorder.

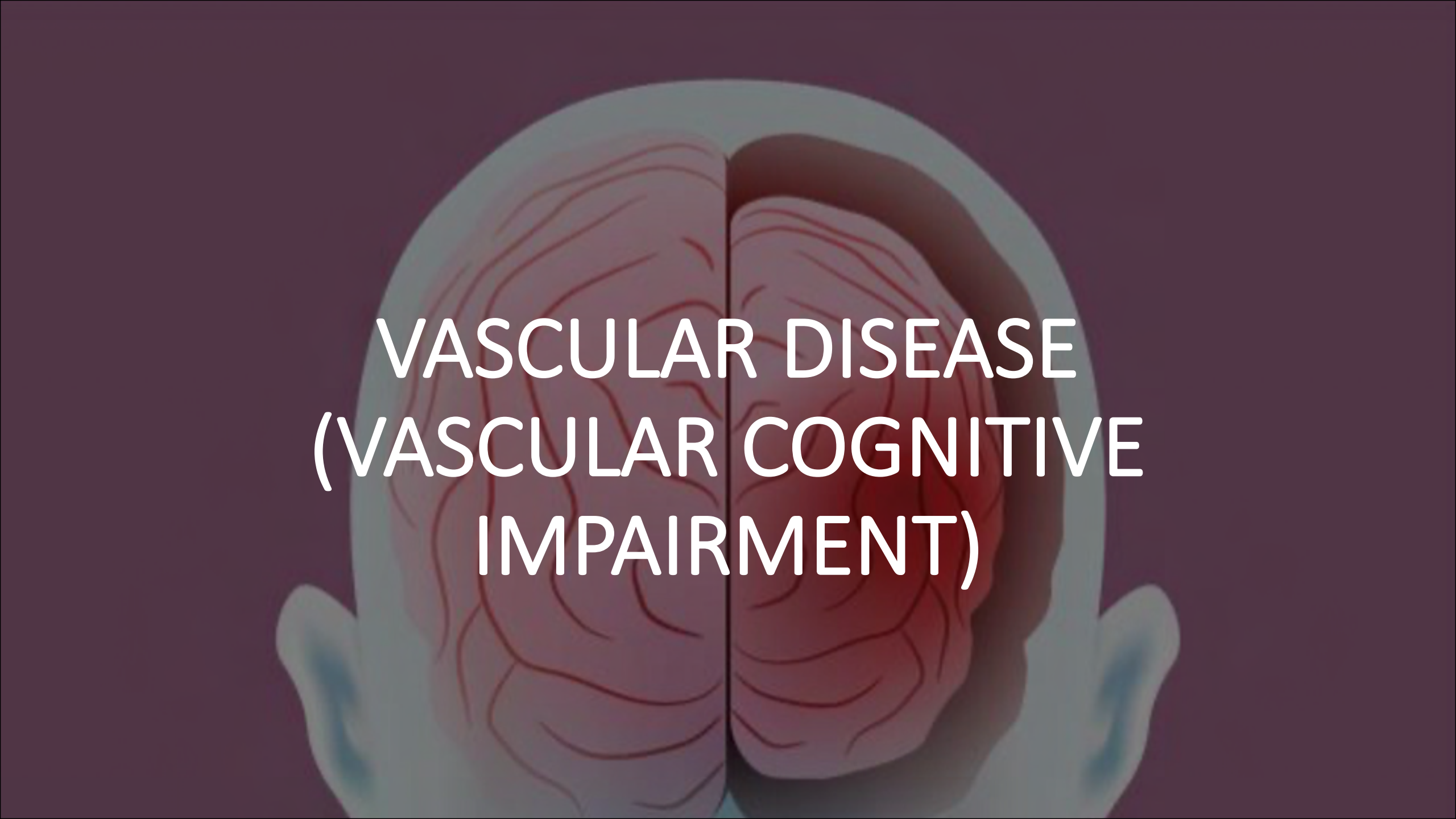
NCD due to AD is probable if there is evidence of causation by one of several single-gene variants.

Treatment

- No cure or truly effective treatment.
- **Cholinesterase inhibitors** (e.g., donepezil, rivastigmine) may slow clinical deterioration.
- **NMDA receptor antagonist:** (e.g, memantine) patients with moderate-to-severe disease.
- Antipsychotic medications: to treat agitation and aggression.
- Supportive care

- **A multidisciplinary approach is necessary.**
- **Any treatment plan must include caregiver support.**

- Because they are associated with **increased mortality** in patients with dementia, low doses should be prescribed for short periods of time.
- Ideally, informed consent should be obtained from patients and/or their designated decision makers.
- **Monitor closely** for side effects.



VASCULAR DISEASE (VASCULAR COGNITIVE IMPAIRMENT)

Vascular dementia

- Vascular dementia (VD) describes gradual cognitive decline caused by small or large vessel disease.

- **Epidemiology**
  - Second most common type of dementia (15–20% of cases)
  - Prevalence increases with age (~ 1–4% in patients ≥ 65 years).

- **Etiology**:
  - VD may occur as a result of a prolonged and severe cerebral ischemia of any etiology
    - Large vessel strokes, usually cortical.
    - Small vessel strokes (lacunar infarcts) to subcortical structures.
    - Microvascular disease affecting the periventricular white matter.
    - Effects vary based on the size, location, and number of infarcts.

- Risk factors:
  1. Hypertension
  2. Diabetes mellitus
  3. Smoking
  4. Hyperlipidemia
  5. Advanced age
  6. Obesity
  7. Atrial fibrillation.
  8. Coronary artery disease.

- **Clinical manifestations:**

Due to large vessel

Multi-infarct dementia: typically, **stepwise deterioration**

Cognitive impairment

Due to small vessel:

- Reduced executive functioning
- Impaired complex attention

Clinical Manifestations

- Presentation and progression of cognitive impairment are variable.
  - Classically demonstrates a stepwise deterioration corresponding with the occurrence of micro-infarcts (i.e., multi-infarct dementia).
  - May present with acute onset followed by partial improvement.
  - May have an insidious onset with gradual decline similar to AD.
- **Complex attention** and **executive function** are the cognitive domains typically affected in small vessel disease.
- Confirmation of the diagnosis requires neuroimaging with clinical correlation.

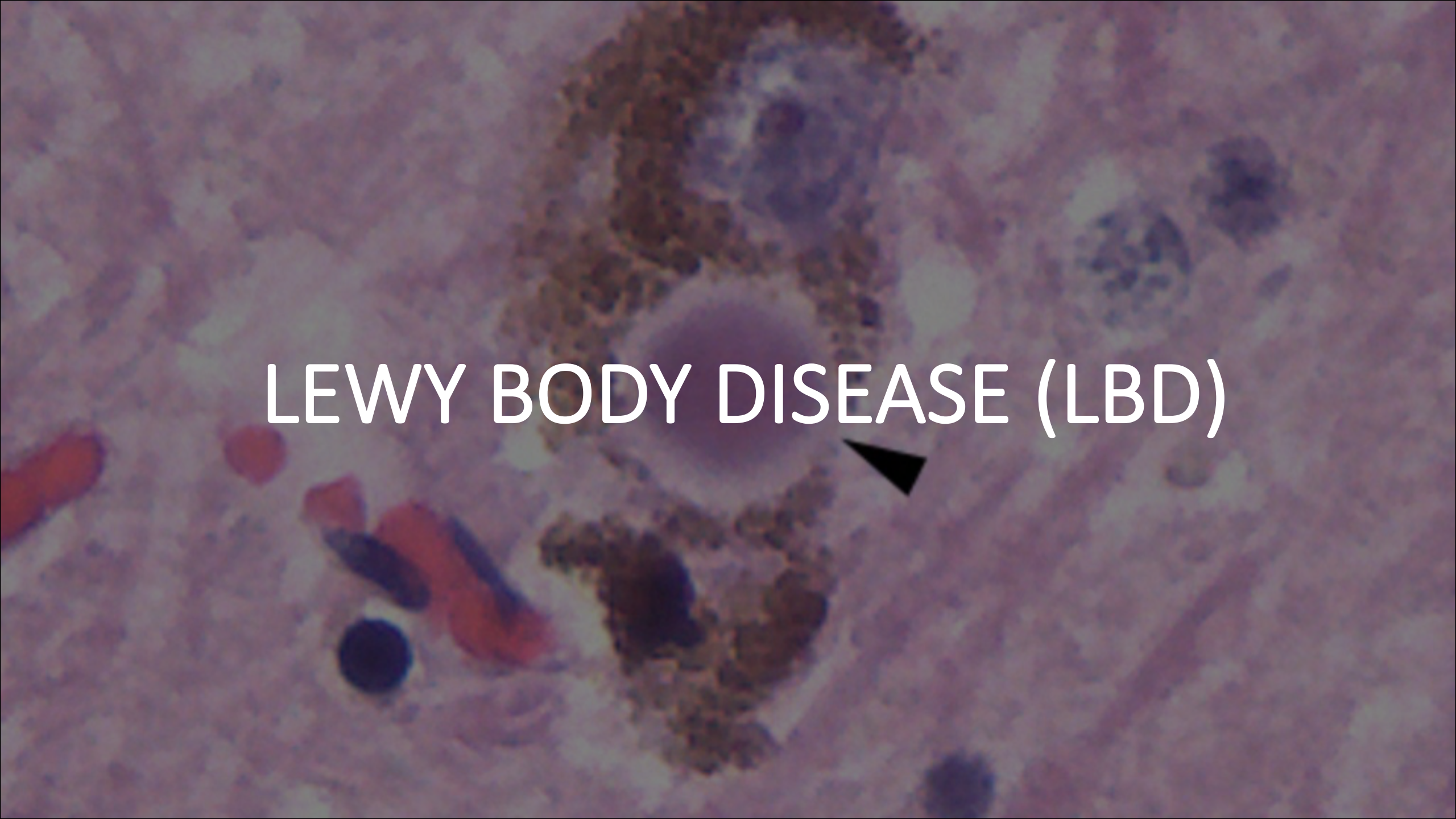
A 68-year-old female is brought to the clinic by her husband. He reports that his wife has recently seemed confused and overly emotional. The patient is able to complete her daily activities, but reports increased difficulty with planning and decision-making. Her medical history is significant for hypertension and transient ischemic attacks (TIAs). A physical exam reveals a carotid bruit.

What is the likely diagnosis?

Mild vascular NCD.

Treatment

- No cure or truly effective treatment.
- Manage risk factors with a goal of preventing future strokes.
- Symptomatic treatment is similar to AD.



LEWY BODY DISEASE (LBD)

Lewy body dementia

- Dementia with Lewy bodies is a less common type of dementia. It is closely related to both Alzheimer's disease and Parkinson's disease.

- Lewy bodies are tiny clumps of protein that develop inside nerve cells. They prevent the cells from communicating properly by disrupting the important chemical messengers between them, eventually causing the cells to die.

As reflected in its name, the major pathologic features of LBD are Lewy bodies (pathologic aggregations of alpha-synuclein) and Lewy neurites in the brain, primarily in the basal ganglia.

Clinical Manifestations

- **CORE FEATURES:**
  - **Waxing and waning** of cognition especially in the areas of attention and alertness.
  - **Visual hallucinations**
  - **Rapid eye movement** (REM) **sleep behavior disorder (**violent movements during sleep in response to dreams)
  - Development of **extrapyramidal signs** (Parkinsonism)

at least 1 year after cognitive decline becomes evident.

- Indicative biomarkers:
  - REM sleep without atonia (RWSA) demonstrated via polysomnography.
  - Evidence of reduced dopamine receptor uptake in the basal ganglia via SPECT or PET

Clinical Manifestations

- Suggestive features:
  - Pronounced **antipsychotic sensitivity** (i.e., extrapyramidal symptoms).
  - Postural instability and recurrent falls.
  - Loss of consciousness or transient unresponsiveness.
  - Autonomic dysfunction.
  - Olfactory agnosia or diminished sense of smell.
  - Nonvisual hallucinations and delusions.
  - Excessive sleepiness.
  - Depression, apathy, and anxiety.

Diagnosis

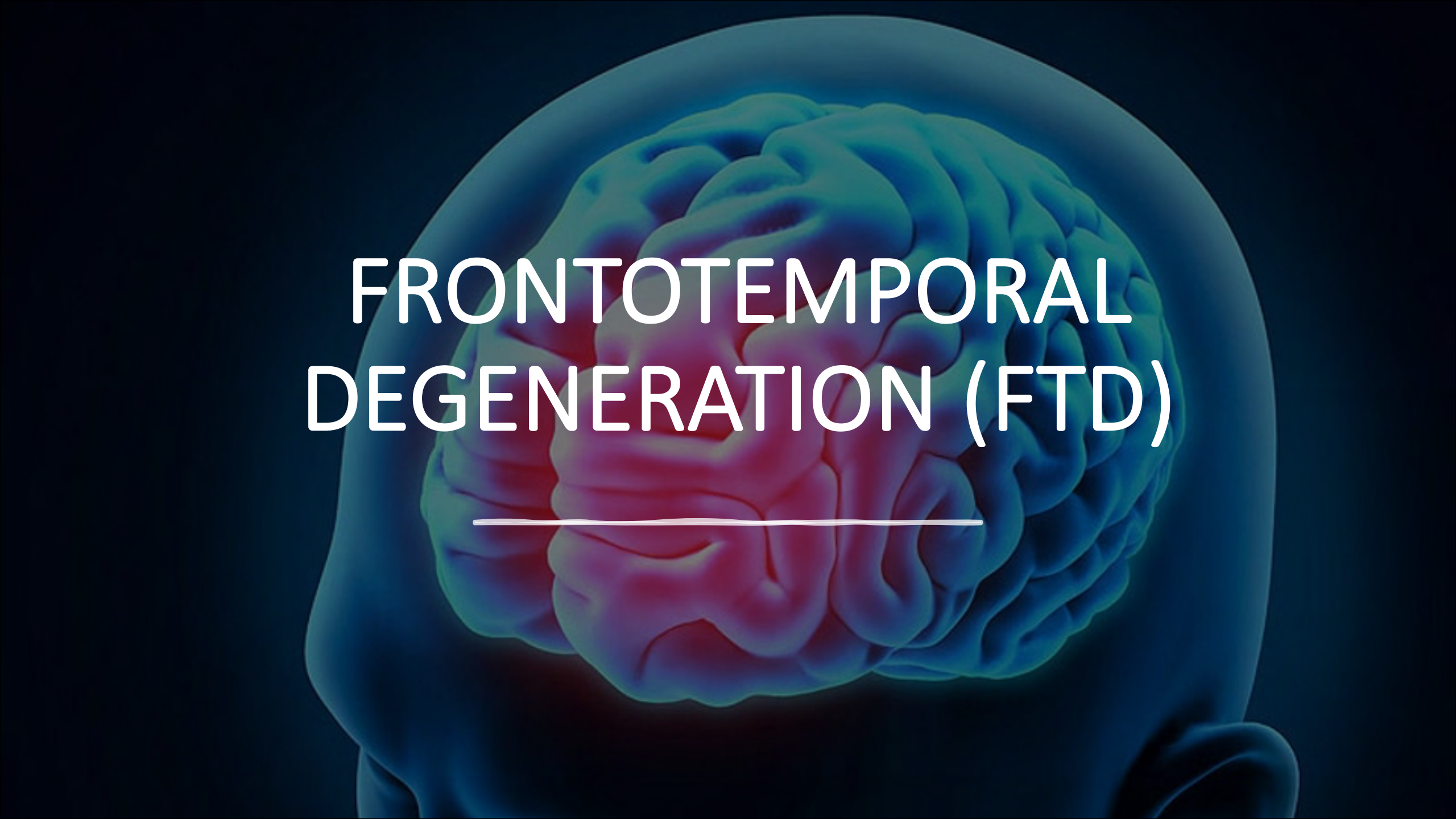
- Definitive diagnosis can only be made with autopsy.

- **Possible** NCD with Lewy bodies: Only one core feature without evidence from indicative biomarkers OR one or more indicative biomarker(s), but no core clinical features.

- **Probable** NCD with Lewy bodies: Two or more core features OR one core feature and one or more indicative biomarker(s).

Treatment

- **Cholinesterase inhibitors** for cognitive and behavioral symptoms.
- **Quetiapine** or **clozapine** for psychotic symptoms.
  - Use the lowest effective dose for the shortest period of time possible.
  - Monitor closely for adverse effects, such as extrapyramidal signs, sedation, increased confusion, autonomic dysfunction, and signs of **neuroleptic malignant syndrome (NMS).**
- Levodopa-carbidopa for Parkinsonism.
  - Not as effective as in idiopathic Parkinson disease.
  - May exacerbate psychosis or REM sleep behavior disorder.
- Melatonin and/or clonazepam for REM sleep behavior disorder.



FRONTOTEMPORAL DEGENERATION (FTD)

FRONTOTEMPORAL DEGENERATION (FTD)

- Frontotemporal dementia (FTD) is a progressive neurodegenerative disease of the frontal and/or temporal lobe generally caused by mutations to proteins in the brain (e.g., Tau, progranulin).
- FTD includes a diverse group of clinical and pathological disorders that typically present between the ages of 45 and 65.
- Approximately 40% are familial, and 10% are autosomal dominant.
- Marked atrophy of the frontal and temporal lobes.

Etiology

- Generally associated with pathological intracellular inclusion bodies (Pick bodies) that are caused by **mutations in tau** (main protein component of Pick bodies)
  or **progranulin** (precursor of granulin, which regulates cell growth) proteins

• Clinical Manifestations

- Cognitive deficits in:
  - **attention**, **abstraction**, **planning**, and **problem solving**.

- **Behavioral variant:**
  - **Disinhibited** verbal, physical, or sexual behavior.
  - Decline in **social cognition** and/or **executive abilities**.

- Overeating or oral exploration of inanimate objects.
- Lack of emotional warmth, empathy, or sympathy.
- Apathy or inertia.
- Perseveration, repetitive speech, rituals, or obsessions.

- **Language variant**
  - Difficulties with **speech** and **comprehension**.

- Relative sparing of learning/memory and perceptual-motor function.
- Many individuals have features of both the behavioral and language variants.
- Increased sensitivity to adverse effects of antipsychotics.

- **Diagnosis:**

  - Definitive diagnosis cannot be made until autopsy.
  - FTD is **probable** if :

  1. frontotemporal atrophy is evident on structural imaging
  2. or hypoactivity is visualized on functional imaging in context of the characteristic clinical signs.

- **Treatment**
  - Symptom-focused.
  - Serotonergic medications (e.g., SSRIs, trazodone) may help reduce disinhibition, anxiety, , repetitive behaviors, and eating disorders.

HIV INFECTION

HIV INFECTION

- HIV is the most common infectious agent known to cause cognitive impairment.
- leads to a complex disease pattern that ultimately results in chronic immunodeficiency.
- HIV can be transmitted sexually, parenterally, or vertically.
- Infection is most common in the young adult population between 20 and30 years of age. The virus infects macrophages and other CD4+ cells, leading to the destruction of CD4 T cells

- **Risk Factors**
- History of severe immunosuppression.
- High viral loads in the CSF.
- Advanced HIV infection.

- **Clinical Manifestations**
  - Variable presentation depending on the part(s) of the brain affected.
  - Decline may be observed in executive functioning, attention, working memory, and psychomotor activity.
  - Psychiatric and neuromotor symptoms may also be present.

- **Diagnosis**
- Mild or major NCD attributable to confirmed HIV infection.
- Elisa, serology

- **Treatment**
- Antiretroviral therapy (ART) improves cognition in some patients.
  - Nucleoside reverse transcriptase inhibitors (NRTIs)
  - e.g: abacavir

- Psychostimulants target fatigue, apathy, and psychomotor retardation.

HUNTINGTON DISEASE (HD)

HUNTINGTON DISEASE (HD)

- Is a neurodegenerative movement disorder characterized by involuntary and irregular movements of the limbs, neck, head, and/or face (chorea).

- This autosomal-dominant inherited disease is caused by mutations (increased number of CAG trinucleotide repeats) in the huntingtin gene which eventually leads to the dysfunction of subcortical motor circuits.

Chromosome 4

- Symptom onset depends on the individual extent of the genetic abnormalities but usually occurs around 40 years of age.

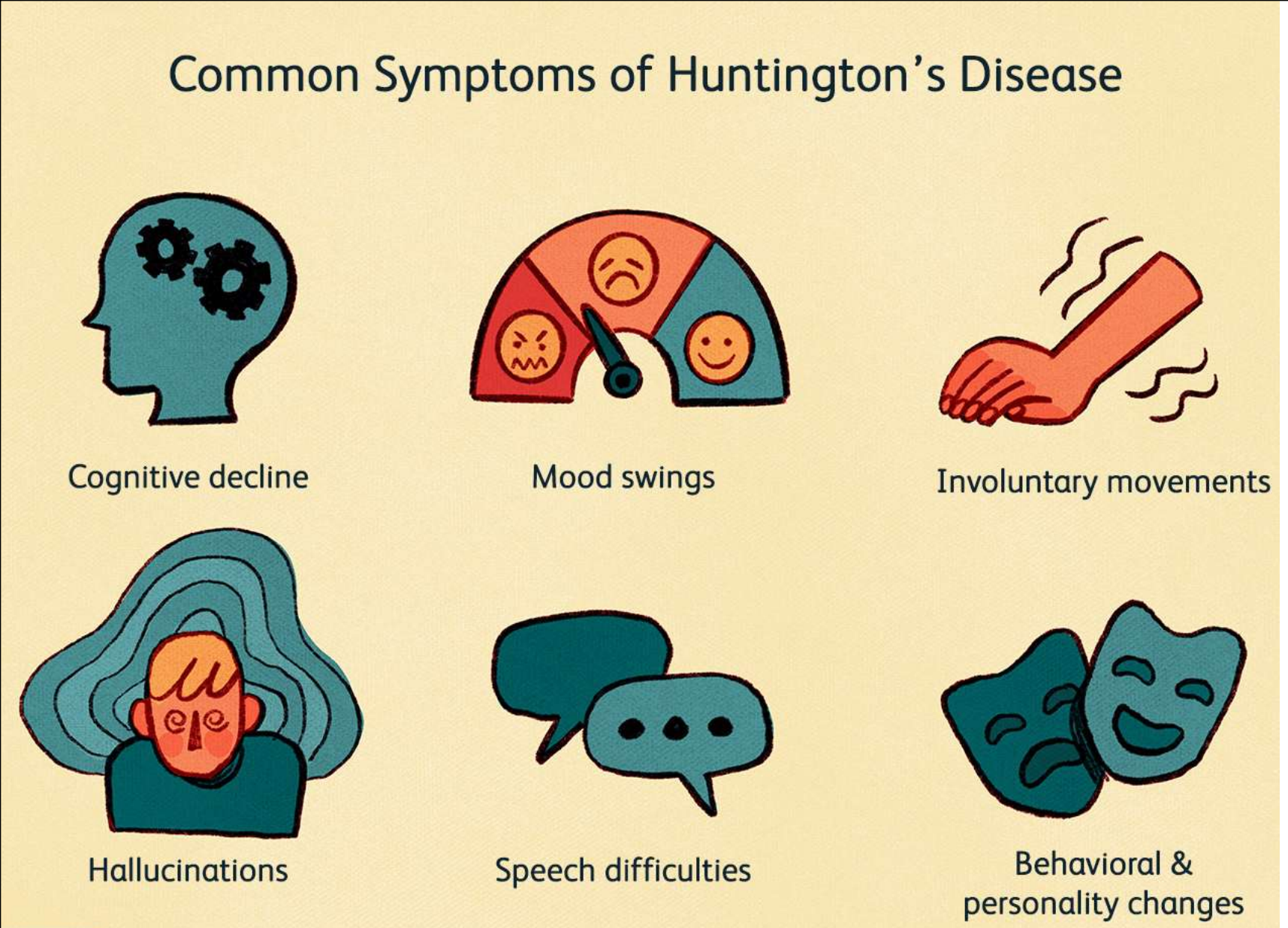
- **Epidemiology:**
- **Peak incidence:** 40 years of age
- One of the most common hereditary diseases of the brain

■ **Increased rate of suicide (7%).**

■ **Patients are often aware of deteriorating mentation.**

- **Etiology:**
- **Increased number of CAG repeats,** in the huntingtin gene on **chromosome 4**
- Inheritance (Autosomal dominant)

■ **<u>Executive function</u> is the primary cognitive domain affected.**



Clinical Manifestations

Characterized by a triad of:

Motor symptoms.

- **Chorea and bradykinesia**

Cognitive symptoms

- **(decline in executive function)**

- **Psychiatric symptoms (depression, irritability, hallucinations)**

Diagnosis

PATIENT HISTORY

GENETIC TESTING (PCR)

IMAGING: CT, MRI. (RARELY USED)

■ **Mild or major NCD may be diagnosed prior to onset of motor signs if an individual is determined to be at risk based on family history or genetic testing.**

Treatment

Symptom-directed therapy

- **Hyperkinetic/choreatic movements**
  - Monoamine-depleting drugs (tetrabenazine)
  - Atypical (2nd generation) antipsychotics.(clozapine)
- **Depression**: SSRIs (e.g., citalopram)

PARKINSON DISEASE (PD)

Parkinson disease

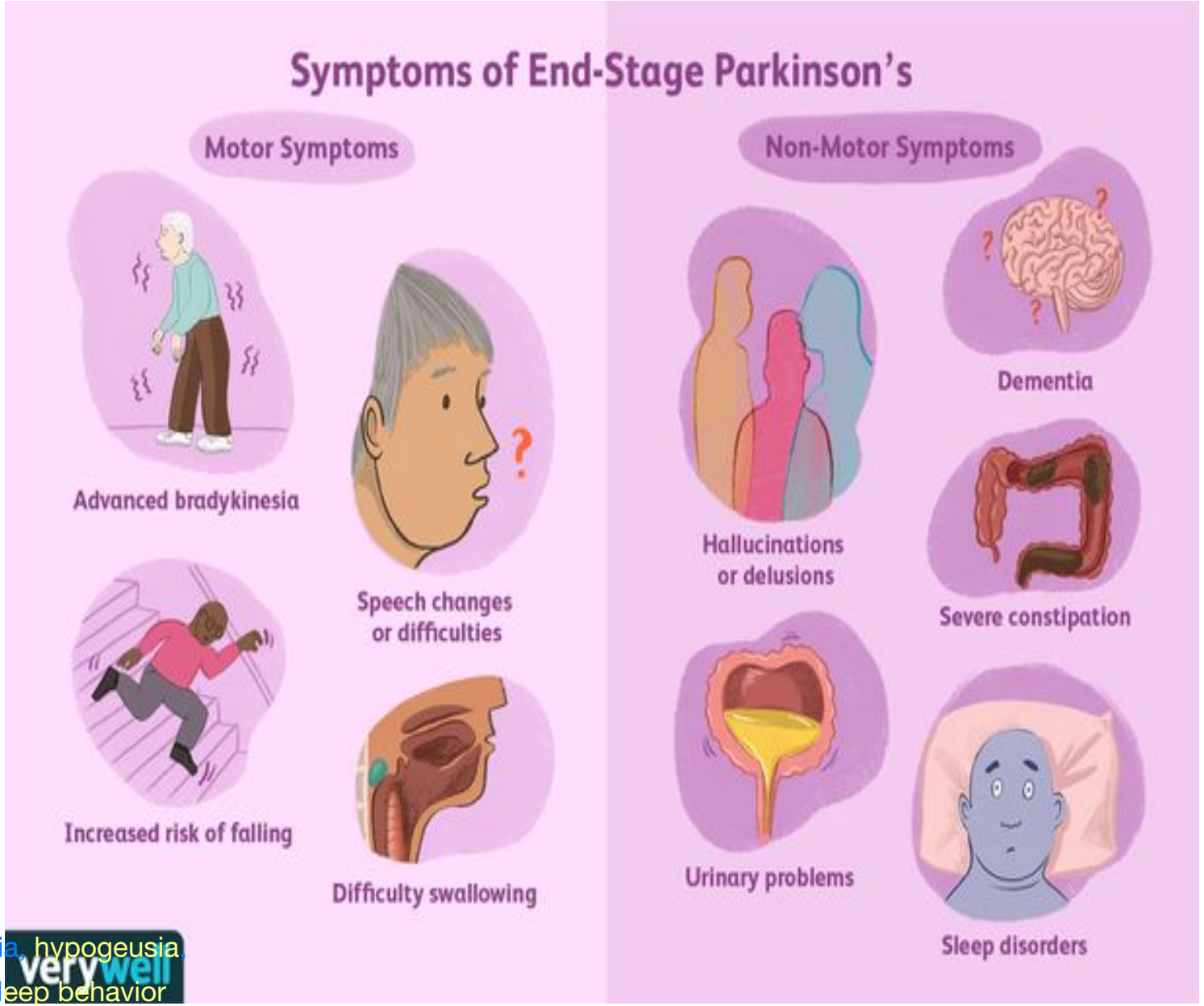
- Parkinson disease (PD) is a neurodegenerative condition that involves the progressive **depletion of dopaminergic neurons in the basal ganglia**, particularly the substantia nigra.

- It's the second most common neurodegenerative disorder following Alzheimer disease

Age of onset: ~ 60 years in sporadic cases

Clinical Manifestations

- **Motor**: rigidity, resting tremor, bradykinesia, and postural instability.
- **Psychotic symptoms**: visual hallucinations and paranoid delusions.
- **Cognitive:** executive dysfunction and visuospatial impairments.
- Depression, anxiety, personality changes



■ Prodromal symptoms and signs (e.g., micrographia, hyposmia, hypogeusia, constipation, personality changes, mood disorders, and REM-sleep behavior disorder) may occur up to two decades before motor abnormalities appear.

- **Diagnosis**
  - Diagnosis of PD requires the presence of **bradykinesia** and either **tremor** or **rigidity**.
  - Associated with asymmetry of motor symptoms and favorable response to dopaminergic therapy.
  - Mild or major NCD is attributed to PD if **cognitive decline appears after the onset of motor symptoms** and no other underlying etiology is identified.
- **Treatment**
  - ■ Motor symptoms are most commonly treated with **carbidopa-levodopa** and/or **dopamine agonists**.

Treatment

- Motor symptoms are most commonly treated with **carbidopa-levodopa** and/or **dopamine agonists**.
- High-frequency deep brain stimulation may lessen severe motor symptoms, but is associated with increased risk of depression.
- Cholinesterase inhibitors are used to target cognitive symptoms and may also ameliorate some of the neuropsychiatric symptoms (hallucinations).
- Psychotic symptoms may respond to a reduction in the dose of dopamine agonists.
- **Low-dose quetiapine** and **clozapine** are the preferred medications for treatment of psychosis. Avoid other antipsychotics since they can worsen the motor symptoms of PD.
- Pimavanserin is a serotonergic medication approved by the FDA to treat PD psychosis.

PRION DISEASE

PRION DISEASE

- A form of subacute spongiform encephalopathy caused by proteinaceous infectious particles (prions).
- Most cases occur sporadically.
- The most common type is **Creutzfeldt–Jakob disease**.

  Variant CJD (vCJD, aka bovine spongiform encephalopathy or mad cow disease) is a rare food-borne prion disease.

- Up to 15% are familial (autosomal dominant).

Clinical Manifestations

- rapidly progressive cognitive decline
- Difficulties with concentration, memory, and judgment.
- Myoclonus in 90% of patients
- Ataxia, nystagmus, and hypokinesia

Diagnosis

- Definitive diagnosis requires analysis of brain tissue obtained via biopsy or autopsy
- A diagnosis of probable CJD requires:
  - Rapid progression of cognitive decline.
  - At least two of the following typical clinical features:
    - Myoclonus.
    - Visual or cerebellar signs.
    - Pyramidal or extrapyramidal signs.
    - Akinetic mutism.
- Supportive findings from at least one diagnostic modality:
  - CSF positive for 14-3-3 proteins.
  - Lesions in the putamen or caudate nucleus on MRI.

Evaluation

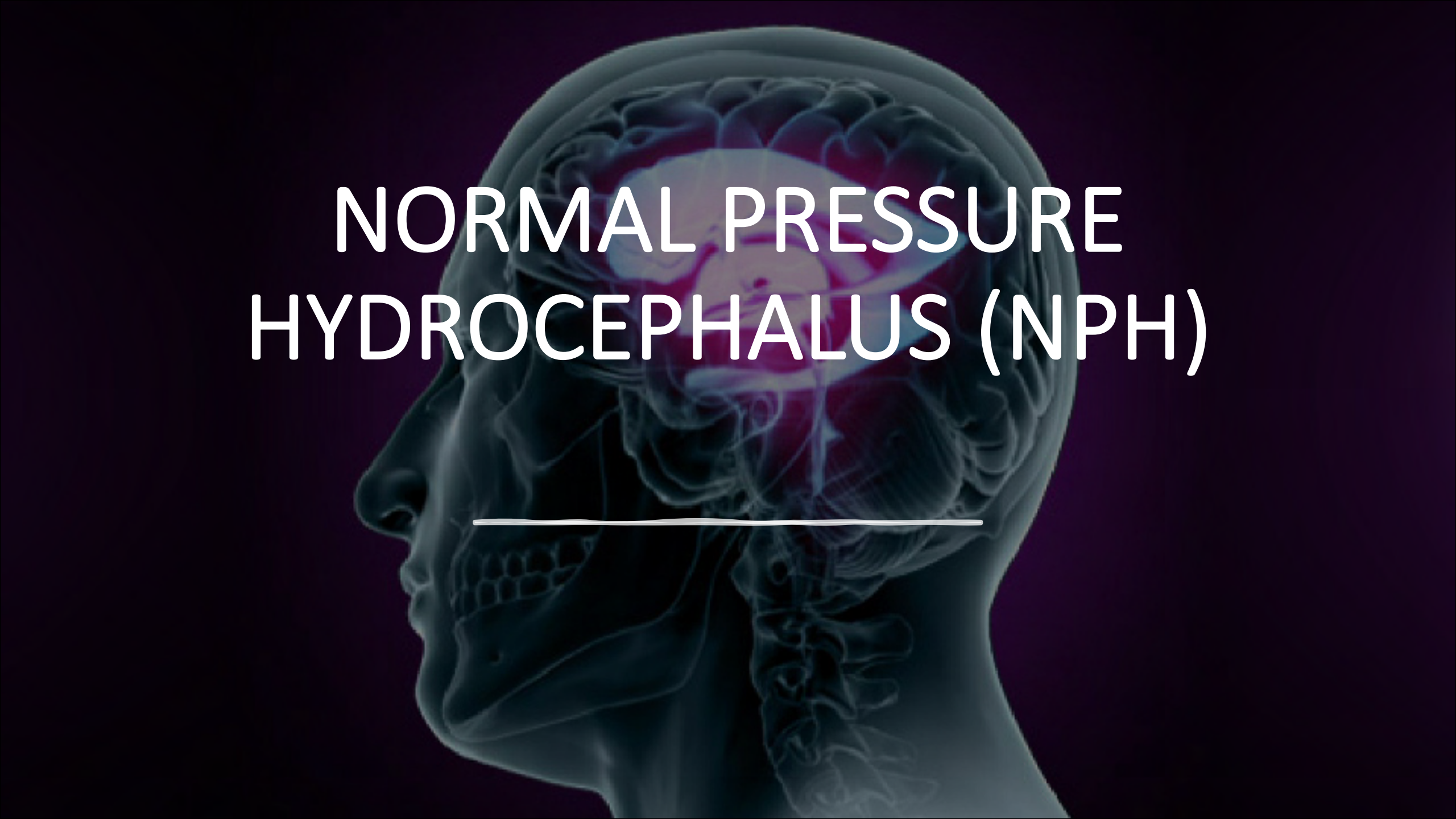
- Brain MRI: Hyperintensities in the caudate head, putamen, or at least two cortical regions on DWI or FLAIR.
- EEG: **Periodic sharp wave complexes**.
- CSF analysis: Positive RT QuIC assay and/or presence of 14-3-3 protein.

Diagnosis

- A diagnosis of probable sCJD requires either of the following scenarios:
  - A neuropsychiatric disorder with a **positive CSF RT-QuIC assay**.
  - **Rapid progression** of cognitive decline with two or more of the typical clinical features listed above AND typical findings on MRI, EEG, or CSF analysis.
- Definitive diagnosis requires analysis of brain tissue obtained via biopsy or autopsy.

Treatment

- Supportive
- No effective treatment exists.
- Most individuals die within 1 year of diagnosis.



NORMAL PRESSURE HYDROCEPHALUS (NPH)

NPH

- NPH is a potentially reversible cause of cognitive dysfunction.
- Enlarged ventricles (on imaging) with a **localized elevation** of cerebrospinal fluid (CSF) pressure but **normal opening pressures** on lumbar puncture.
- The etiology is either **idiopathic** or secondary to obstruction of CSF reabsorption sites due to infection (meningitis) or hemorrhage (subarachnoid or intraventricular).

Clinical manifestations

- **Gait disturbance** (“Wobbly”).
  - Most likely to be the first manifestation.
  - Slow with short steps.
  - Broad-based with outwardly rotated feet.

Feet appear to be stuck to the floor (magnetic gait).

Postural instability leads to recurrent falls.

- **Urinary incontinence** (“Wet”).
  - May begin as urinary urgency.
  - In later stages, apathy may contribute

Gait disturbance may interfere with reaching the toilet before urinary incontinence.

- **Cognitive impairment** (“Wacky”).
  - Insidious onset.
  - Executive dysfunction.
  - Psychomotor retardation.

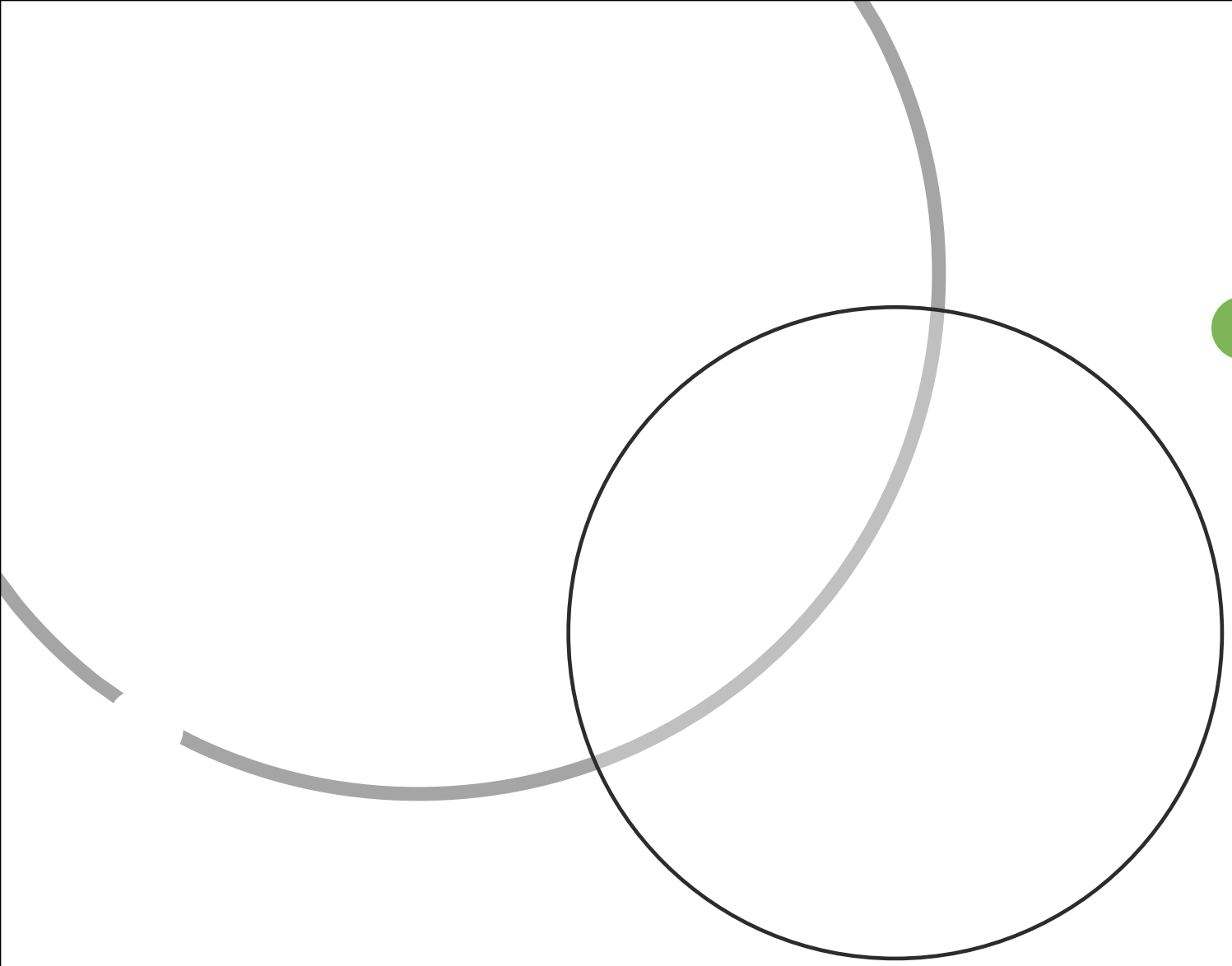
- Decreased attention.
- Apathy.

- Neuroimaging shows enlargement of ventricles out of proportion to cortical atrophy.

Localized elevation of cerebrospinal fluid (CSF) pressure but normal opening pressures on lumbar puncture.

Treatment

- Placement of a shunt (usually ventriculoperitoneal) may improve symptoms.
- Cognitive impairment is least likely to improve.



Thank you