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# Overview of Alzheimer's and Other Dementias

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- Defining dementia
- Effects of dementia on the brain
- Stages and symptoms of Alzheimer's disease
- Treatment options and medications
- Current research

## Overview

- Defining dementia
- Effects of dementia on the brain
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## Overview

– Dementia is defined as the loss of cognitive function that interferes with a person's day-to-day activities.

- Thinking
- Remembering
- Reasoning
- Personality
- Behavior



# What Is Dementia?

- Normal changes in memory with aging:
  - Forgetting names or appointments
  - Having trouble sorting out complex problems
  - Having difficulty learning new things (computers, etc.)

*These changes do not affect a person's ability to manage day-to-day activities.*

**How Is Dementia Different from Normal Aging?**

- Medication side effects
- Alcohol effects
- Hormone or vitamin imbalances
- Depression

**What Other Conditions Can Be Confused with Dementia?**

- Can lead to problems with attention and memory
- Can be confused with lack of initiation, a common early sign of dementia
- May be seen together with or precede dementia



## Depression

- Feeling sad, hopeless, or guilty most of the time
- Feeling tired or having low energy
- Crying a lot
- Having thoughts of suicide or death
- Sleep problems (too much or too little)
- Changes in appetite or weight (up or down)
- Loss of interest and pleasure in activities

## Depression Warning Signs



- Studies estimate only 10-40% of elderly get care
- Overall US suicide rate 12/100,000
- White males peak from 20-40 and again over 65
- Rate in 85 and up at 50/100,000
- Est. 75% of elderly who suicide saw MD within month prior
- 20% of older pts. who suicide saw MD **that day**
- 25% of all completed suicides in patients over the age of 65

## Geriatric Suicide

## New

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- Dementia due to
  - Alzheimer's disease
  - Lewy Body disease
  - Vascular disease
  - Pick's disease
  - HIV
  - Parkinson's disease

## Older

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- Chronic Brain Syndrome
- Organic Brain Syndrome
- Senility
- Acute Confusional State
- Hardening of the Arteries

# Dementia Terminology

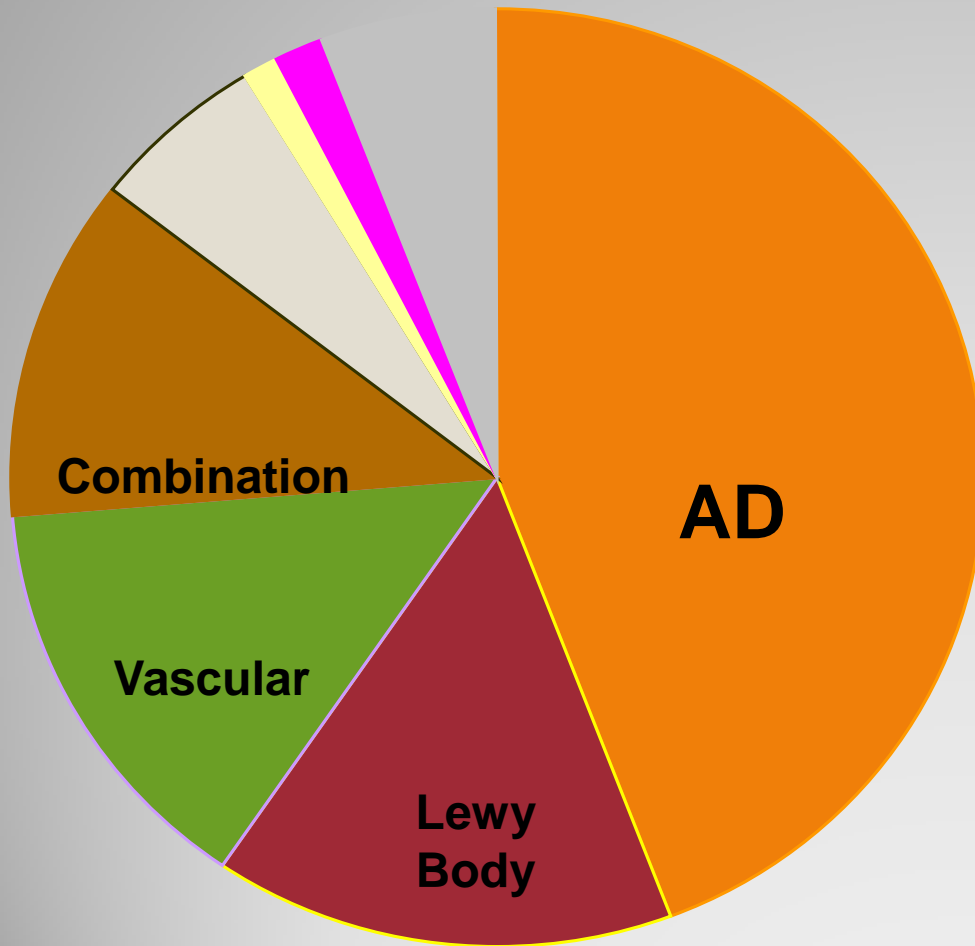
- Dementia can be caused by various disorders including:
  - Alzheimer's disease
  - Lewy Body disease
  - Vascular dementia
  - Fronto-temporal dementia
  - Parkinson's disease

## What Is Dementia?

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**What Is Dementia?**

# Causes of Dementia



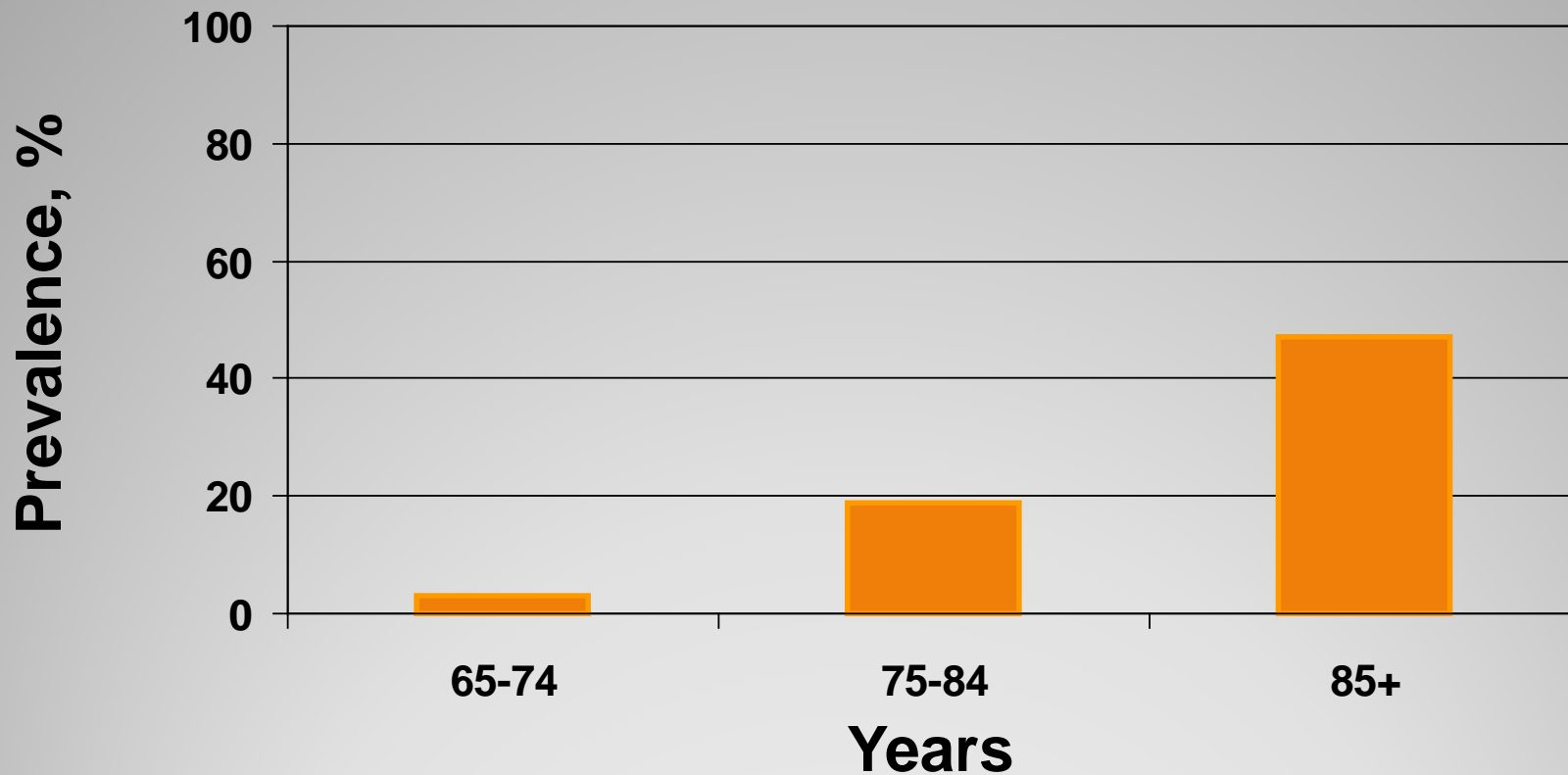
- Alzheimer's disease
- Lewy Body
- Vascular/Multi-Infarct
- Combination
- Brain Tumors
- Parkinson's disease
- Psychiatric Conditions
- Unknown

- The most common form of dementia (up to 80% of all dementia cases)
- Prevalence increases with aging
- 2 main forms:
  - o Early onset (accounts for <10% of cases)
    - symptoms develop before age 60
    - Highly linked to 3 genes on chromosomes 1, 14, 21
  - o Late onset (>90% of cases)
    - symptoms usually develop after age 70
    - Linked to genetic risk factor apolipoprotein E4

## Alzheimer's Disease

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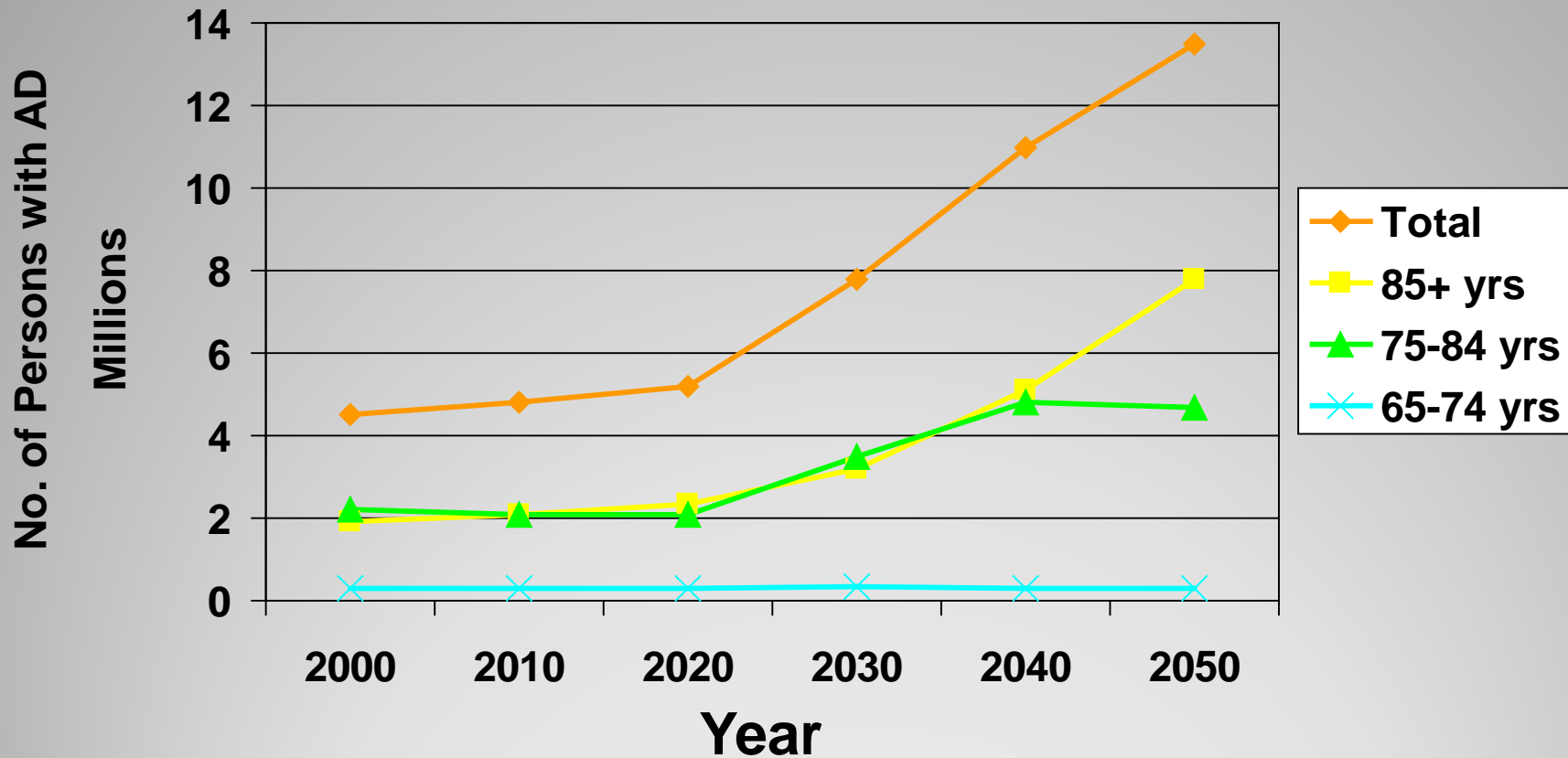
## Alzheimer's Disease



## Alzheimer's Disease Prevalence: Changes with Aging

Evans et al., JAMA 1989



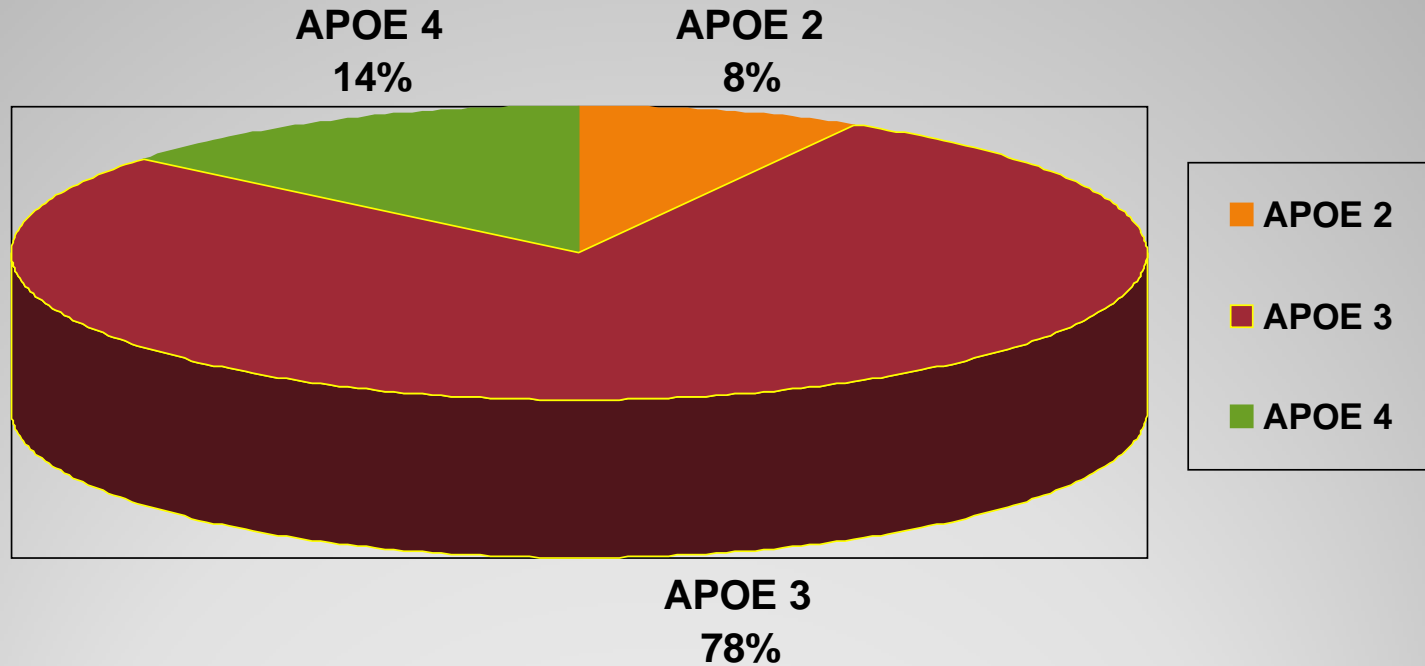


## Alzheimer's Disease Prevalence in the United States

- Age
- Family history of AD
- Apolipoprotein E4 (APOE4) – genetic risk
- Low sex steroids/high gonadotropins
- Low education level
- Head trauma with loss of consciousness
- Down syndrome

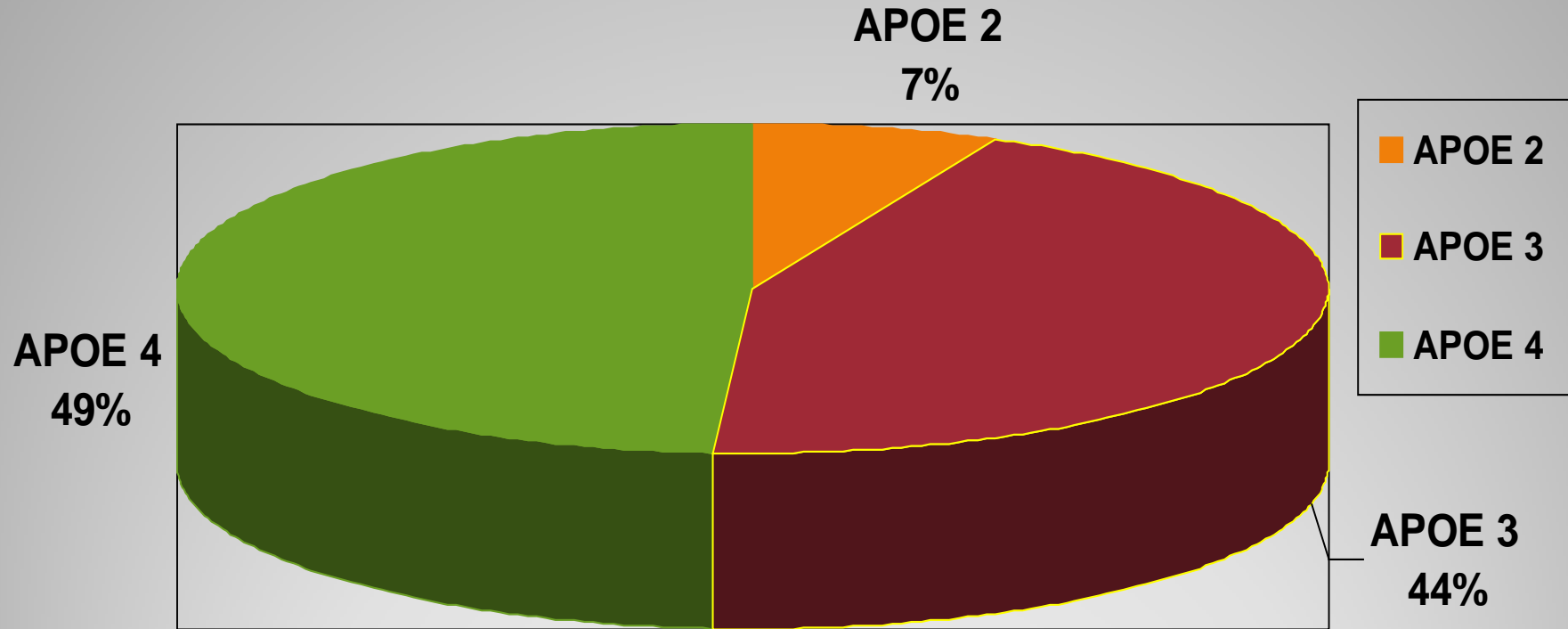
## **Risk Factors for AD**

# APOE allele frequencies in general population



**AD Risk Factors:  
APOE 4**

# APOE allele frequencies in persons with dementia



**AD Risk Factors:  
APOE 4**

Jonker C, Arch Neurol 1998;55:1065-1069

– Vascular risk factors associated with AD:

- High cholesterol
- High blood pressure
- Obesity
- Diabetes
- Low activity levels

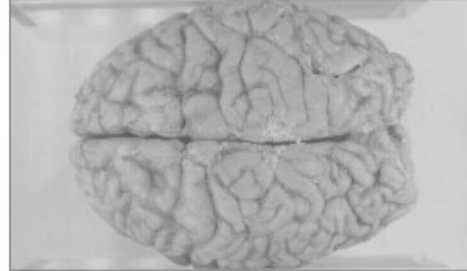


## Risk Factors for AD

- Defining dementia
- Effects of dementia on the brain
- Stages and symptoms of Alzheimer's disease
- Treatment options and medications
- Current research

## Overview

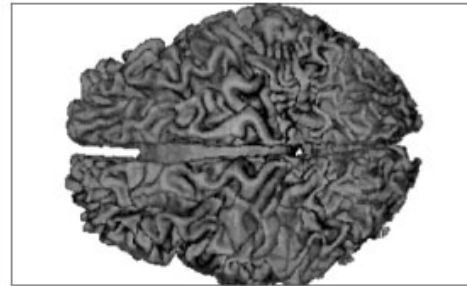
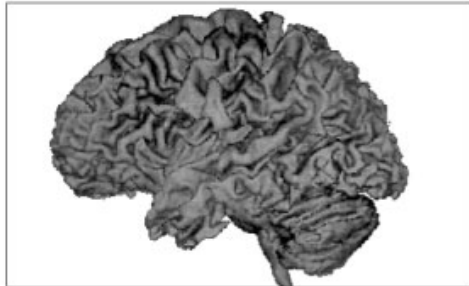
A. The brain of a normal elderly person



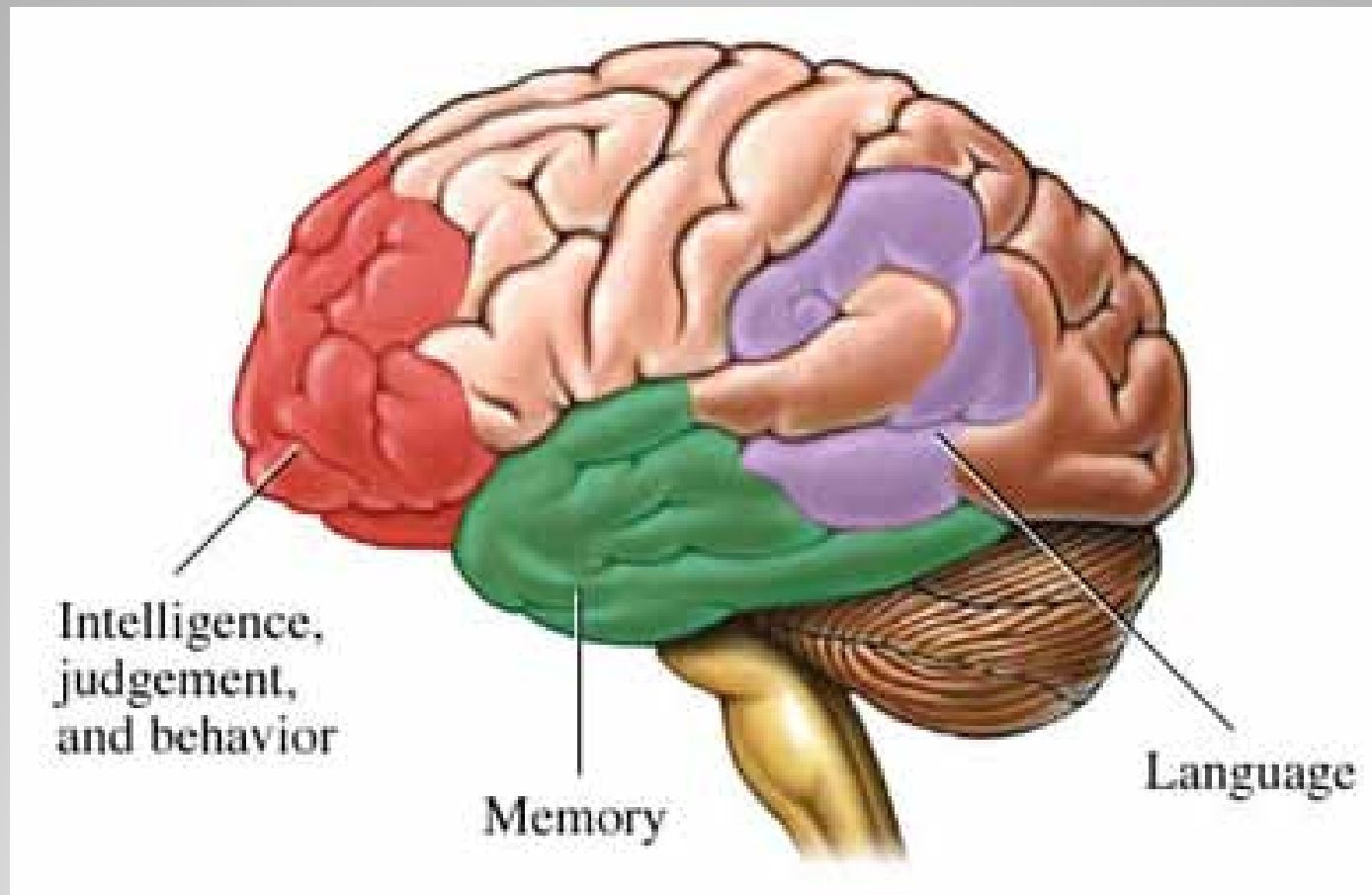
B. The brain of a person with Alzheimer's disease



C. The brain of a person with alcoholism

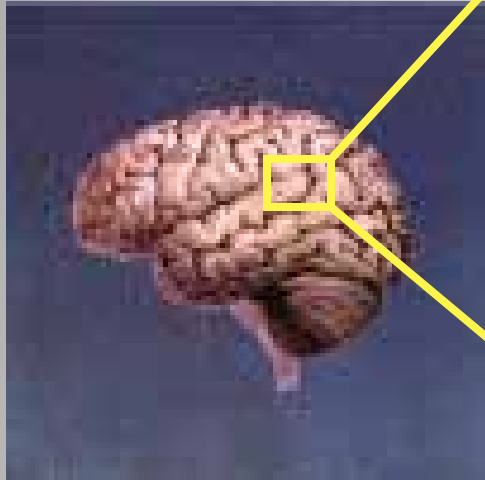


# Effects of Alzheimer's on the Brain

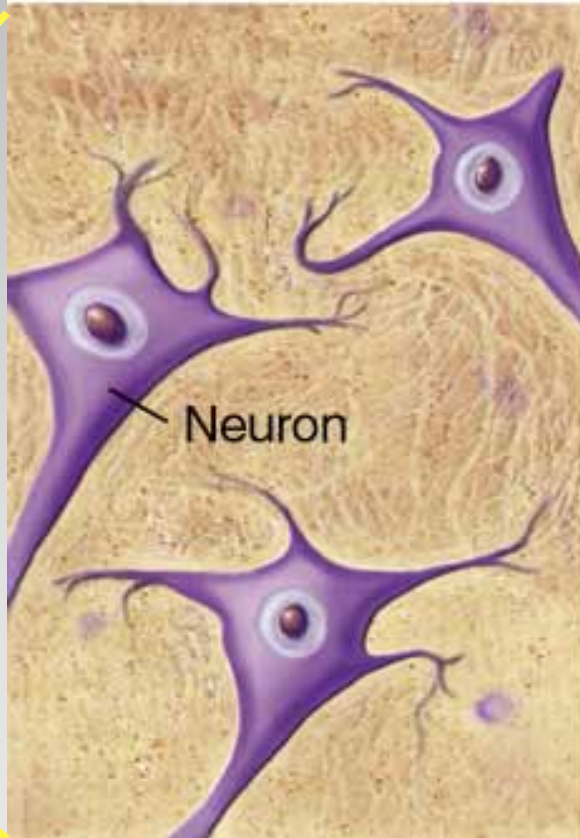


## Effects of Alzheimer's on the Brain

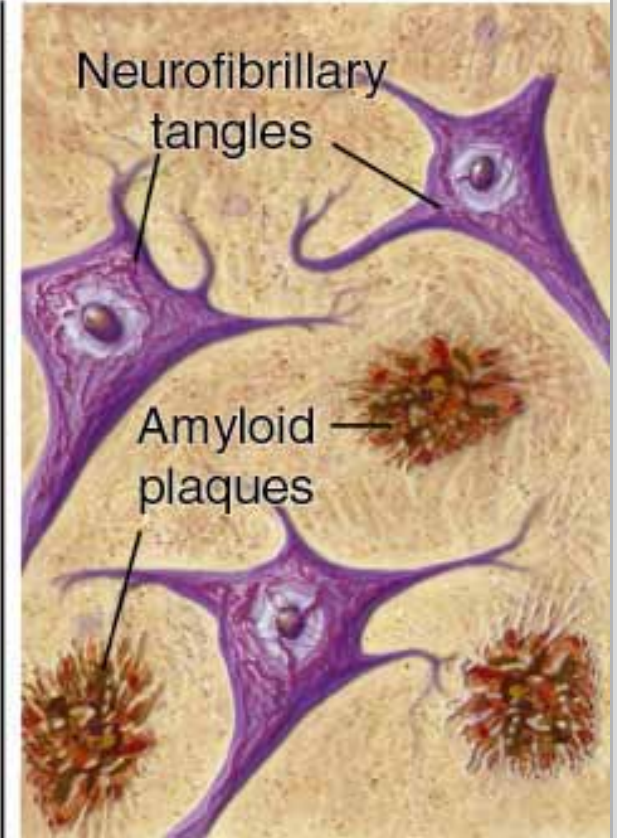




Normal

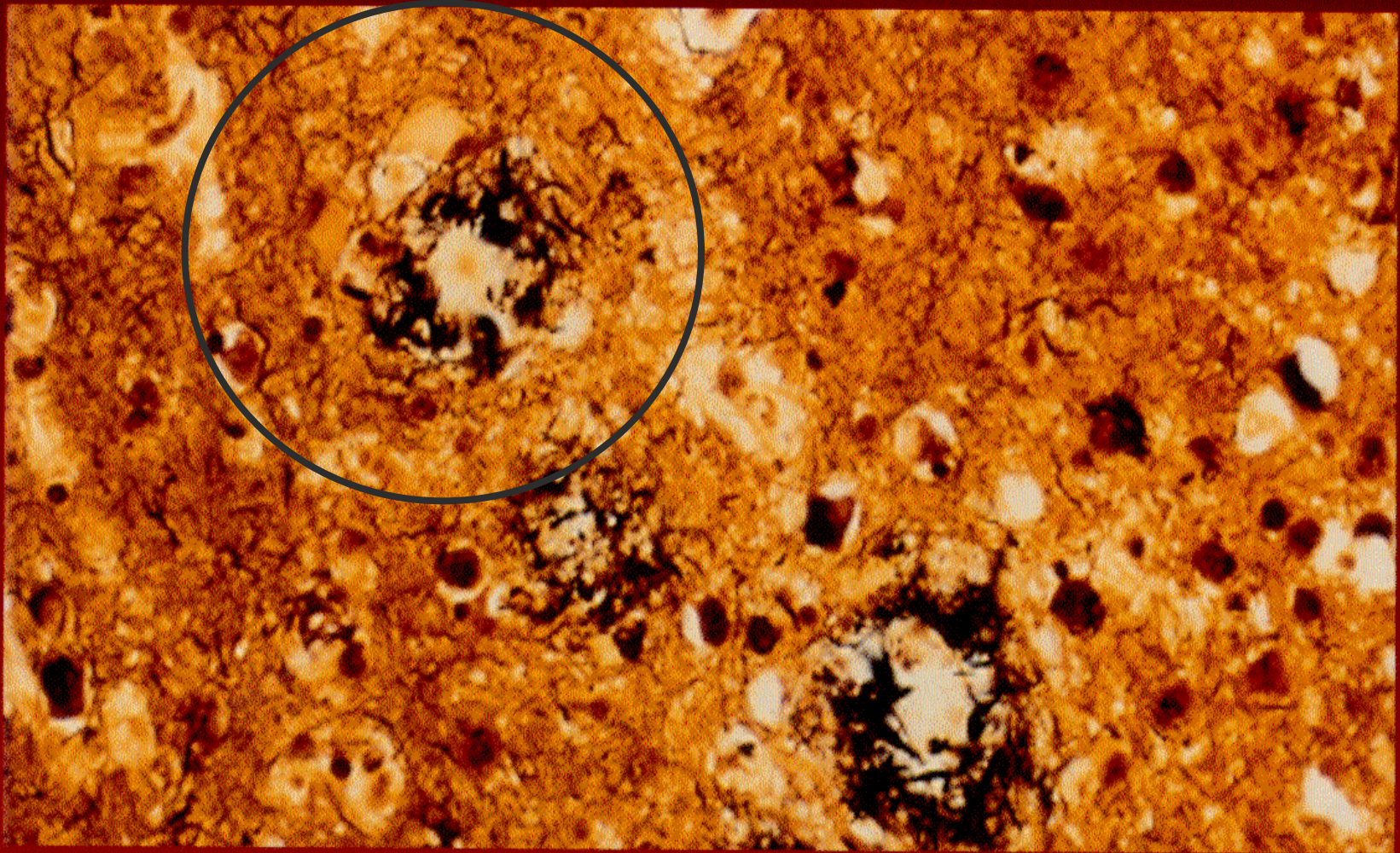


Alzheimer's

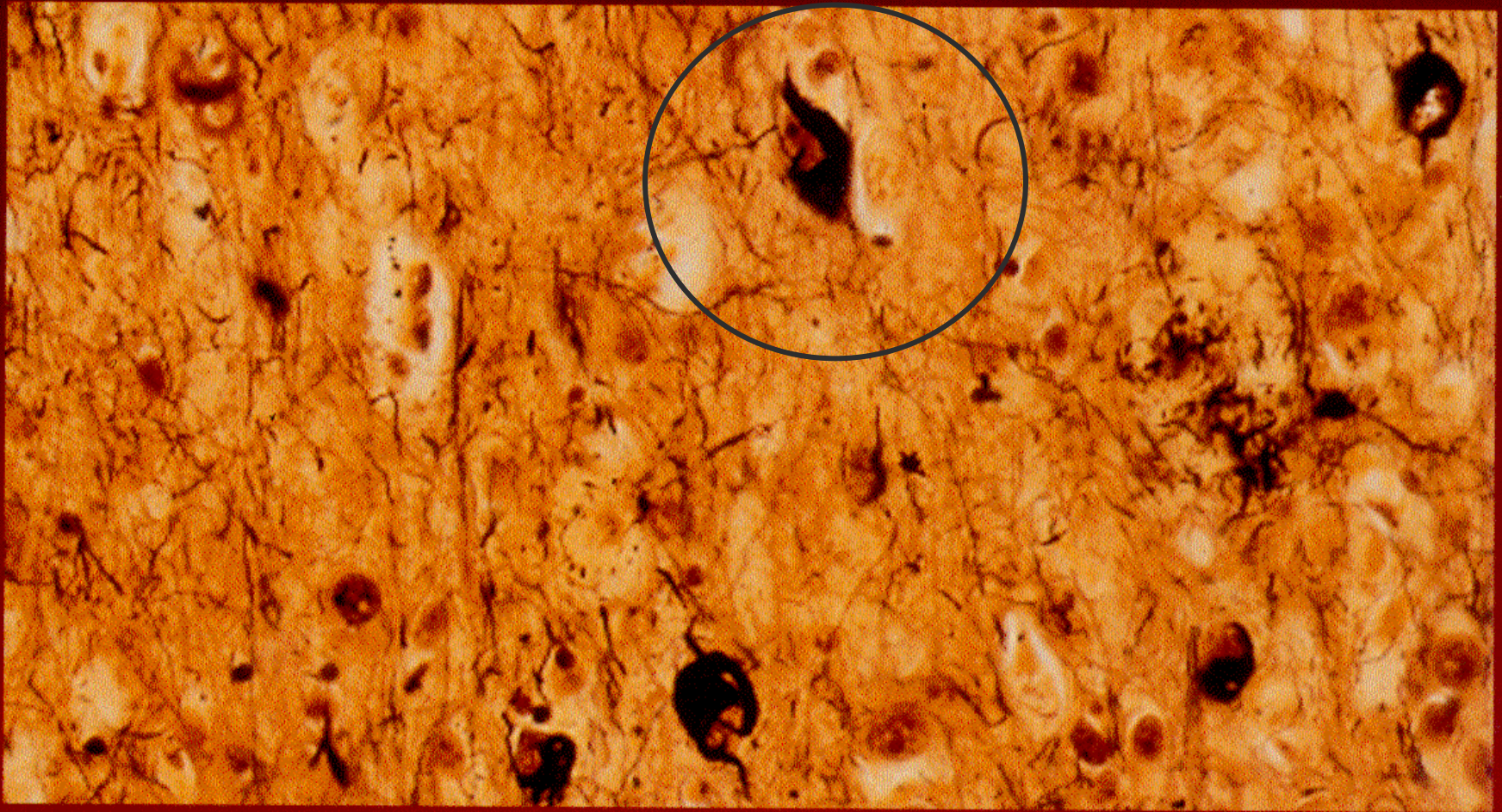


# Effects of Alzheimer's on the Brain

# AMYLOID PLAQUES

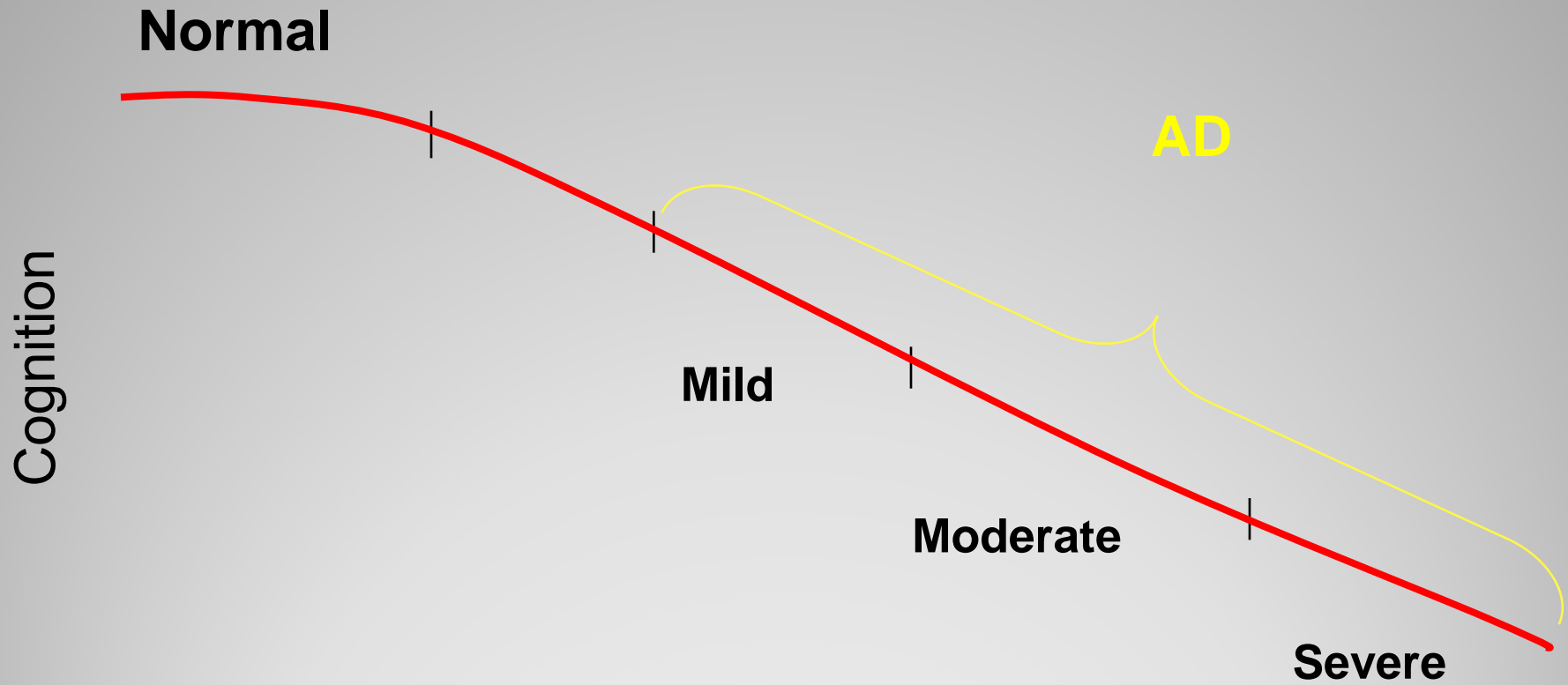


# NEUROFIBRILLARY TANGLES

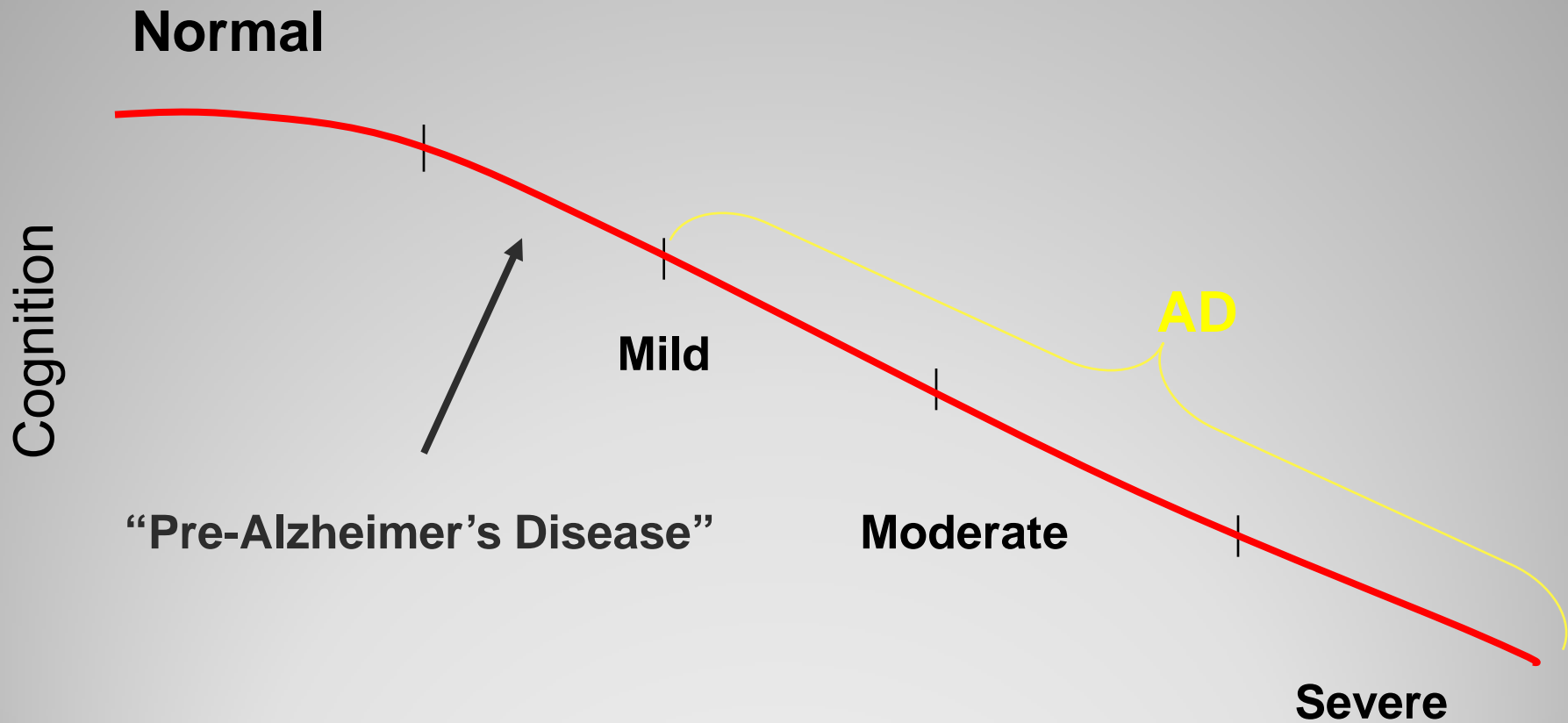


- Defining dementia
- Effects of dementia on the brain
- Stages and symptoms of Alzheimer's disease
- Treatment options and medications
- Current research

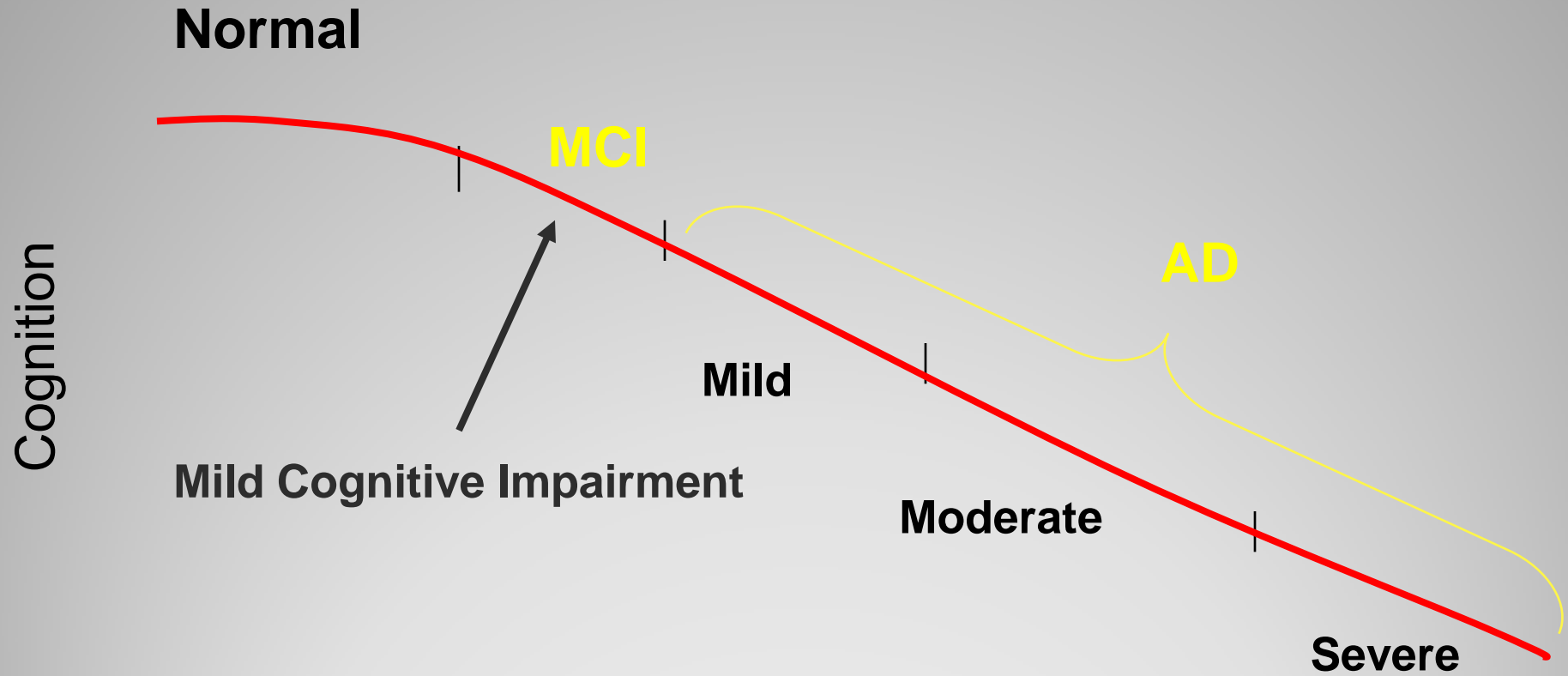
## Overview



# Stages of Alzheimer's Disease



# Stages of Alzheimer's Disease



# Stages of Alzheimer's Disease

## – Characterized by:

- Memory complaint, preferably corroborated by an informant
- Impaired memory function for age and education
- Preserved general cognitive function
- Intact social/occupational function
- Not demented on testing

**Mild Cognitive Impairment (MCI)**



- Mild AD characterized by:
  - Short-term memory loss
  - Difficulty performing familiar tasks
  - Altered judgment
  - Language changes
  - Changes in mood, behavior, personality
  - Disorientation to time and place
  - Problems with abstract thinking

## Stages of Alzheimer's Disease

- Moderate AD characterized by:
  - Worsening memory loss
  - Difficulty performing familiar tasks
  - Poor judgment
  - Language changes
  - Changes in mood, behavior, personality
  - Disorientation to time and place
  - Problems with abstract thinking
  - Changes in sensory perception
  - Physical changes

## Stages of Alzheimer's Disease

- Severe AD characterized by:
  - Little or no short-term memory
  - Inability to perform tasks
  - Lack of judgment
  - Unable to communicate
  - Physical decline

## Stages of Alzheimer's Disease

- Delusions
- Suspiciousness
- Hostility
- Hallucinations
- Feelings of persecution
- Incoherence
- Overexcitability
- Emotional withdrawal or isolation
- Apathy
- Social withdrawal
- Lack of feelings or inappropriate emotion (e.g., laughing at the death of a loved one)

**What Are Some Behavioral Changes Seen with Dementia?**

- Clinical diagnosis – no one test can confirm the disease
- Constellation of:
  - History from patient and family
  - Cognitive testing
  - Physical exam
  - Lab tests (to rule out other conditions)
  - CT scan or MRI scan of the brain (test for amyloid deposition and if any concern for mini-strokes, etc.)
  - Genetic evaluation



## How Do You Diagnose Alzheimer's Disease?

- Memory task
  - “What were the 3 items I gave you to remember a few minutes ago?”
- Other areas of thinking assessed
  - Language
  - Judgment
  - Comprehension
  - Attention
  - Visual-spatial

## Cognitive Testing

- 30 point scale published in 1975
- Quick, universal, easy to give
- Sensitive and specific
- Must be consistent with asking, scoring
- Tests orientation, registration, attention/calculation, recall, language, and praxis
- Generally 24 or lower think possible dementia
- Mild cognitive impairment 20-24
- Moderate impairment 10-20
- Severe impairment <10
- With Alzheimer's, typically lose 2-4 points/year

## Mini-Mental Status Exam (MMSE)

- Simple but informative
- Tests memory, language comprehension, executive function, visuospatial, visuomotor, concentration, fine motor skills, math, visual fields.
- Ask to draw face, place numbers, draw hands to read either 11:10 or 8:20
- Either score as correct/incorrect or give one point each for drawing complete circle, numbered correctly positioned, all 12 numbers present, hands correct

## Clock Draw Exam



- Alzheimer's disease
- Lewy Body disease
- Vascular dementia
- Fronto-temporal dementia
- Parkinson's disease

## Other Causes of Dementia

– Characterized by:

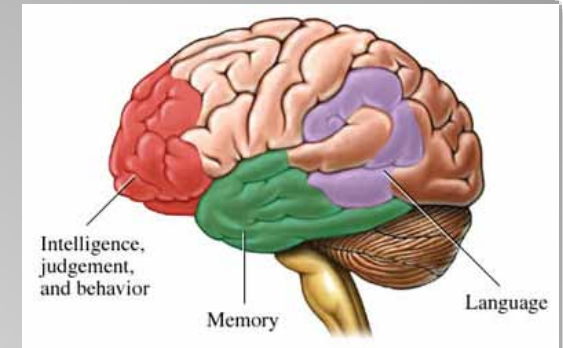
- Fluctuating cognition, attention, and alertness
- Recurrent visual hallucinations
- Parkinsonism
- Recurrent falls
- Syncope (fainting spells)
- Increased sensitivity to medicines used to control agitation (Haldol)
- Delusions
- Medications for Parkinson's may worsen hallucinations and delusions

## Lewy Body Disease

- Quick-onset of memory problems
- Risk factors for stroke (high blood pressure, diabetes, high cholesterol, etc.)
- “Step-wise” progression
- Commonly seen together with AD
- Will often see focal neurological signs

## Vascular Dementia

- Group of disorders affecting the frontal and temporal lobes (includes Pick's disease)



- Early findings may include apathy, anger, loss of inhibitions, rudeness, lack of empathy, changes in sexual behavior, and/or poor hygiene
- Memory loss occurs later in disease
- Patients lack awareness or concern that their behavior has changed

## Frontotemporal Dementia (FTD)

- Characterized by:
  - Tremors
  - Limb stiffness
  - Difficulty with speech
  - Difficulty initiating movement
- Late in the disease may develop memory problems
- If Parkinson's symptoms develop at the same time as memory loss, it most likely is Lewy Body disease

## Parkinson's Disease

- Autosomal dominant
- 5 to 7/100,000 prevalence
- Average age onset 40 yr. with progression and death in 17 years.
- Subcortical dementia with atrophy of caudate nucleus
- Triad
  - Dementia
  - Chorea (intermittent jerking limbs, trunk)
  - Positive family history
- Personality changes- irritability, apathy, typically prior to chorea
- Depression common in up to 50%

## Huntington's Disease

- Less than 2%, onset 60-70 yr. old
- Triad
  - Progressive dementia
  - Gait apraxia (fail to alternate legs)
  - Urinary incontinence
- Caused by impaired CSF circulation with ventricular dilation
- HCT/MRI - ventricular dilation with minimal atrophy
- CSF pressure, EEG, lab tests - normal
- Series of LPs monitoring for gait improvement

## Normal Pressure Hydrocephalus

- Prion - proteinaceous infective agent lacking DNA, RNA
- 1/1,000,000 annual incidence
- Rapidly progressive neurodegenerative disorder, fatal average 6 months
- Clinically - early fatigue, insomnia, anorexia, progression to dementia, behavioral disturbances, myoclonus
- Transmitted by corneal transplant, intracerebral EEG electrodes, tainted human growth hormone

## Creutzfeldt-Jakob Dementia (CJD)



- Cognitive impairment in 50% chronic alcoholics
- Direct toxic effects of alcohol and secondary vitamin deficiencies
- See confusion, gaze palsy, nystagmus, ataxia, retrograde and anterograde amnesia, peripheral neuropathies
- Chronic thiamine deficiency
- HCT/MRI - may be normal or show cerebral atrophy, hemorrhages in mammillary bodies
- EEG - normal

## Wernicke-Korsakoff

- Defining dementia
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## Overview

- Education and emotional support to the patient and their families
- Safety review
- Caregiver support
- Behavioral interventions
- Medical therapy

## **Treatment of Alzheimer's Disease**

- Medications used to treat Alzheimer's disease
- Medications used to treat behavioral symptoms (such as wandering and agitation)
- Medications used to treat depression and anxiety in Alzheimer's patients
- Potential preventive therapies

## Medical Therapy for AD

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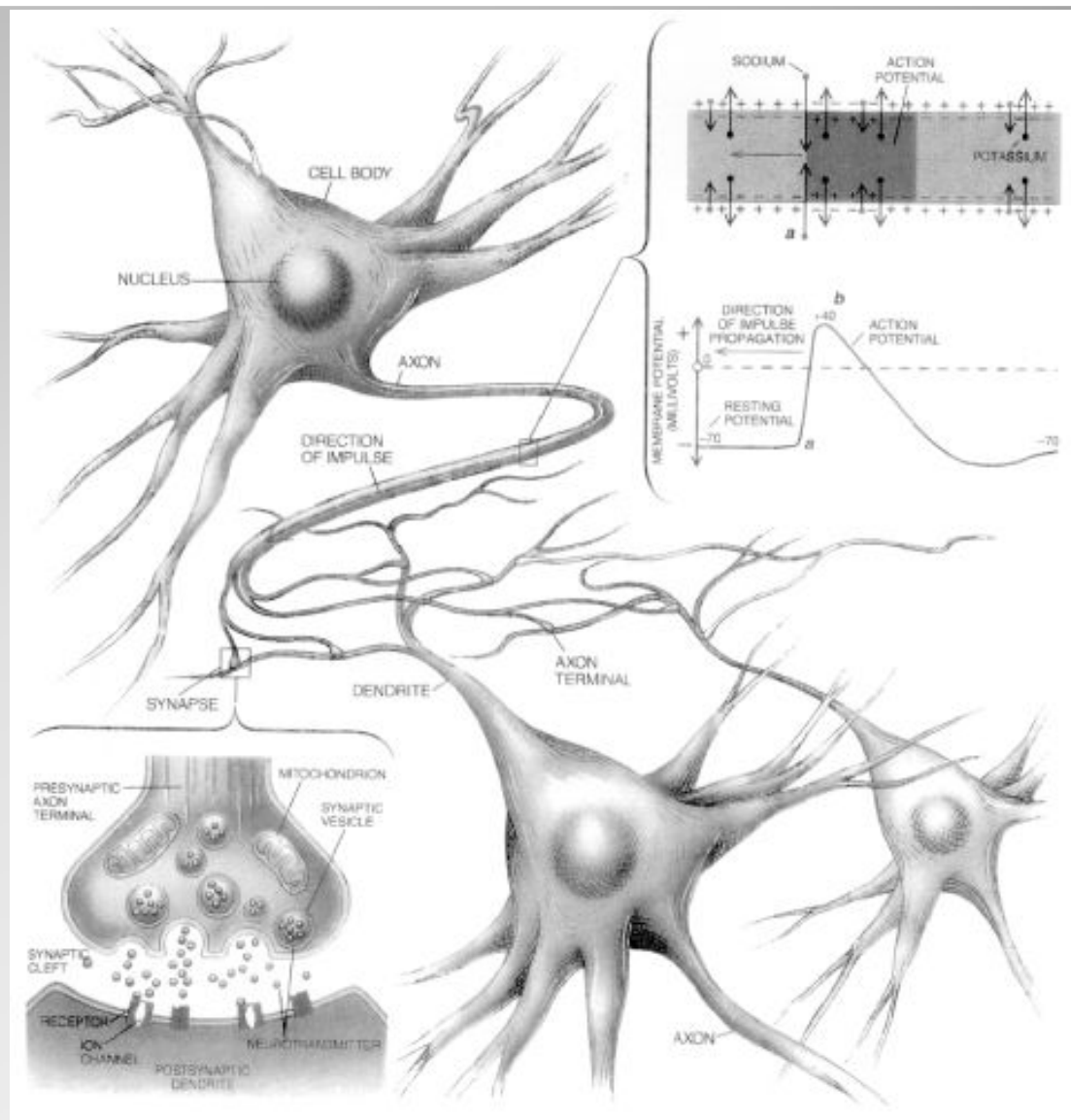
## Medical Therapy for AD

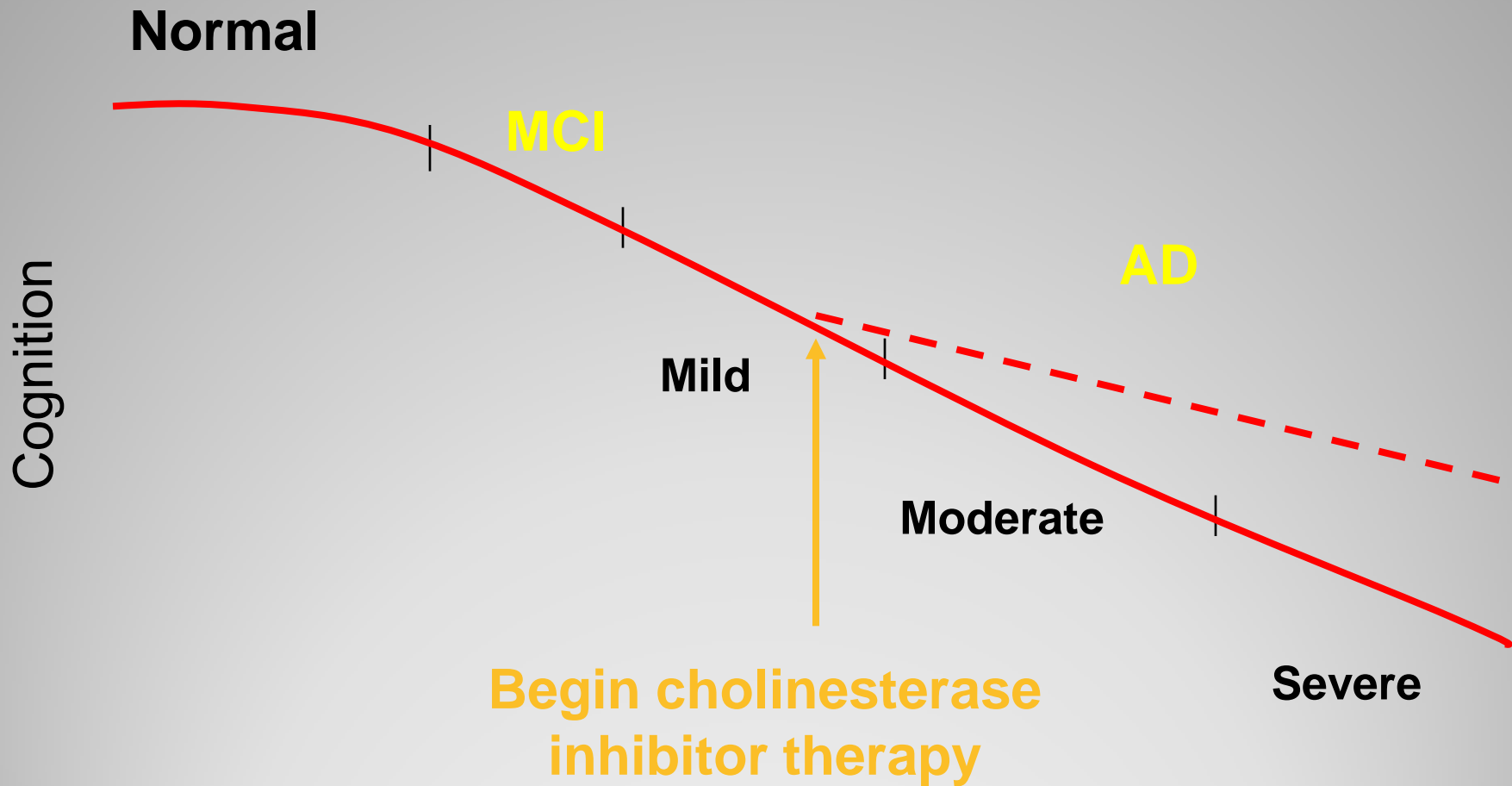
## FDA Approved Medications

- Acetylcholinesterase inhibitors (Mild to Mod AD)
  - Tacrine (Cognex)
  - Donepezil (Aricept)
  - Rivastigmine (Exelon)
  - Galantamine (Reminyl)
- NMDA receptor antagonist (Mod to Severe AD)
  - Memantine (Namenda)

**Medications used to treat  
Alzheimer's disease**

Acetylcholinesterase inhibitors block an enzyme which breaks down acetylcholine in the space between nerve cells





# Stages of Alzheimer's Disease



Cognition

Normal

MCI

Mild

AD

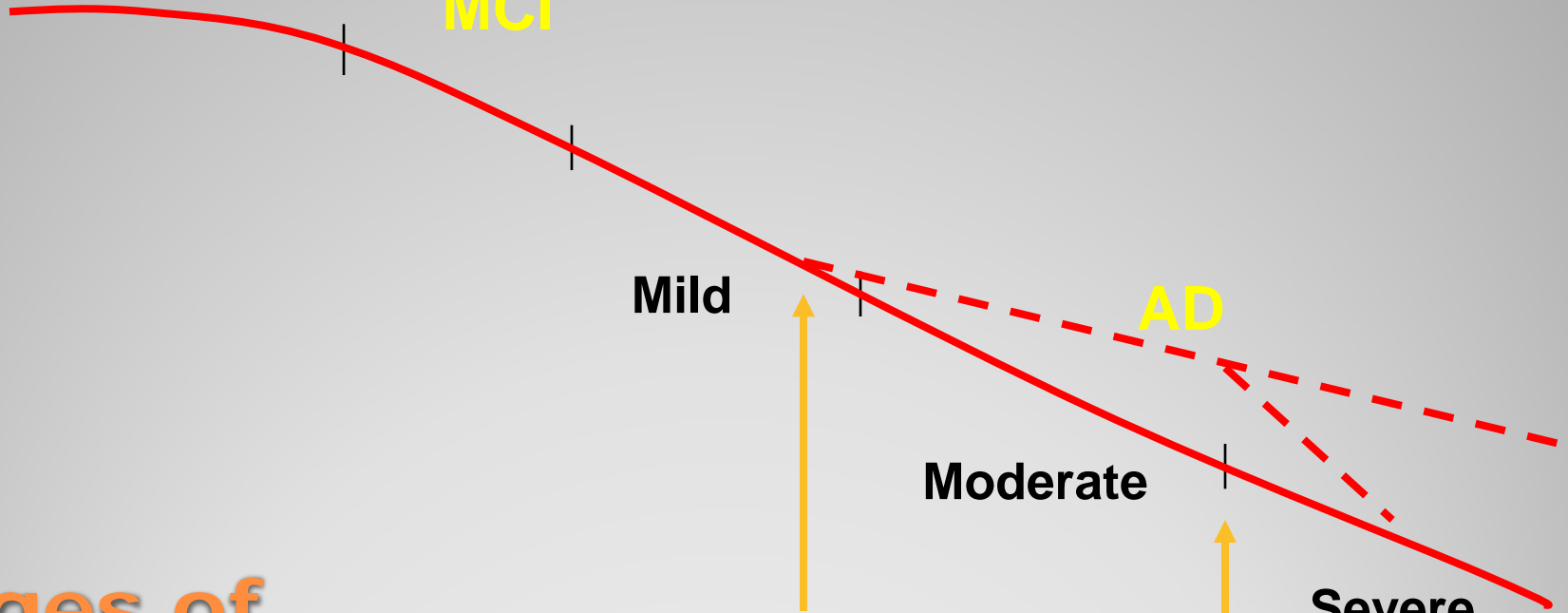
Moderate

Severe

# Stages of Alzheimer's Disease

Begin cholinesterase inhibitor therapy

Stop cholinesterase inhibitor therapy



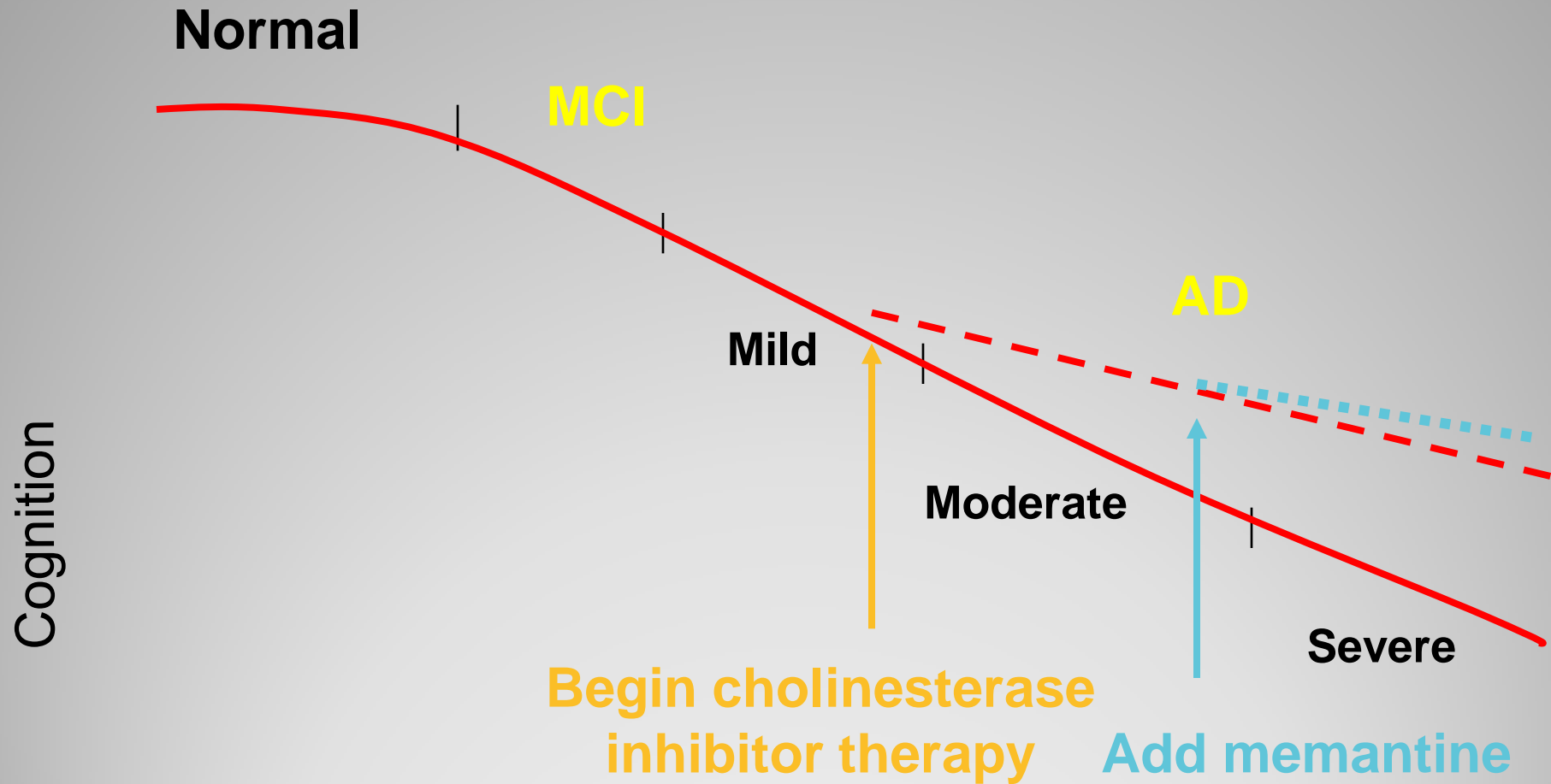
## – Cholinergic drugs

- Delay the progression of memory loss
- Delay time to nursing home placement
- Improve behavioral symptoms
- Help relieve some caregiver burden

**Visuospatial**

- Memantine (Namenda)
  - Works by protecting cells from too much glutamate, a chemical released in excess by damaged brain cells in Alzheimer's disease
  - Approved by FDA in January 2004
  - Useful in combination with cholinesterase inhibitors
  - Indicated for moderate to severe AD (MMSE score <14)

## NMDA Antagonists



# Stages of Alzheimer's Disease

- Medications used to treat Alzheimer's disease
- Medications used to treat behavioral symptoms (such as wandering and agitation)
- Medications used to treat depression and anxiety in Alzheimer's patients
- Potential preventive therapies

## Treatment of Alzheimer's Disease

# Medications may not be needed!

- Agitation
  - Risperidone (Risperdal)
  - Olanzapine (Zyprexa)
  - Quetiapine (Seroquel)
  - Haloperidol (Haldol) – avoid in persons with Lewy Body disease
- Insomnia
  - Trazodone
  - AVOID BENEDRYL (INCLUDED IN TYLENOL P.M.) AND SEDATIVES LIKE VALIUM!

**Medications used to treat behavioral symptoms**

- Medications used to treat Alzheimer's disease
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## Treatment of Alzheimer's Disease

- Depression
  - Fluoxetine (Prozac)
  - Paroxetine (Paxil)
  - Sertraline (Zoloft)
  - Citalopram (Celexa)
  - Venlafaxine (Effexor)
- Anxiety (use with caution!- may worsen symptoms)
  - Lorazepam (Ativan)
  - Alprazolam (Xanax)
  - Buspirone (Buspar)

**Medications used to treat depression and anxiety**



- Mood and anxiety symptoms may improve with cholinergic drugs
- Some medications used for anxiety (like Ativan) may actually lead to increased agitation
- Increased socialization may help with some depression and anxiety symptoms

**Medications used to treat depression and anxiety**

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- Alzheimer's Association research link
  - <http://www.alz.org>
- Alzheimer Research Forum
  - <http://www.alzforum.org/home.asp>
- Alzheimer's Disease Education & Referral (ADEAR) Center (National Institute on Aging)
  - <http://www.alzheimers.org/nianews/nianews.html>

**Current AD Research – International and National**

- UW Medical School and Madison VA GRECC Wisconsin Comprehensive Memory Program
  - o Clinical trials for:
    - Women and men with AD
    - Adult children of persons with AD (*Wisconsin Registry for Alzheimer's Prevention [WRAP]*)
    - Persons with Mild Cognitive Impairment (MCI)
    - Healthy adults without memory complaints

**Current AD Research – Local**

- Current areas under investigation at Wisconsin Comprehensive Memory Program:
  - Functional MRI
  - Hormone therapy (women and men)
  - Isoflavonoids
  - Statin therapy (AD prevention and treatment)

**(608) 263-2582 or toll free 1-866-MEM-PROG**

**Current AD Research – Local**



**There is hope...**

