NEUR 1520 Neuroscience Study Guide for Exam 2: Lecture 16: The Aging Brain and Alzheimer's

Sources: the lecture slides and The Mind's Machine, Chapter 4. Nothing else.

Each heading is one book learning objective. [L13 s08] = Lecture 13, slide 8. [MM p124] = book page 124.

(teal italics) = plain meaning of the word before it. ⚠ **Do not mix up = a look-alike pair to keep apart.** **Amber dotted words** = names printed on the figure beside them.

Contents

4.4.1 Describe the current model of processes underlying the degeneration seen in Alzheimer's disease 1

4.4.2 Critique the amyloid hypothesis of Alzheimer's 3

4.4.3 Discuss how brain imaging may help us understand the mechanism(s) of Alzheimer's 4

Click a line to jump to it. The PDF side panel (bookmarks) has the same parts.

4.4.1 Describe the current model of processes underlying the degeneration seen in Alzheimer's disease

⚠ **Do not mix up: Tangle NUMBER tracks how bad cognitive impairment is; tangles are probably SECONDARY to plaques.** [MM p140]

Review, low licking and grooming: methyl groups are added and gene expression is reduced. [L16 s02, L16 s03]

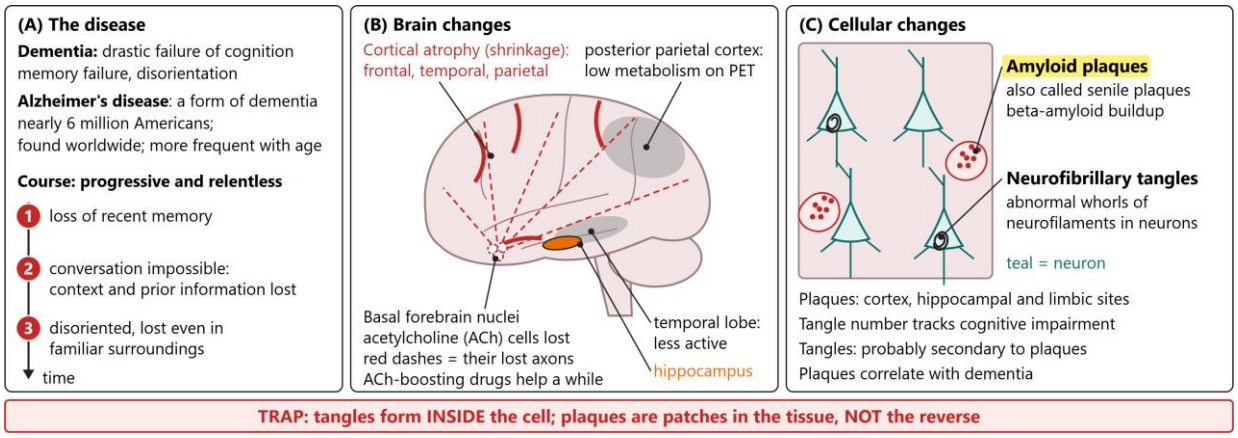
Review, high licking and grooming: no methyl groups are added and gene expression is high. [L16 s02, L16 s03]

Slower responses seem inevitable with aging, but many cognitive abilities change little until advanced age. [MM p138]

Most people reaching an advanced age lead happy, productive lives, at a slower pace. [MM p138]

PET scans: cerebral metabolism normally stays almost constant as we age. [MM p138]

Alzheimer's disease instead shows a dramatic decline in brain activity. [MM p138]



Alzheimer's disease course, brain changes, and the cell changes in plaques and tangles [MM p139]

On the figure: dementia · Alzheimer's disease · cortical atrophy · posterior parietal cortex · amyloid plaques · senile plaques · neurofibrillary tangles · basal forebrain

Dementia: drastic failure of cognitive ability, including memory failure and disorientation. [L16 s05, MM p139]

Alzheimer's disease: a form of dementia; may appear in middle age, more frequent in the aged. [L16 s05, MM p139]

Nearly **6** million Americans have Alzheimer's, a number that will keep growing as the population ages. [MM p139]

Alzheimer's is found worldwide with almost no geographic differences. [MM p139]

Alzheimer's frequency **increases** with aging up to age **85** to **90.** [MM p139]

People reaching that age symptom-free become less and less likely to ever develop them. [MM p139]

So Alzheimer's is a disease, not simply wear and tear in the brain. [MM p139]

Staying physically and mentally active reduces risk, also refuting the idea that brains simply wear out. [MM p139]

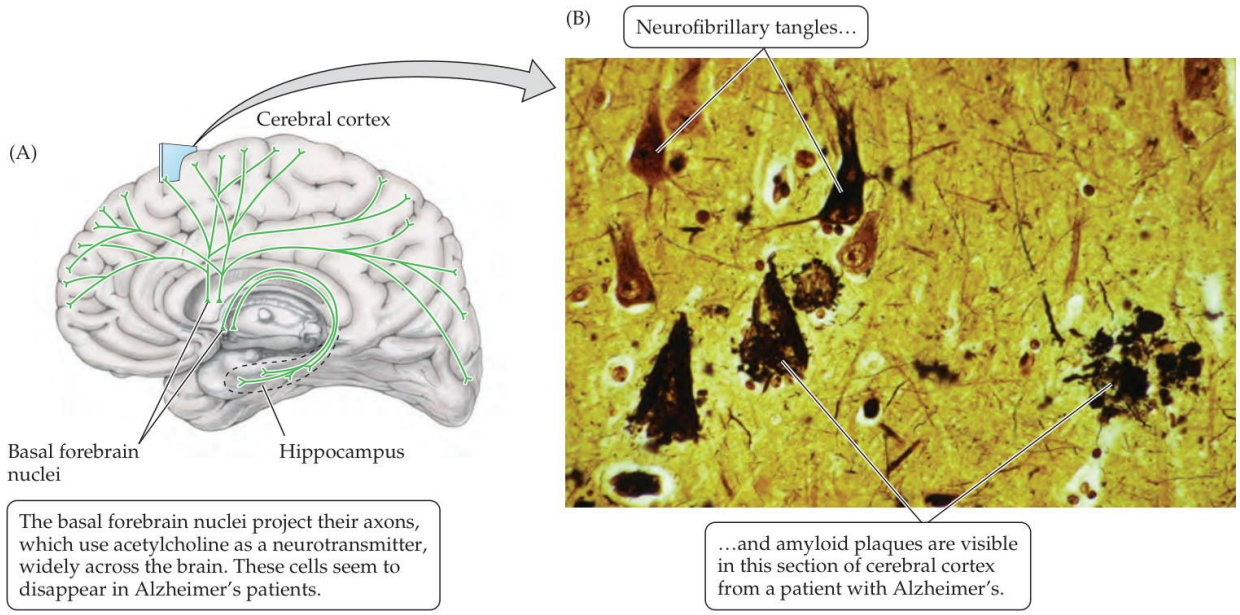
1. Begins as memory loss of recent events. [L16 s05, MM p139]

2. Memory loss grows so extensive that conversation is impossible: context and prior information are lost. [L16 s05, MM p139]

3. Cannot answer simple questions, such as what year it is or where they are. [MM p139]
4. Becomes disoriented, easily lost even in familiar surroundings; decline is progressive and relentless. [MM p139]

Brain shows striking **cortical atrophy** *(shrinking of the cortex)*, especially frontal, temporal, and parietal areas. [L16 s05, MM p139]

PET: marked reduction of metabolism in **posterior parietal cortex** and parts of the temporal lobe. [L16 s05, MM p139]



Basal forebrain acetylcholine axons across the cortex, with tangles and plaques in cortex tissue [MM p139]

On the figure: basal forebrain · hippocampus · neurofibrillary tangles · amyloid plaques · acetylcholine

Amyloid plaques (also **senile plaques**): patches formed by buildup of **beta-amyloid** *(protein that piles up)*. [L16 s08, MM p139]

Amyloid plaques appear in cortex, **hippocampus**, and associated limbic system sites. [MM p139]

Amyloid plaque: small brain area with abnormal cellular and chemical patterns; plaques correlate with dementia. [MM p139]

Beta-amyloid: a protein that accumulates in amyloid plaques in Alzheimer's disease. [L16 s08, MM p139]

Neurofibrillary tangles: abnormal whorls of **neurofilaments** *(threads inside nerve cells)* tangled inside the cell. [L16 s08, MM p140]

The number of tangles is directly related to the size of cognitive impairment. [MM p140]

Neurons in the **basal forebrain** that make **acetylcholine (ACh)** *(a neurotransmitter)* are gradually lost. [L16 s08, MM p140]

Basal forebrain nuclei send ACh axons widely across the brain; these cells seem to disappear. [L16 s09, MM p139]

Drugs that boost ACh signaling may reduce some symptoms for a time. [MM p140]

1. Beta-amyloid builds up. [L16 s08, MM p139]
2. Amyloid plaques form in cortex, hippocampus, and limbic sites. [L16 s08, MM p139]
3. Neurofibrillary tangles form, probably as a secondary response to plaques. [MM p140]
4. More tangles go with more cognitive impairment. [MM p140]

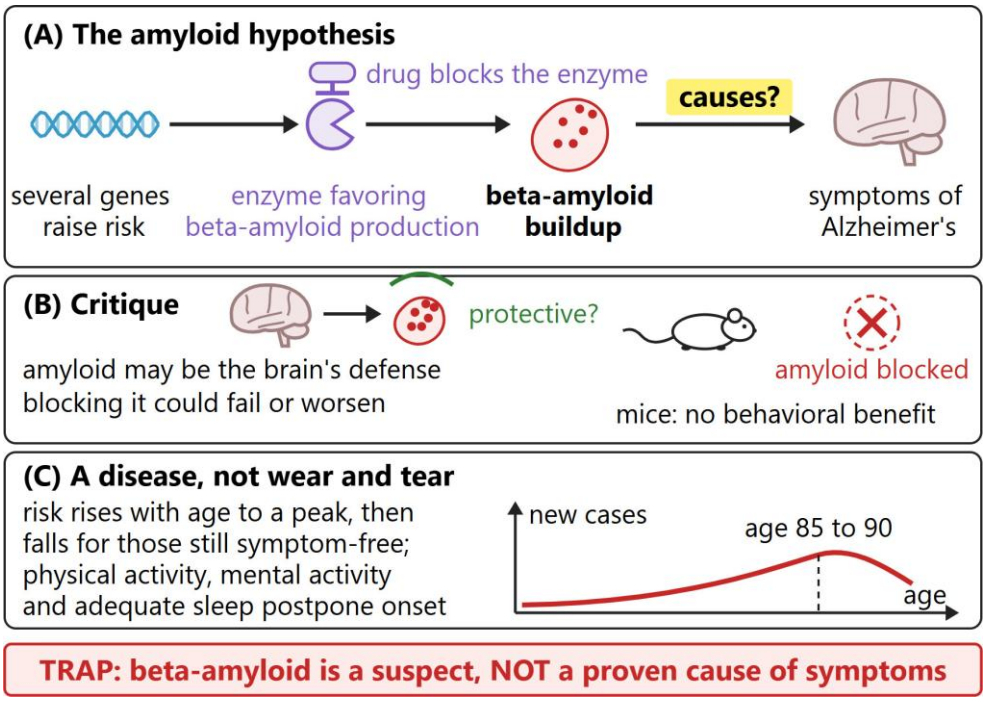
Three cellular changes in Alzheimer's

Change	What it is	Key point
Amyloid plaques	Patches of beta-amyloid buildup	In cortex, hippocampus, limbic sites
Neurofibrillary tangles	Whorls of neurofilaments inside cells	Number tracks cognitive impairment
ACh neuron loss	Basal forebrain neurons die	ACh drugs ease symptoms briefly

Table source: [L16 s08, MM p139, MM p140]

4.4.2 Critique the amyloid hypothesis of Alzheimer's

⚠ **Do not mix up: Beta-amyloid is a suspect, NOT a proven cause: it may be the brain's response.** [MM p140]



The amyloid hypothesis, its critique, and risk with age [MM p141]

On the figure: amyloid hypothesis · beta-amyloid · buildup · mice · physical activity · mental activity

The **amyloid hypothesis** *(beta-amyloid buildup causes the symptoms)*: skepticism is growing. [MM p140]

Beta-amyloid is a suspected cause because amyloid plaques correlate with dementia. [MM p139, MM p141]

Several genes affect beta-amyloid **buildup** in plaques and **increase** Alzheimer's risk. [MM p141]

Amyloid levels on PiB imaging correlated with who would develop Alzheimer's. [MM p140]

Treatment strategy: drugs that interfere with enzymes favoring beta-amyloid production. [MM p140]

Growing skepticism: does beta-amyloid actually cause the symptoms of Alzheimer's? [MM p140, MM p141]

Alternative: amyloid may be the brain's defense, something the brain does to avoid symptoms. [MM p140]

If so, blocking amyloid production would not help and might even worsen the disease. [MM p140]

Support for the doubt: several manipulations in **mice** blocked amyloid but gave no behavioral benefit. [MM p140]

Genes and experience interact: **physical activity**, **mental activity**, and adequate sleep can postpone onset of Alzheimer's. [MM p140, MM p141]

Best current way to avoid Alzheimer's: remain physically and mentally active. [MM p140]

Critique of the amyloid hypothesis

For amyloid as cause	Against amyloid as cause
Plaques correlate with dementia	Blocking amyloid in mice: no behavior benefit
Genes raising amyloid raise risk	Amyloid may be a protective response
PiB amyloid predicts who develops it	Blocking amyloid might worsen disease

Table source: [MM p139, MM p140, MM p141]

4.4.3 Discuss how brain imaging may help us understand the mechanism(s) of Alzheimer's

⚠ Do not mix up: Only HIPPOCAMPAL formation size, NOT general brain shrinkage, correlated with memory decline in aging. [L16 s06, MM p138]

Question: is mild memory impairment tied to shrinking of specific regions, or general brain shrinkage? [L16 s06, MM p138]

Participants: healthy, cognitively normal people aged **55** to **87.** [L16 s06, MM p138]

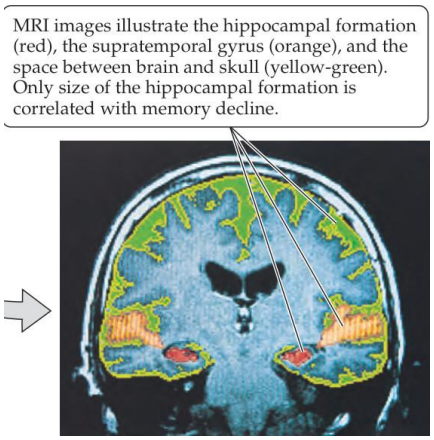
Methods: memory tests, plus brains measured from **MRI** *(scan of brain structure)* images. [L16 s06, MM p138]

Effects of sex, age, IQ, and overall brain atrophy were removed statistically. [MM p138]

Result: **only hippocampal formation** volume correlated with memory decline. [L16 s06, L16 s07, MM p138]

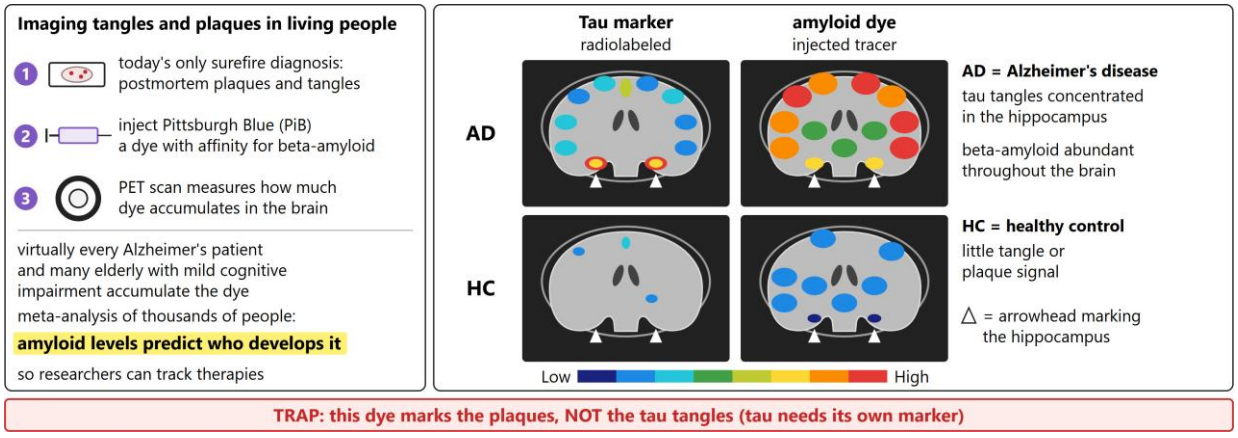
MRI colors: hippocampal formation red, **supratemporal gyrus** orange, space between brain and skull yellow-green. [L16 s07, MM p138]

Only hippocampal size correlated: supratemporal gyrus and skull space (general shrinkage) did not. [L16 s06, L16 s07, MM p138]



Coronal MRI showing the hippocampal formation, supratemporal gyrus, and skull space [MM p138]

On the figure: MRI · hippocampal formation · supratemporal gyrus



Imaging plaques and tangles: Pittsburgh Blue PET and tau marker in Alzheimer's brains and healthy controls [MM p140]

On the figure: Pittsburgh Blue · affinity · PET scan · meta-analysis · tau tangles · healthy control

Only surefire diagnosis now: postmortem brain exam showing amyloid plaques and neurofibrillary tangles. [MM p140]

Pittsburgh Blue (PiB): injected dye with an **affinity** *(tendency to bind)* for beta-amyloid. [L16 s10, MM p140]

A **PET scan** *(brain scan of an injected tracer)* then shows how much dye accumulates in the brain. [MM p140]

Virtually every brain of a person with Alzheimer's accumulates PiB. [MM p140]

So do brains of many elderly people with mild cognitive impairment. [MM p140]

Meta-analysis of thousands: PiB amyloid levels correlated with who would develop Alzheimer's. [MM p140]

Implication: easier to track how well therapies for Alzheimer's work. [MM p140]

Injected **radiolabeled markers** *(radioactive tags that show on scans)* can image **tau tangles**. [L16 s10, MM p140]

PiB marks beta-amyloid plaques, **NOT** tau tangles; tau needs its own radiolabeled marker. [L16 s10, MM p140]

Alzheimer's brain: tau tangles concentrated in the hippocampus, compared with a **healthy control**. [L16 s10, MM p140]

Alzheimer's brain: beta-amyloid abundant throughout the brain; healthy control shows low amyloid. [L16 s10, MM p140]

PET also shows reduced metabolism in posterior parietal and temporal cortex in Alzheimer's. [L16 s05, MM p139]

Imaging tangles vs plaques

Scan target	Marker	Alzheimer's brain (AD)	Healthy control (HC)
Tau tangles	Radiolabeled marker	Concentrated in hippocampus	Little signal
Beta-amyloid	Pittsburgh Blue (PiB)	Abundant throughout brain	Low

Table source: [L16 s10, MM p140]