

# Alzheimer's Disease

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# Alzheimer's Disease: More Than Memory Loss

- **Progressive memory impairment**
- **Language affected**
- **Poor visual recognition**
- **Learnt sequences lost**
- **Impaired social or occupational function**
- **Changes in personality, behavior, and judgment**

# Making the Diagnosis of Alzheimer's Disease

- **History**
- **Physical**
- **Neurologic and Mini–Mental exam**
- **Blood tests**
- **Imaging studies: CT, MRI**

# Symptoms of Alzheimer's Disease

1. Memory loss affecting skills
2. Difficulty performing familiar tasks
3. Problems with language
4. Disorientation regarding time or place
5. Impaired judgment
6. Problems with abstract thinking
7. Misplacing objects
8. Changes in mood or behavior
9. Changes in personality
10. Loss of initiative

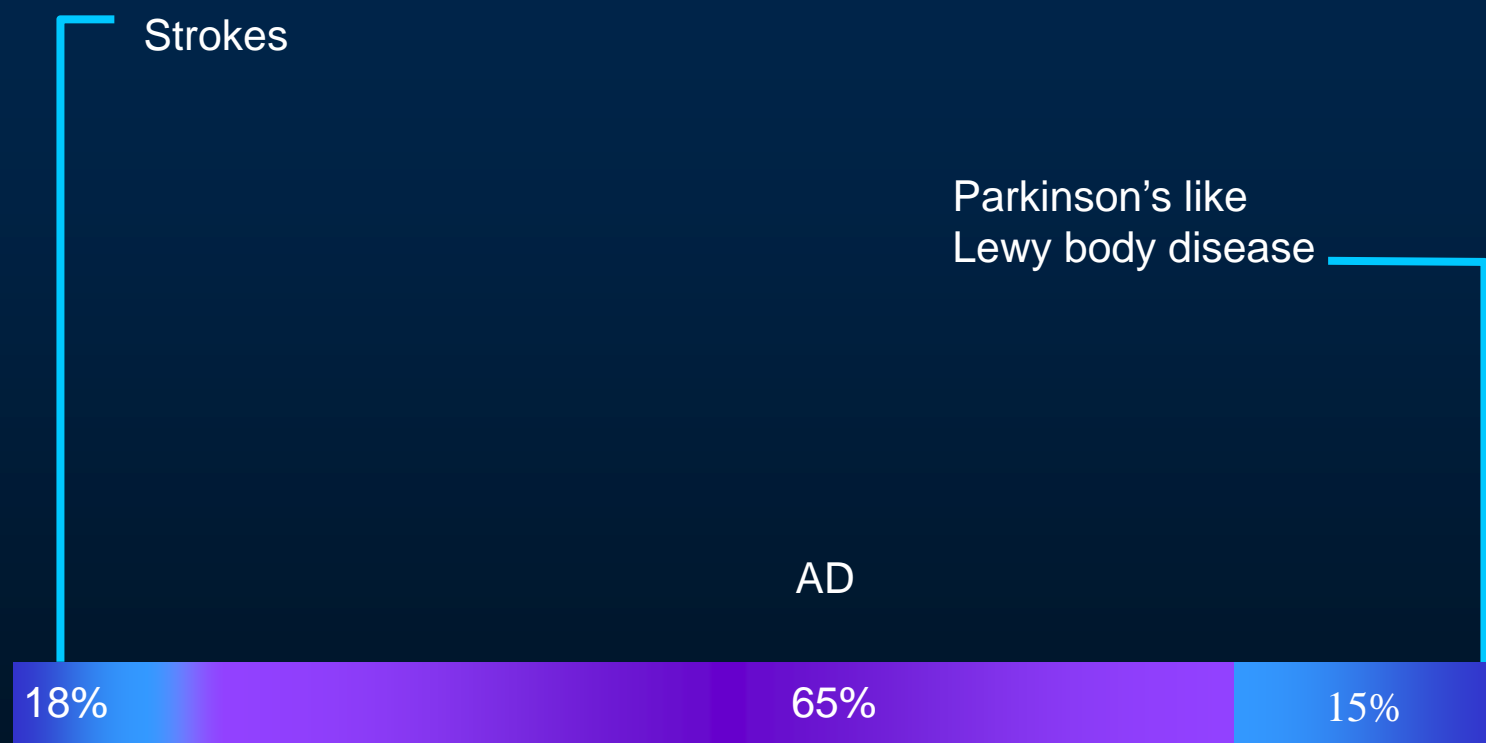
# Barriers to Early Detection of Alzheimer's Disease

- **Misidentification by the family of early signs as normal aging process**
- **Social skills often maintained in early AD**
- **Denial and lack of insight by patient**
- **Reluctance to report symptoms — stigma**
- **Lack of definitive screening tools**

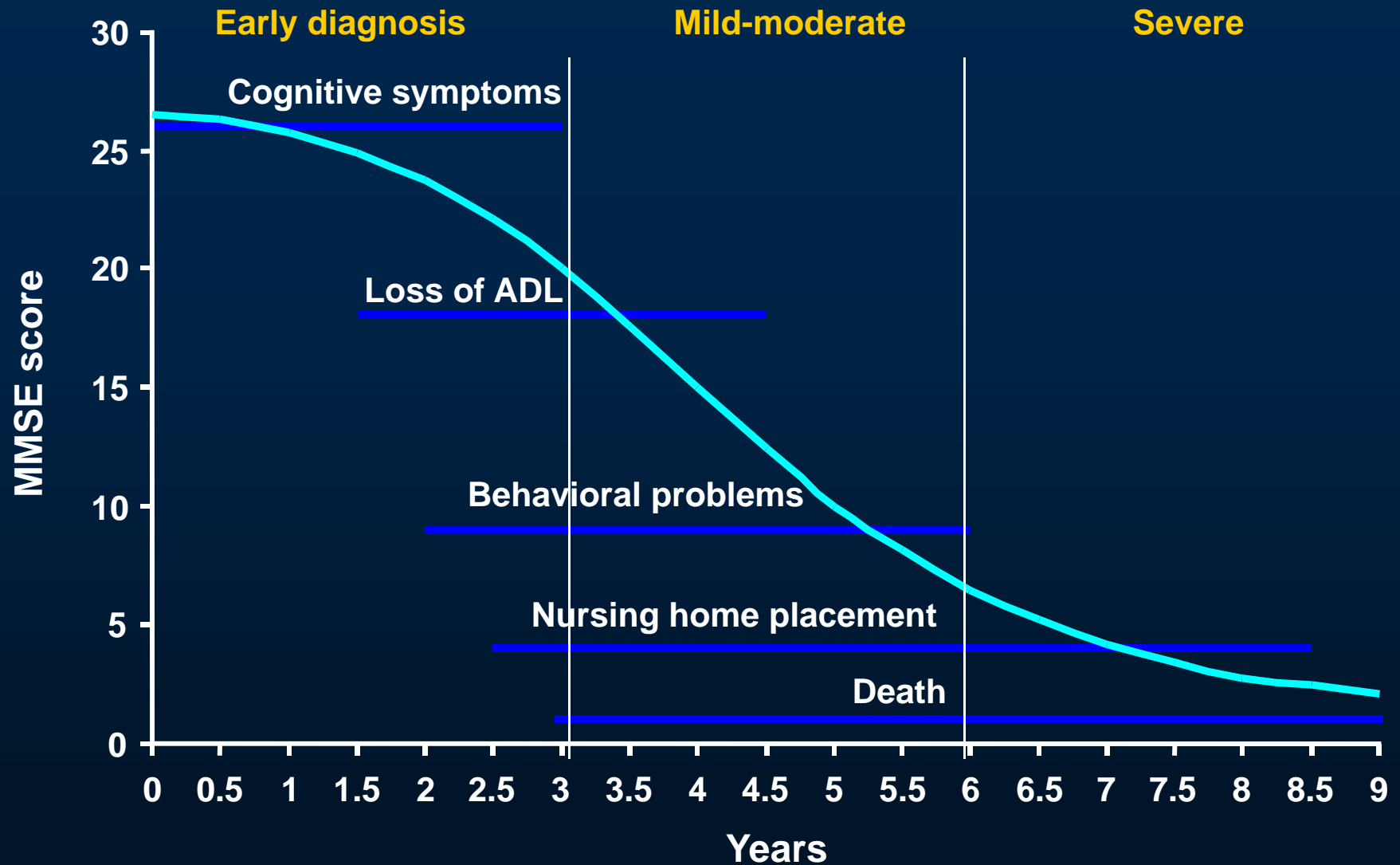
# Prevalence and Impact of AD

- **AD is the most common cause of dementia**
- **Affects 10% of the population over the age of 65 and 50% over the age of 85**
- **Approximately 4 million AD patients in the United States**
- **Annual treatment costs = \$100 billion**
- **AD is the fourth leading cause of death in the United States**
- **The overwhelming majority of patients live at home and are cared for by family and friends**

# Differential Diagnosis of Dementia



# Progress of AD





# Patient Functioning as Disease Progresses

## Stages of Alzheimer's Disease

	Mild	Moderate	Severe
Activities of daily living (ADLs)	Problems with routine tasks	Needs help with basic ADLs (e.g., feeding, dressing, bathing)	Progresses to total dependence on caregiver (e.g., feeding, toileting)
Behavior	Changes in personality	Anxiety, suspicion, pacing, insomnia	Agitation, wandering
Cognition	Confusion and memory loss	Difficulty recognizing family and friends Chronic loss of recent memory	Loss of speech Misidentifies or is unable to recognize familiar people

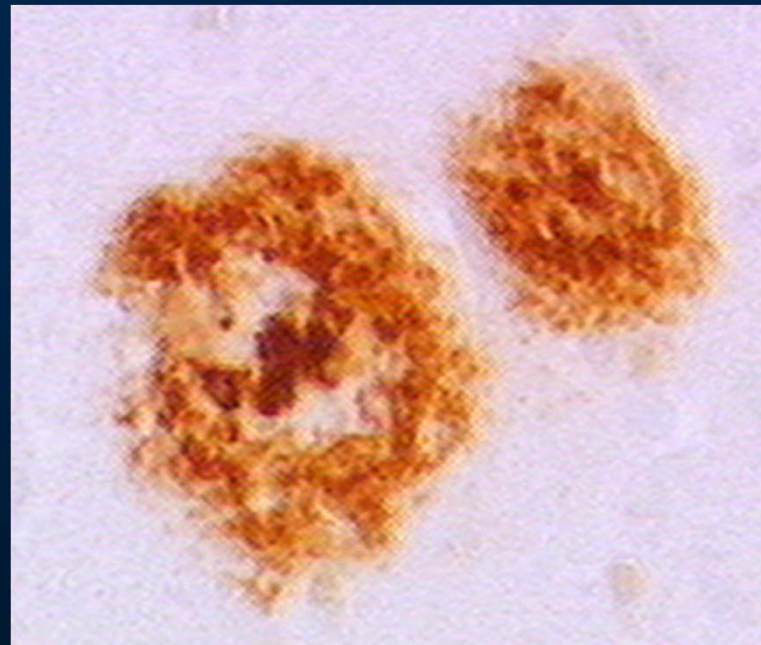
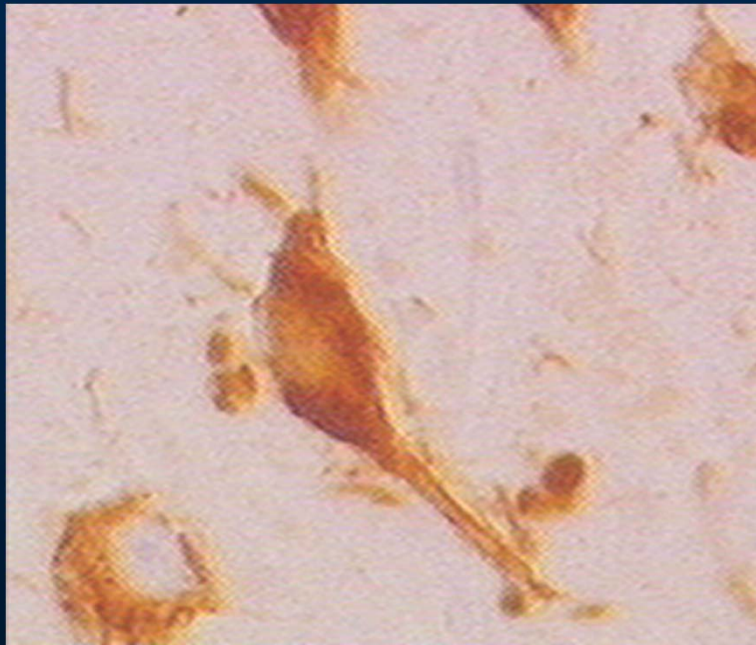
# Impact of Alzheimer's Disease on Caregivers

- **More than 70% of patients with Alzheimer's disease live at home, and almost 75% of home care is provided by family and friends**
- **46% to 59% of caregivers are depressed, according to various studies**
- **Caregivers get more medical illnesses than non-caregivers**

# Alzheimer's Disease in the Long-Term Care Setting

- **Alzheimer's disease affects a significant population in long-term care facilities**
  - **1.5 million people resided in certified nursing facilities from 1999 to 2000**
  - **Approximately 45% of nursing home residents have AD**

# Neurofibrillary Tangles and Amyloid Plaques



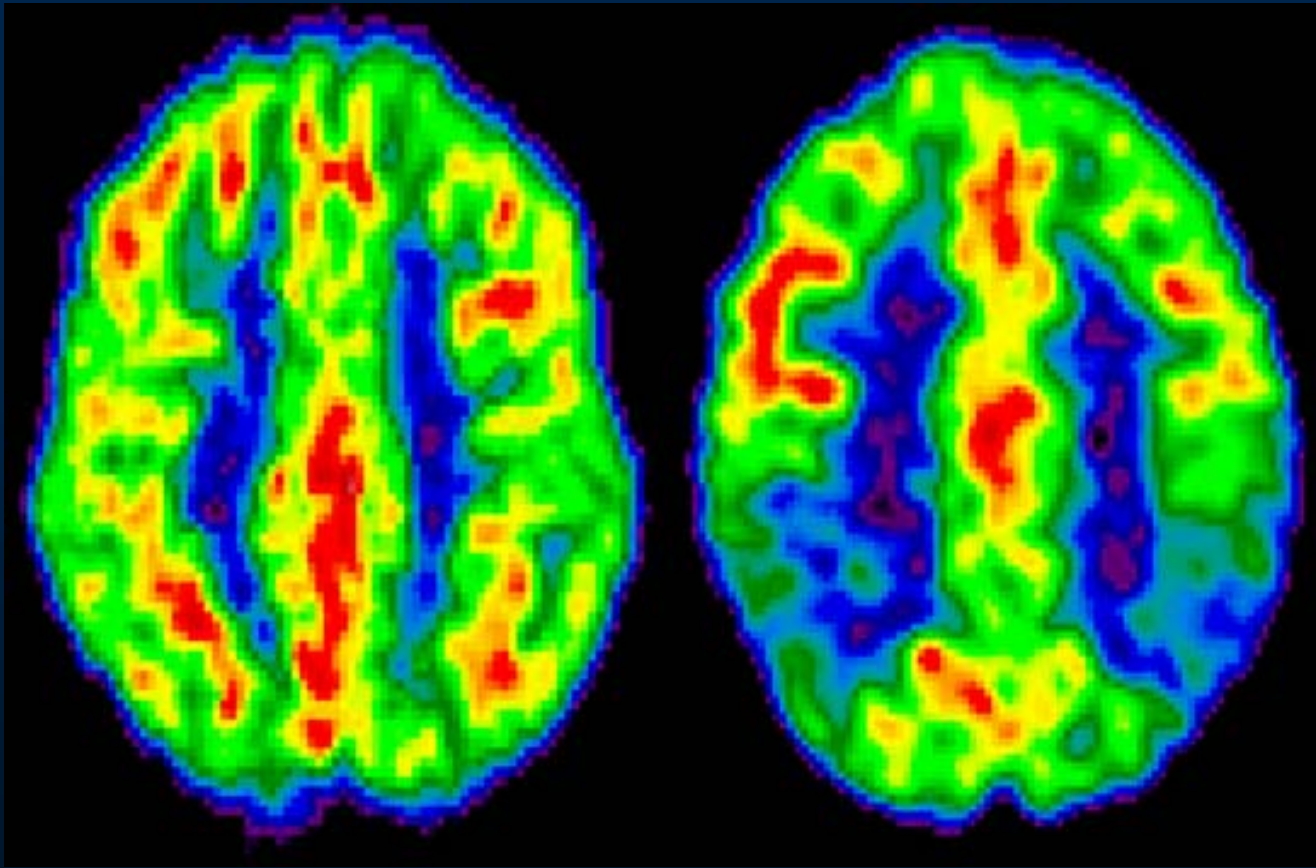
# Brain Scans

- **CT/MRI are especially indicated for:**
  - **Headache**
  - **Abrupt or rapid onset of cognitive decline**
  - **Onset of dementia before age 65**
  - **Gait changes or motor signs**
  - **Seizures**

# SPECT and PET

- **Cerebral blood flow and glucose metabolism can be measured by single photon emission computed tomography (SPECT) and positron emission tomography (PET)**
- **SPECT and PET typically show reduced activity in the parietal lobes in AD**

# Typical AD PET Scan



Provided courtesy of M. Mega, MD, PhD, Department of Neurology, UCLA School of Medicine.

# Laboratory Tests

- Complete blood count
- Serum electrolytes (including calcium)
- Liver function tests
- BUN and creatinine
- Thyroid-stimulating hormone
- Serum vitamin B<sub>12</sub> level
- ESR
- HIV Serology



# Tests

- Apolipoprotein E genotyping
  - **Not recommended for screening**
    - 50% of AD patients do not carry APOE  $\epsilon$ 4

Roses AD. *Ann Neurol.* 1995;38:6-14. Kurz A et al. *Alzheimer Dis Assoc Disord.* 1998;12:372-377.

Tapiola T et al. *Neurobiol Aging.* 2000;21:735-740.

Padovani A., et al *Arch Neurol* 59:71-75, January 2002

# Possible Risk Factors

- Age
- Family history
- Female gender
- Low testosterone
- Head injury
- Strokes
- Depression
- Elevated plasma homocysteine levels
- APO E genotype and Down's syndrome

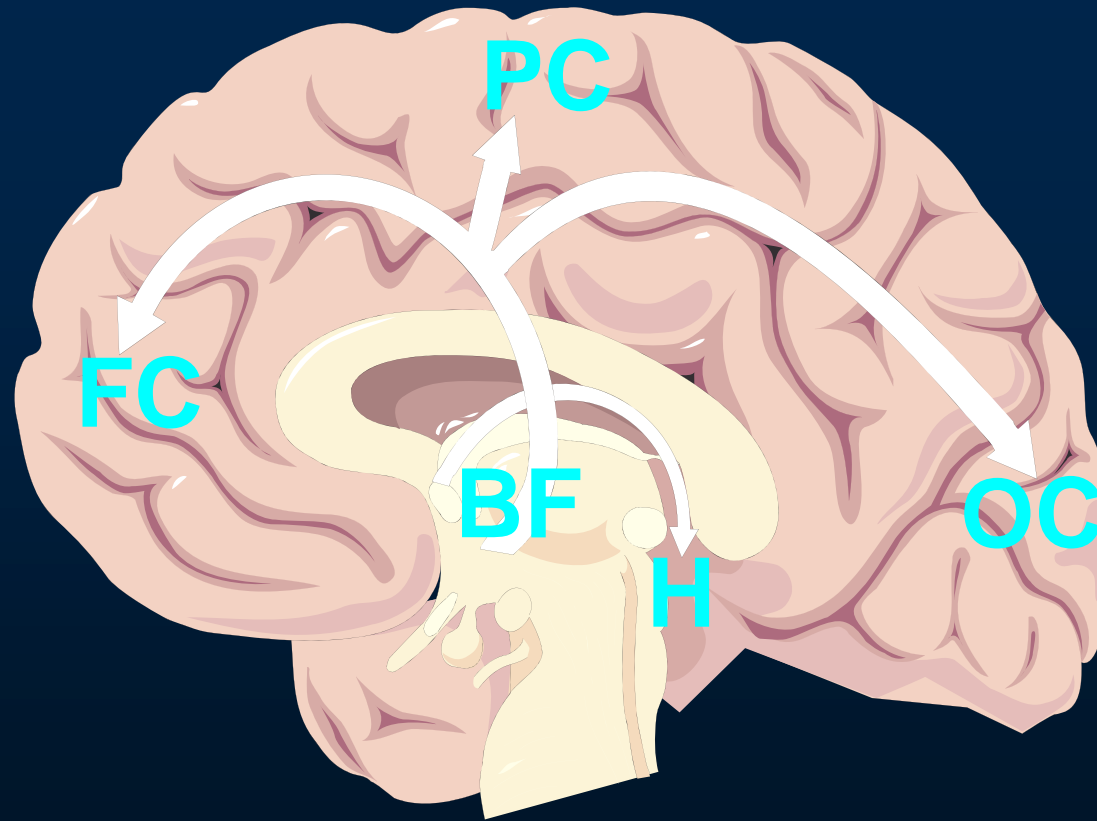
# Risk Reduction?

- ? Cholesterol lowering agents
- ? Antioxidants: Vitamin E and C
- ? Anti-inflammatories
- ? Estrogen
- ? Reduce Homocysteine: Folate
- Aspirin

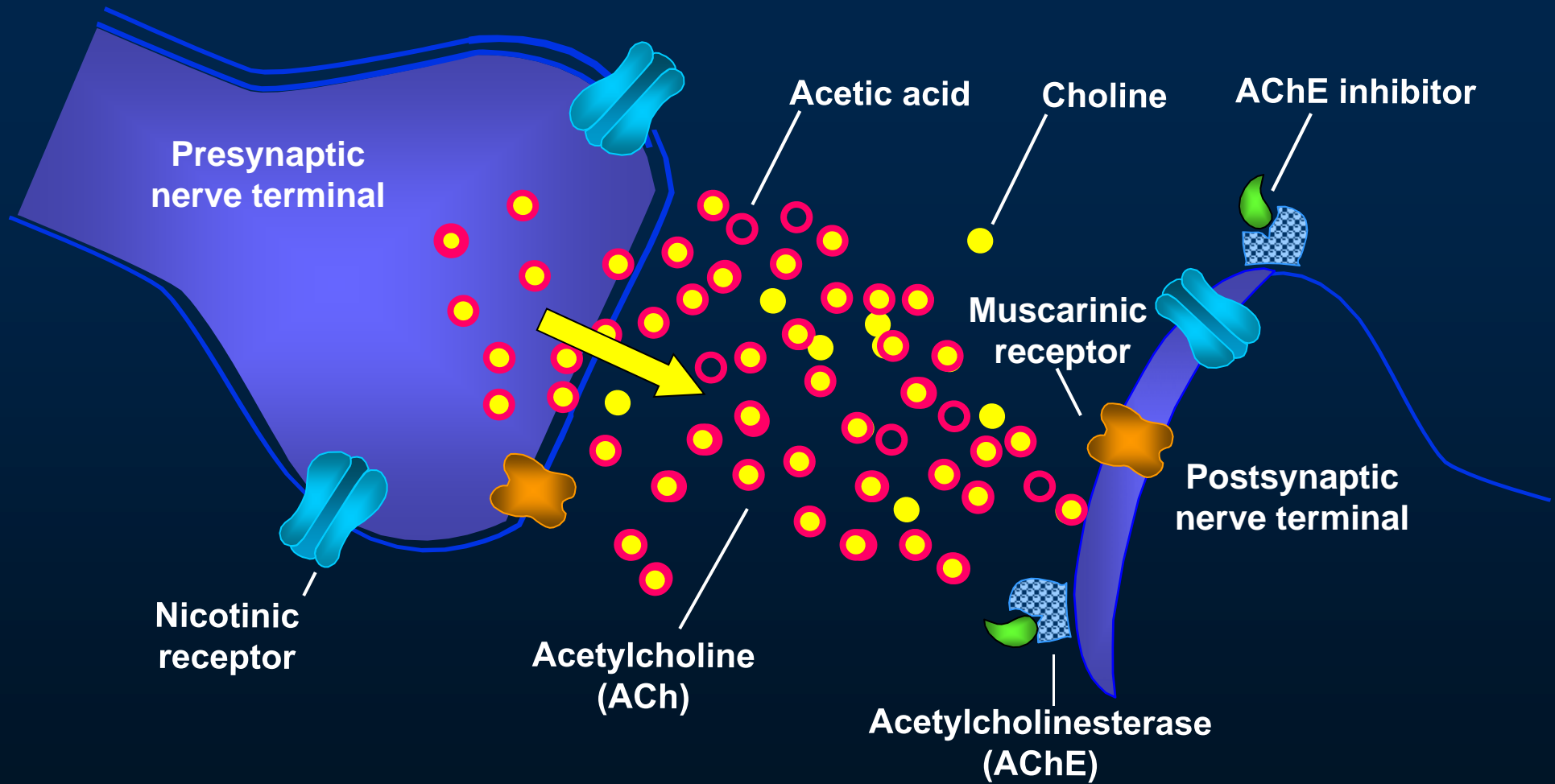
# Other Topics

- **Advance Directives**
- **DMV reporting**
- **Community Social Services**

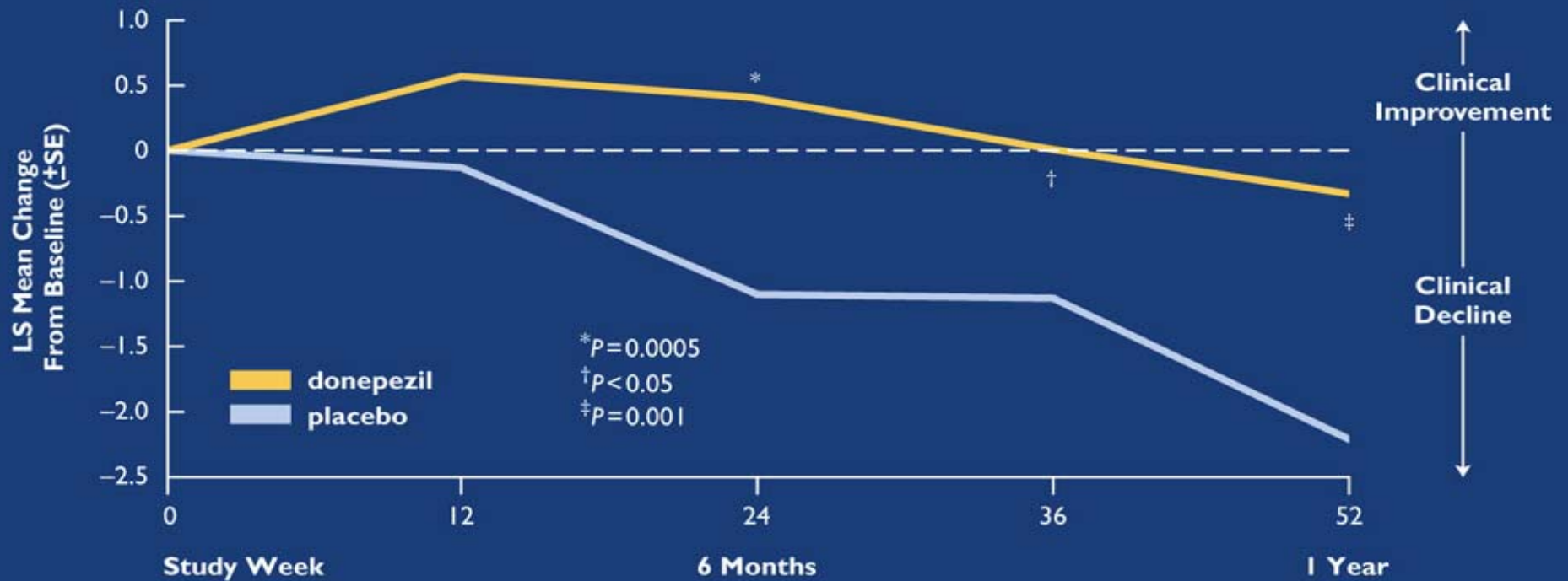
# Cholinergic Pathways From the Basal Forebrain



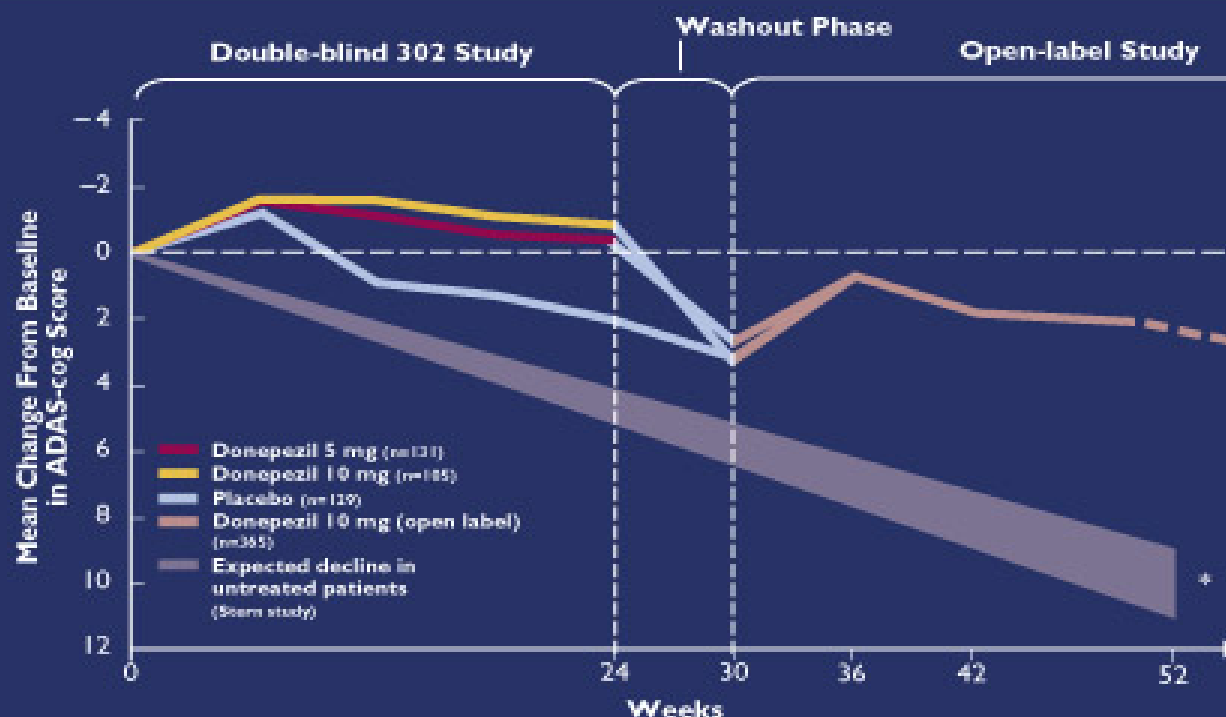
# Acetylcholinesterase Inhibition



# Donepezil significantly improved cognition versus placebo as measured by MMSE scores in a 1-year, multinational clinical trial



## Treatment benefits were lost when donepezil was discontinued as measured by the decline in ADAS-cog scores in an open-label extension of Study 302



\*Other studies have estimated the decline to range from 6 to 12 points annually.

Doody, Geldmacher, Gordon, Perdomo, et al, 2001.

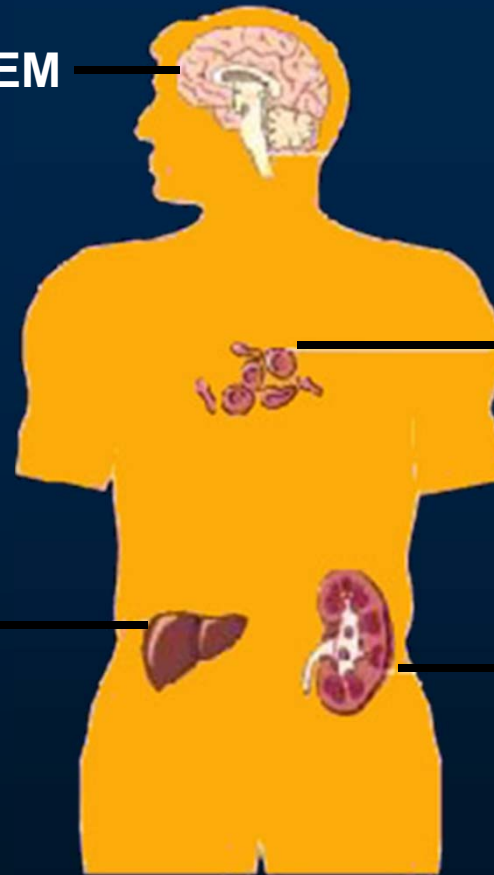
Stern, Mohs, Davidson, Schmeidler, et al, 1994.



# Metabolism of medications

## CENTRAL NERVOUS SYSTEM

Inhibits the target enzyme in the central nervous system



## PLASMA

Blood plasma half-life is hours

## METABOLISM

Metabolism is via simple enzyme hydrolysis

## KIDNEYS

Metabolite is excreted

# Most frequent adverse events in a 1-year, multinational, placebo-controlled clinical trial\*

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- **Asthenia (8% versus 4% placebo)**
- **Syncope (6% versus 3% placebo)**
- **Vertigo (8% versus 2% placebo)**

\*Occurring in  $\geq 5\%$  and at least twice the rate of placebo-treated patients.

# ADVERSE EVENTS REPORTED IN CONTROLLED CLINICAL TRIALS RECEIVING RIVASTIGMINE (6-12 MG/DAY)

Body System / Adverse Event	Titration		Maintenance	
	Placebo (n = 868)	Exelon® (6-12 mg/day) n = 1189)	Placebo (n = 788)	Exelon® (6-12 mg/day) (n = 987)
<b>Percent of Patients with any Adverse Event</b>	<b>66</b>	<b>86</b>	<b>56</b>	<b>69</b>
Nausea	9	43	4	17
Vomiting	3	24	3	14
Dizziness	9	17	4	9
Headache	10	15	5	6
Diarrhea	9	15	4	8
Anorexia	2	14	2	5
Abdominal Pain	4	10	3	5
Fatigue	4	7	1	3
Dyspepsia	4	7	1	3
Confusion	6	7	3	4

# Visit and Dosing Schedule

Visit	Donepezil	Rivastigmine
Baseline	Start 5 mg/day qd	Start 1.5 mg/day bid
Week 2	–	↑ to 3 mg/day bid
Week 4	↑ to 10 mg/day qd	↑ to 4.5 mg/day bid
Week 6	Telephone interview	↑ to 6 mg/day bid
Week 8	–	Telephone interview
Week 12	Study completion	Study completion

- Study medication was dosed in accordance with approved product labeling
- Dose reductions were permitted if current dose was not tolerated

# Memantine

- **Combination treatment**
  - **Additional treatment with 10 mg twice daily of memantine**
  - **Dual-treated patients showed significantly greater improvement, and less decline**
  - **Less nausea and diarrhea**

# Treatment of Depression, Agitation, Insomnia and Hallucinations

- **Avoid Tricyclic Antidepressants and Benadryl**
- **Insomnia: Trazadone**
- **Depression: SSRI's**
- **Behavior problems: Aricept, Exelon, Reminyl**
- **Hallucinations: Risperidal, Zyprexa or Geodon**

Thank You!