Duke Dementia Family Support Program

Caregiver Connections

An Educational Webinar Series with the Experts

The presentation will begin shortly.

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DukeHealth

Dementia 101

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Outline

1. How do memory and thinking change as we age?
2. How do we diagnose mild cognitive impairment (MCI) and dementia?
3. What causes MCI and dementia?
4. How do we treat MCI & dementia?

Memory and thinking change with age....

"Normal" Aging

- Making a bad decision once in a while.
- Occasionally paying a bill late - but able to fix it when reminded.
- Forgetting which day it is and remembering later.
- Sometimes forgetting which word to use.
- Losing things from time to time.

Concerning Changes

- Making poor judgements and decisions a lot of the time.
- Problems taking care of monthly bills.
- Losing track of the time, date, or time of year.
- Trouble having a conversation.
- Misplacing things often and being unable to find them

Adapted from https://www.nia.nih.gov/health/infographics/forgetfulness-normal-or-not

What do we mean by SCI, MCI, and dementia?

Normal Cognition

Subjective Cognitive Impairment (SCI)

- I notice subtle changes in my memory and thinking
- Cognitive assessment is normal.
- These changes do not interfere with my day-to-day activities.

Mild Cognitive Impairment (MCI)

- There are changes in my memory and thinking that I and others notice.
- These changes are picked up on cognitive assessments.
- These changes do not interfere with my day-to-day activities.
- These changes aren't caused by another medical or psychiatric problem.

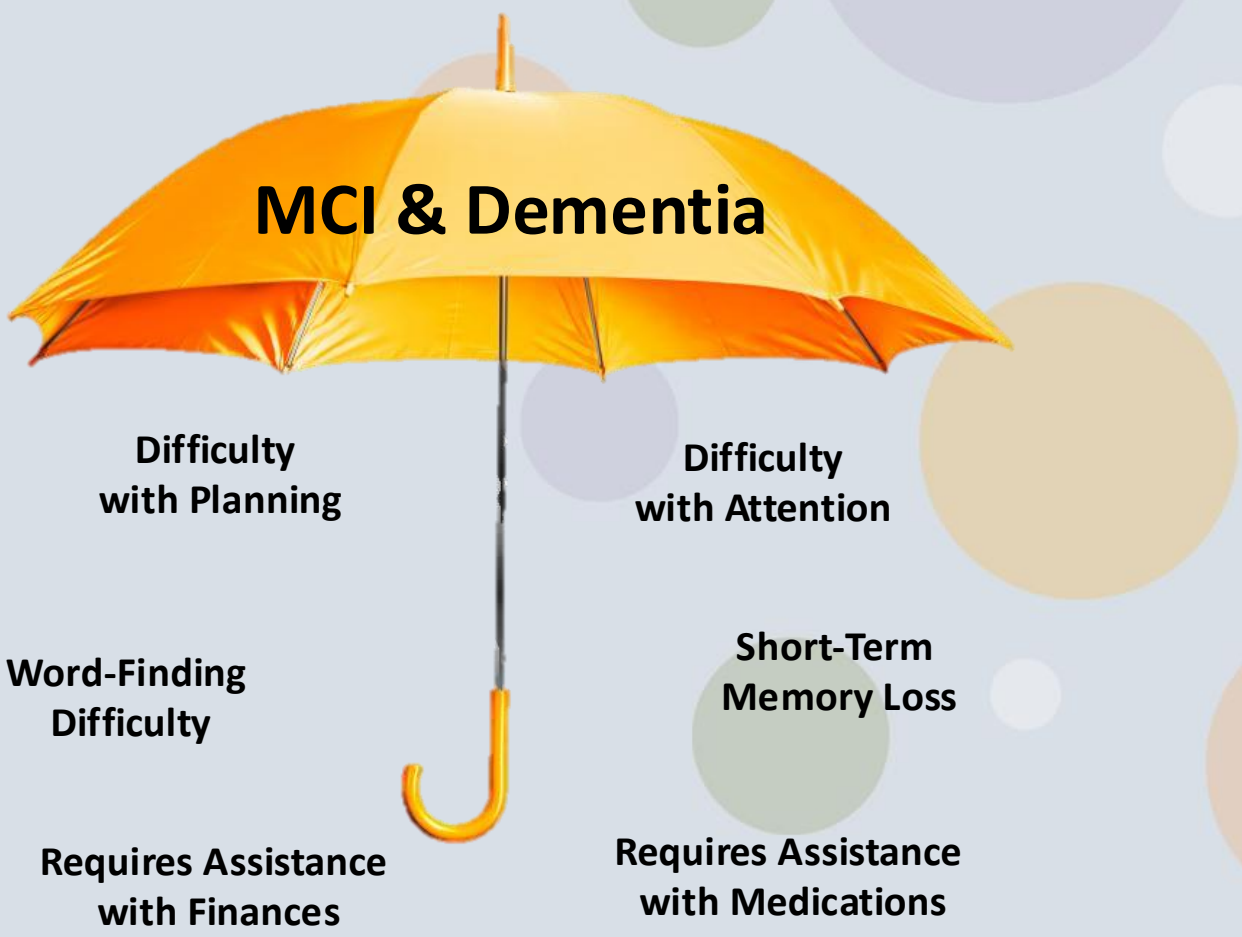
Dementia

- There are changes in my memory and thinking that I and others notice.
- These changes are picked up on cognitive assessments.
- I need extra help with day-to-day activities.
- These changes aren't caused by another medical or psychiatric problem.

MCI and dementia are “umbrella” terms

- MCI and dementia are syndromes or “umbrella” terms which describe a group of symptoms that occur together.
- They describe cognitive symptoms and their impact on function.
- They don’t tell us what’s going on in the brain that is causing the symptoms.
- There are different diseases that can cause MCI and dementia.

Syndromes or “Umbrella” Terms

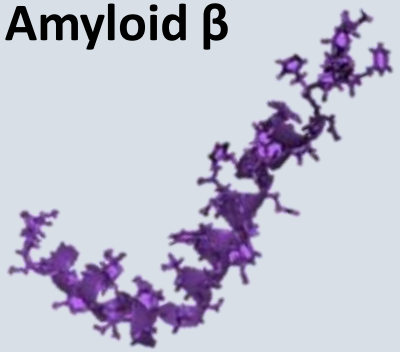


What diseases cause MCI/dementia?

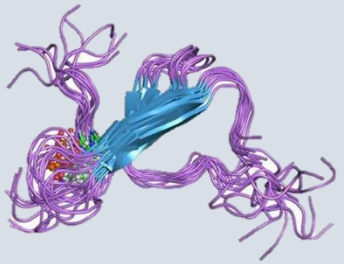
Alzheimer's Disease

- Most common cause of dementia and MCI that progresses to dementia.
- Accounts for 60-80% of cases of dementia.
- Often starts with trouble learning/remembering new information.
- Defined as the build up of two proteins: amyloid plaques and tau tangles.

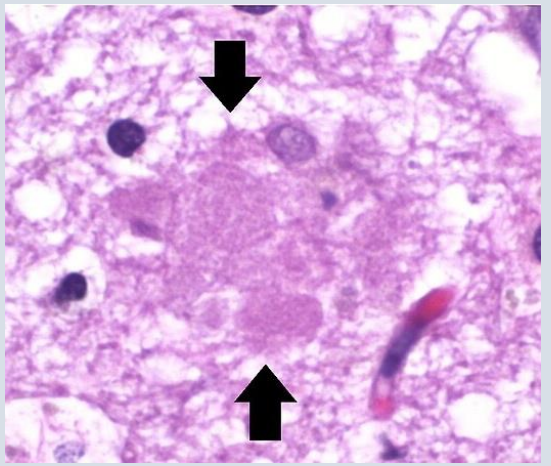
Amyloid β



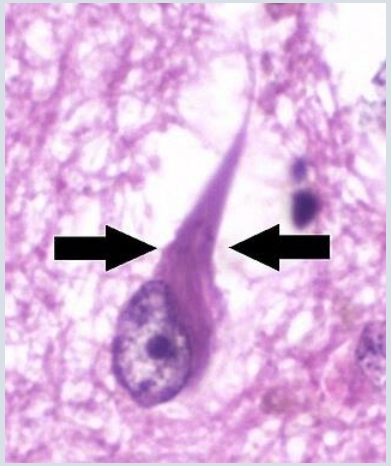
Neurofibrillary Tau



Amyloid Plaques



Tau Tangles

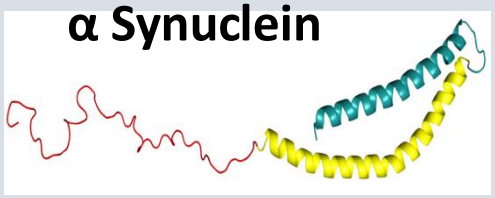


What diseases cause MCI/dementia?

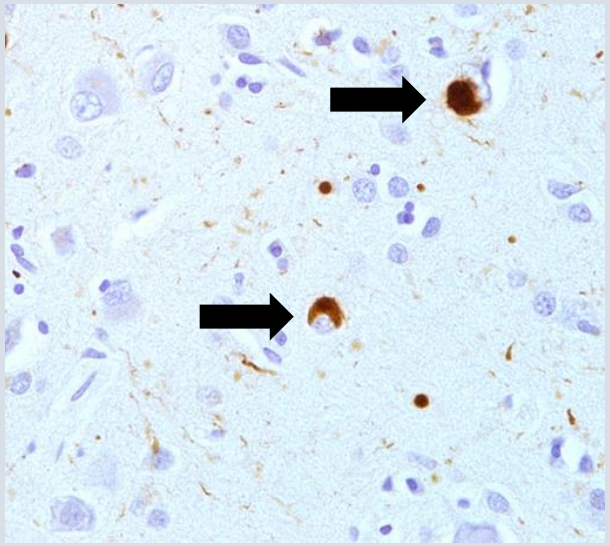
Lewy Body Disease

- Accounts for 10-15% of dementia cases.
- Progressive changes in memory and thinking.
- Mixed Lewy body and Alzheimer's disease is common.
- Other symptoms can include:
  - Cognitive fluctuations
  - Visual hallucinations
  - Acting out dreams
  - Constipation
  - Balance problems, dizziness, tremor, shuffling gait

α Synuclein



Lewy Bodies

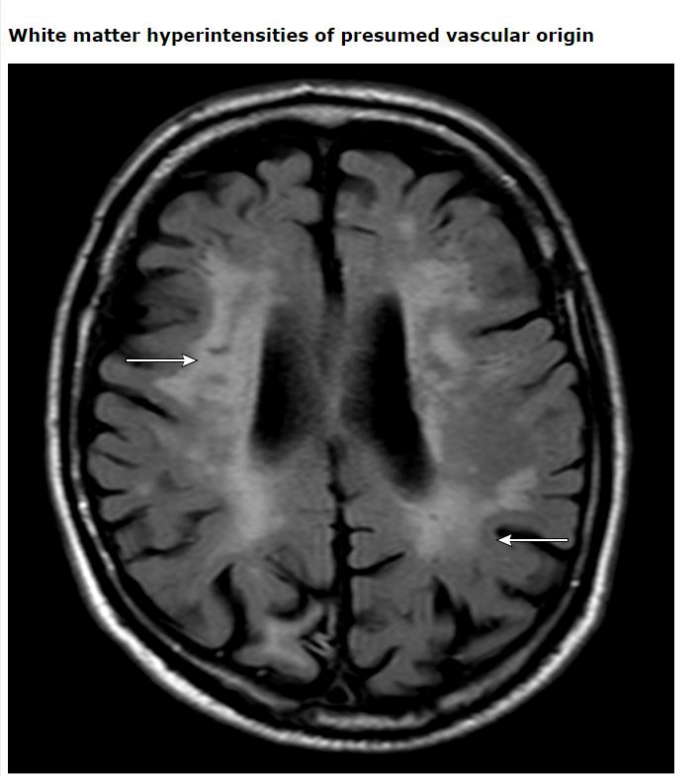


Movalley. *Immunostaining (brown) of alpha-synuclein in Lewy Bodies and Lewy Neurites in the neocortex of a patient with Lewy Body Disease* (21 Oct 2011). *Wikimedia Commons*. CC0 1.0

What diseases cause MCI/dementia?

Vascular Brain Injury (strokes, small-vessel disease)

- Refers to vascular disease in the brain and its contribution to cognitive impairment.
- Many people diagnosed with vascular dementia also have Alzheimer's disease.
- Vascular disease often contributes to cognitive impairment in combination with other causes of MCI/dementia.

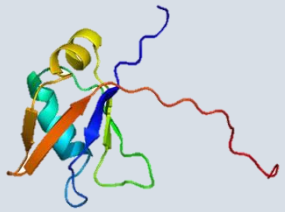


What diseases cause MCI/dementia?

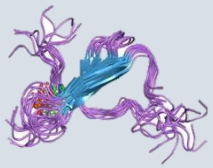
Frontotemporal Dementia

- Symptoms typically develop at a younger age, usually in the 50s.
- Accounts for ~10% of dementia in people under 65.
- A substantial minority have a strong family history; some have identifiable genetic mutations.
- Behavioral variant presents with changes in personality and behavior.
- Primary progressive aphasia (speech/language-led dementia): nonfluent and semantic variants.

TDP-43



Tau



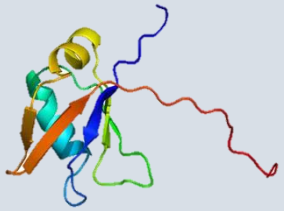
And Others

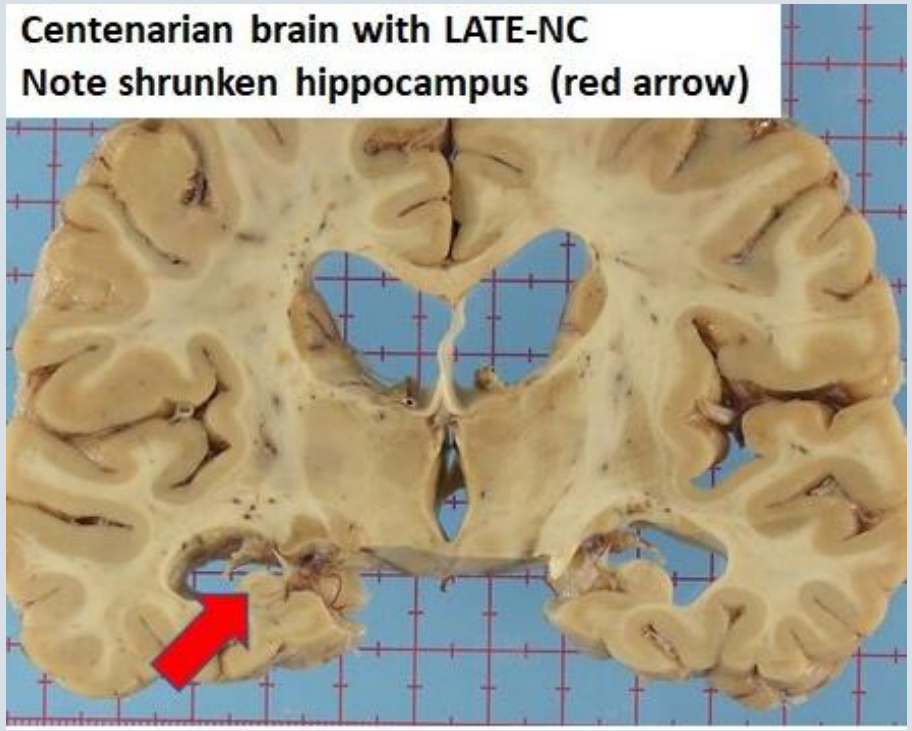
What diseases cause MCI/dementia?

LATE

- Limbic-predominant age-related TDP-43 encephalopathy
- Can look like Alzheimer's, especially with memory-predominant symptoms in older adults.
- Typically occurs in people over 75. Present in over 20% of people 85 and older.
- Suspected when testing for Alzheimer's is negative.
- May progress more slowly than Alzheimer's disease.
- Can occur with Alzheimer's disease.

TDP-43

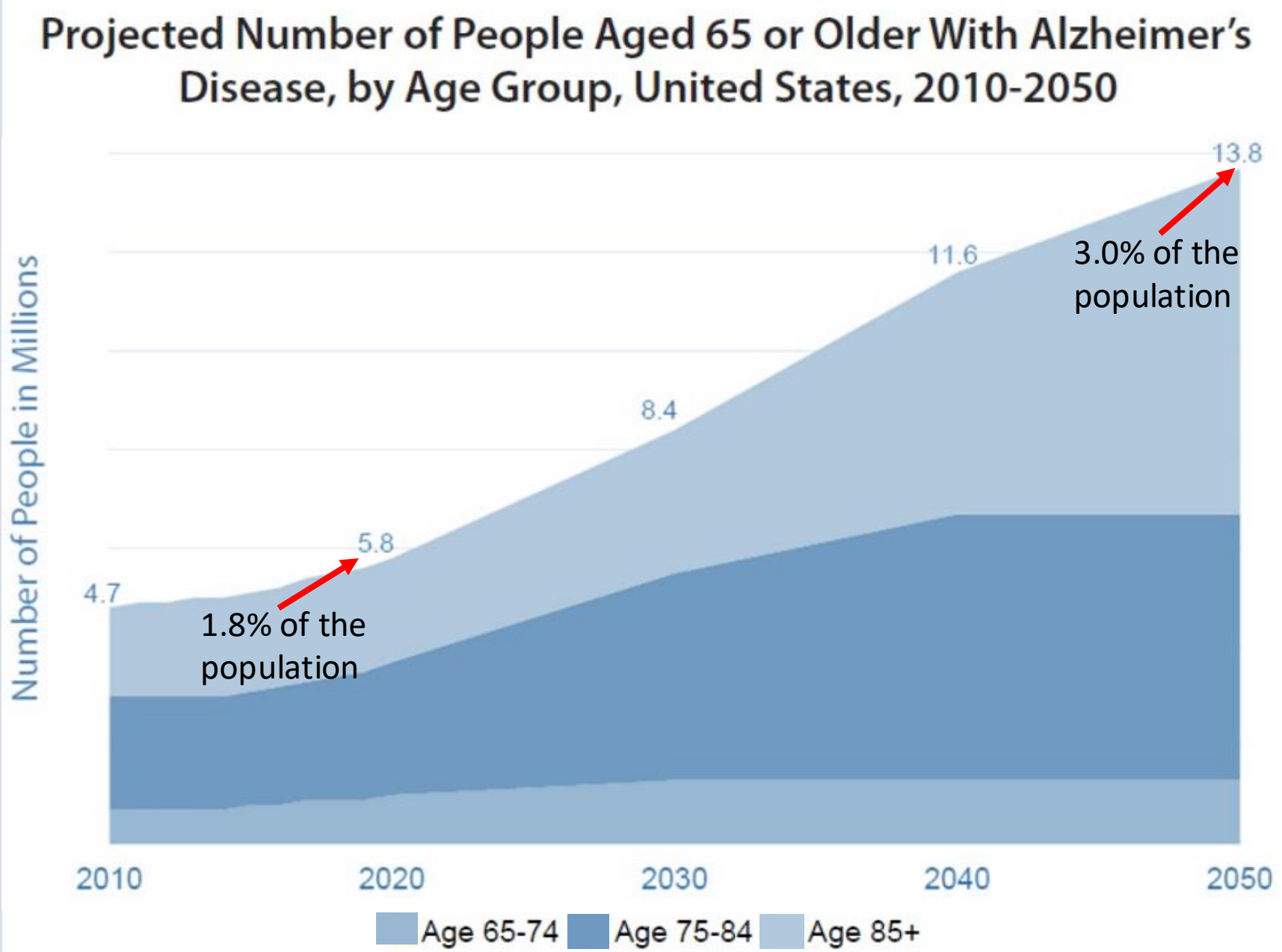




10% of Adults ≥ 65 have AD

2/3 of Americans with AD are women

Risk in African-Americans is 2X higher than whites



Source: Created from data in Hebert LE, Weuve J, Scherr PA, Evans DA. Alzheimer disease in the United States (2010-2050) estimated using the 2010 Census. *Neurology* 2013;80(19):1778-83.

Alzheimer's disease 6th Leading Cause of Death in the US

Annual attributable cost per person is ~$50–60k

Total expenditures on dementia >$200 billion

Some good news?

- As our population ages, more people are living with MCI and dementia.
- Dementia rates at a population level may be stabilizing or falling in some countries.
- About ~45% of dementia risk may be addressed by modifiable factors across the lifespan.
- New symptomatic and disease-modifying treatments are expanding options.

How do we diagnose MCI and dementia?

- Find out when symptoms began and how they have changed over time.
- Perform a cognitive and neurological assessment.
- Look for other factors that may contribute to symptoms.
- Consider additional testing and develop a treatment plan.

↓Cognition

Medications

- Benadryl, amitriptyline, tolterodine, paroxetine
- Ambien, sedatives, muscle relaxants, pain medications

Sleep Problems

- Sleep apnea & Insomnia

↓Cognition
↑Dementia Risk

Medical Problems

- Heart, liver, kidney disease
- Untreated high blood pressure
- Poorly-controlled diabetes

Mood Problems

- Depression & Anxiety

Sensory

- Hearing & Vision Impairment

Lifestyle Factors

- Alcohol and tobacco
- Physical inactivity
- Poor diet
- Social isolation
- Cognitive Disengagement

What other factors can affect memory and thinking?

How do we make a clinical diagnosis?

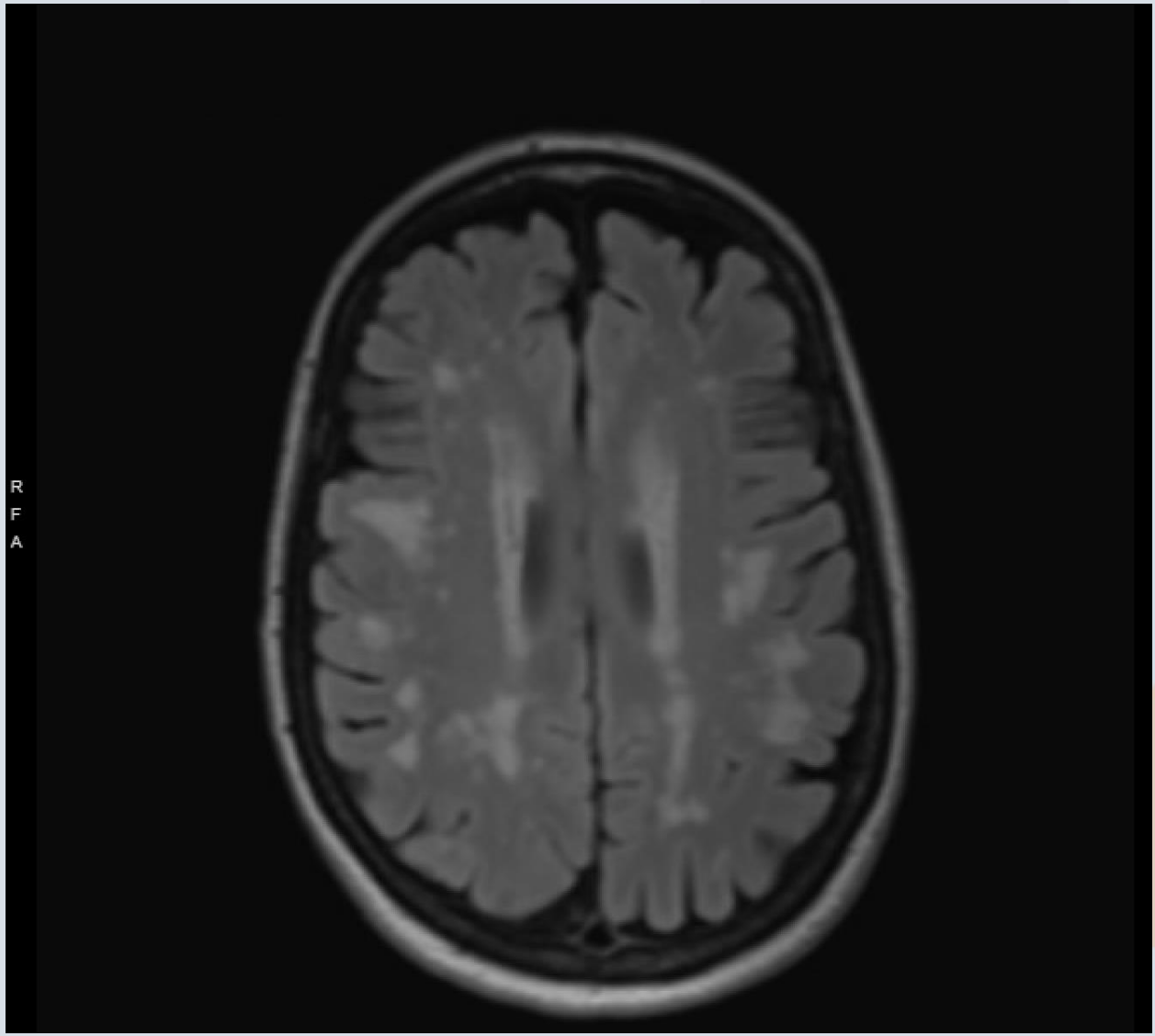
	Patient & Care Partner-Reported Symptoms	Cognitive Assessment	Functional Assessment
Normal Cognition	Normal	Normal	Normal
Subjective Cognitive Impairment (SCI)	Abnormal	Normal	Normal
Mild Cognitive Impairment (MCI)	Abnormal	Abnormal	Normal
Dementia	Abnormal	Abnormal	Abnormal

How do we use brain imaging in our evaluation?

- Routine brain imaging is **often normal** in patients with MCI and dementia.
- We mainly use standard brain imaging (MRI) to **rule out other problems** in the brain that can lead to changes in memory and thinking.
- Specialized brain imaging can help identify the cause of MCI or dementia.

MRI

- Most common routine brain imaging



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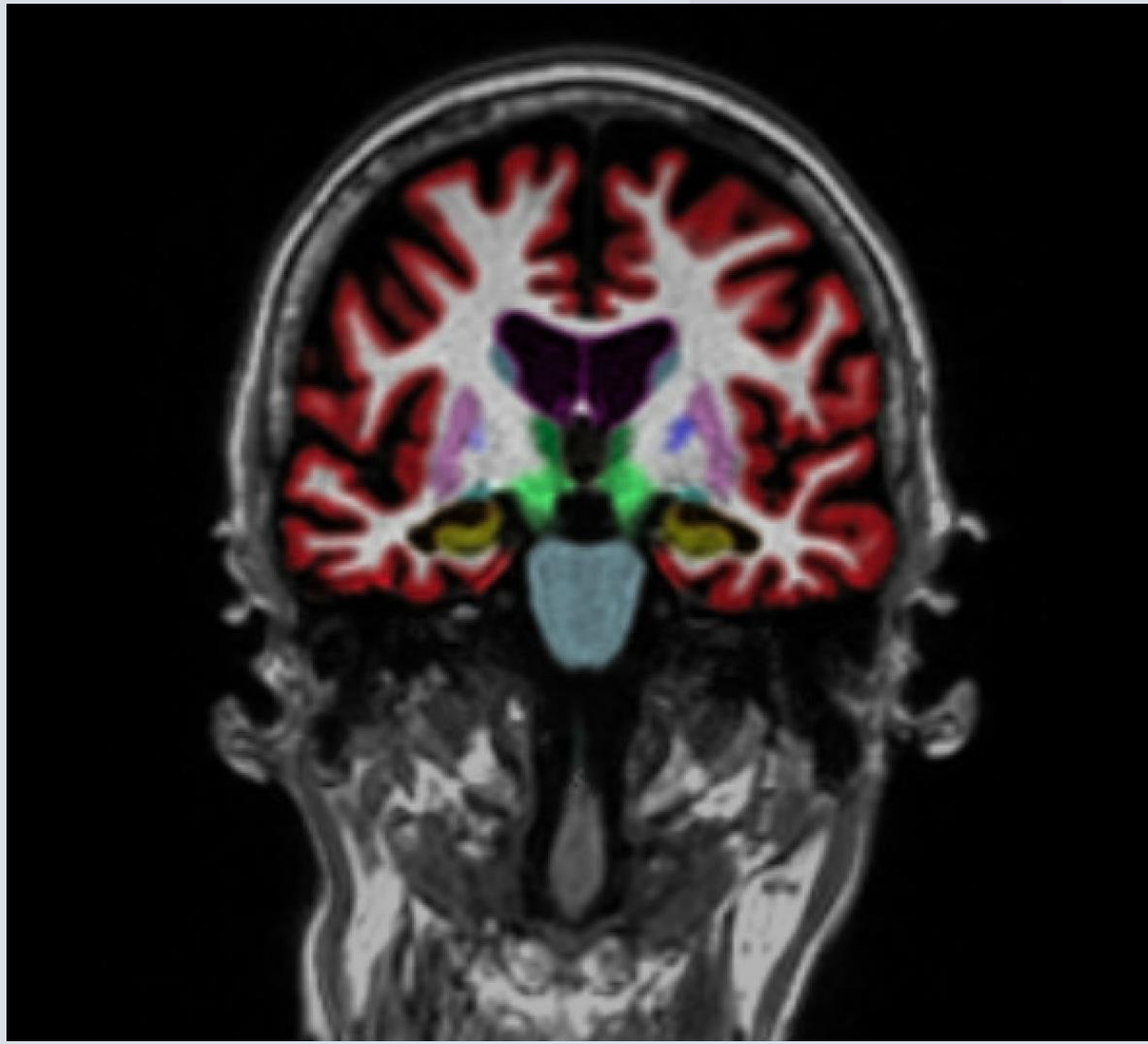
MRI

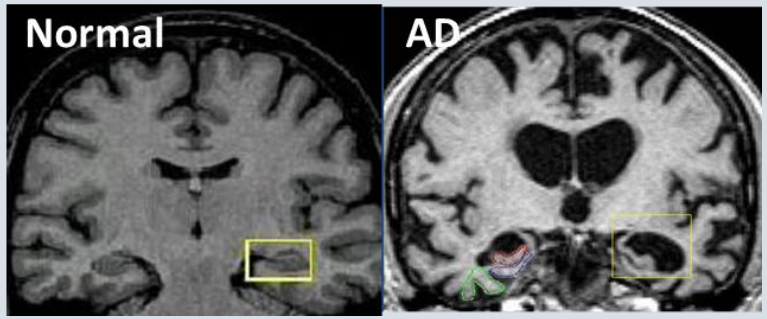
- Most common routine brain imaging



Diagnosis of Alzheimer's Disease

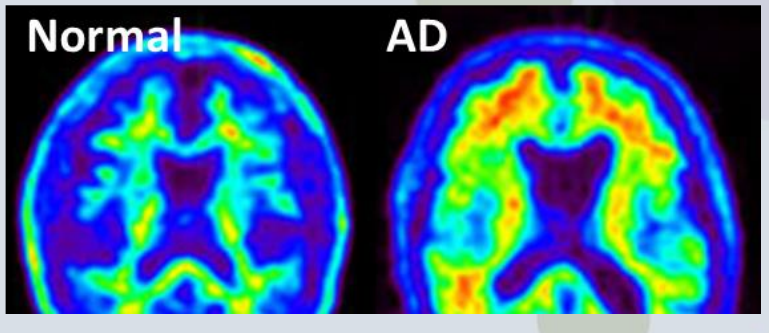
Imaging

MRI



- *Rules out other causes; may show patterns that support a diagnosis.*

Amyloid PET



- *Shows whether amyloid plaques are present.*

Fluid

Lumbar Puncture

Measure Alzheimer's disease proteins in spinal fluid

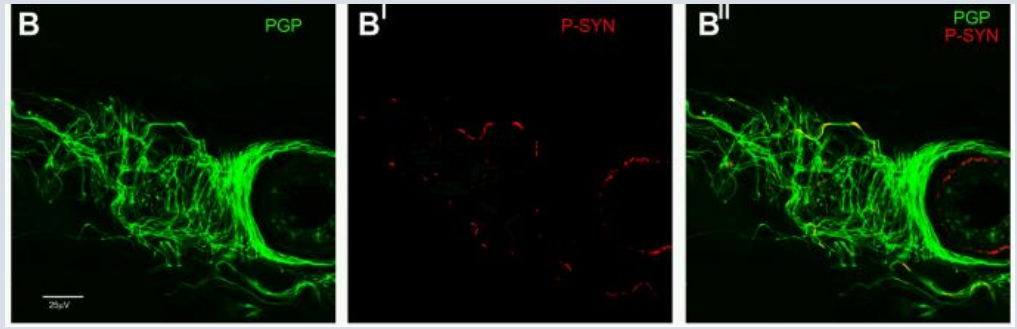
Blood Tests

A newer option that can estimate likelihood of amyloid pathology; used with clinical evaluation (not a standalone screen).

Diagnosis of Other Causes of Dementia

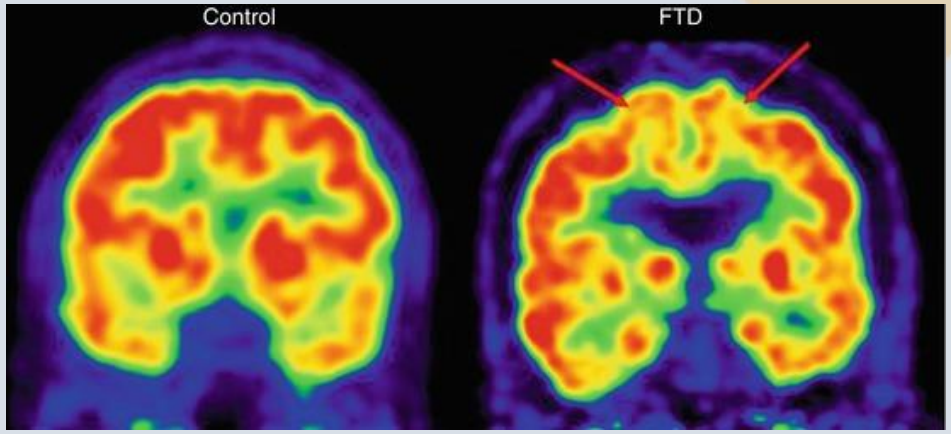
Lewy Body Disease

- Sometimes specialized tests can support Lewy body disease (e.g., certain imaging; skin biopsy biomarkers).



Frontotemporal Dementia

- We can do an FDG PET scan to evaluate for changes in brain metabolism.
- We can perform genetic testing to identify variants that cause frontotemporal dementia.



Donadio, V. *et al.* Skin α-synuclein deposits differ in clinical variants of synucleinopathy: an in vivo study. *Sci. Rep.* **8**, 14246 (2018).

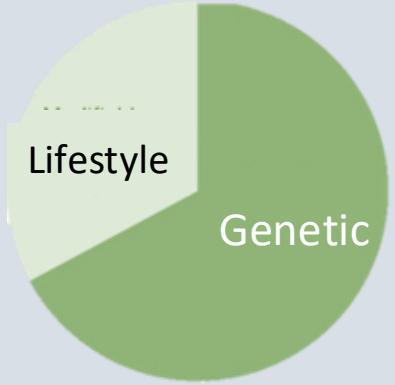
Diagnosis of Other Causes of Dementia

LATE

- LATE is suspected in some older adults with memory-predominant symptoms when Alzheimer biomarkers are negative, but we currently can’t confirm it with a single definitive test during life.

APOE Genotype

- APOE genotype is the **strongest genetic risk factor** for Alzheimer's disease.
- APOE-ε3 is the most common version and is considered to have a neutral effect on the Alzheimer's — neither decreasing nor increasing the risk.
- APOE-ε4 increases risk for Alzheimer's and is associated with earlier onset in certain populations.
- The effect of APOE on Alzheimer's risk is greater in women. The effect of APOE on Alzheimer's risk may be weaker in African-Americans



APOE genotype accounts for 5-10% of the genetic risk. Other genes play a role too.

Alzheimer's Disease Risk

APOE Genotype	ε2/ε2	ε2/ε3	ε3/ε3	ε2/ε4	ε3/ε4	ε4/ε4
% US	1%	12%	60%	2%	21%	2%
Risk	40% Less Likely	40% Less Likely	Average Risk	2.6x More Likely	3.2x More Likely	14.9 More Likely

Serrano-Pozo, et al. "APOE and Alzheimer's Disease: Advances in Genetics, Pathophysiology, and Therapeutic Approaches." *The Lancet Neurology* 20, no. 1 (January 2021): 68–80. https://doi.org/10.1016/S1474-4422(20)30412-9.

How do we treat MCI and dementia?

- Address modifiable risk factors (especially for MCI).
- Increase cognitive resilience.
- Promote overall health and well-being.
- Consider medications that help with memory and thinking symptoms.
- Consider anti-amyloid treatment for early Alzheimer's disease.

Approach to Treatment

Adapt & Prepare

- Complete advanced care planning.
- Plan for future care needs.
- Cognitive rehabilitation with Speech or Occupational Therapy

Address Risk Factors

- Address modifiable risk factors (hearing, blood pressure, etc.)
- Exercise, diet, social engagement, cognitive engagement

Symptomatic Treatments

- Improve symptoms of disease, but do not affect the disease process or address underlying issue that caused the disease
- Donepezil (Aricept) or Memantine (Namenda).
- Antidepressants

Disease-Modifying Treatments

- Addresses the underlying problem causing the disease, which slows down or preventing disease progression
- Lecanemab (Leqembi) & Donanemab (Kisunla) for Alzheimer’s disease

Symptomatic Treatments for Dementia

Cholinesterase Inhibitors

- Increase acetylcholine in the brain.
- Includes:
  - Donepezil (Aricept)
  - Rivastigmine (Exelon)
  - Galantamine (Razadyne)

NMDA-Receptor Antagonists

- Decreases excessive glutamate signaling in the brain.
- Includes:
  - Memantine (Namenda)

These do not stop the disease; they may modestly help symptoms for some people.

Cholinesterase Inhibitors

- Most helpful in mild–moderate Alzheimer's; donepezil can be used in severe stages. Effects are modest and vary by person.
- Often particularly helpful for hallucinations/attention in Lewy body dementia.
- No evidence of benefit in frontotemporal dementia.

Cholinesterase Inhibitors

Side Effects

- Upset stomach, nausea, diarrhea, and decreased appetite occur in 20-30% of people.
- Insomnia, vivid dreams, and other sleep problems These side effects may be more common with donepezil.
- Less commonly, can slow the heart rate and cause muscle cramps.
- Cholinesterase inhibitors are generally safe.

NMDA-Receptor Blocker

- Decreases excessive glutamate signaling in the brain.
- Helps improve memory and thinking and function.
- Benefits are generally modest at best and may be greater in more advanced disease.
- Limited evidence of benefit in Lewy Body disease.
- Not recommended in frontotemporal dementia.

NMDA-Receptor Blocker

Side Effects

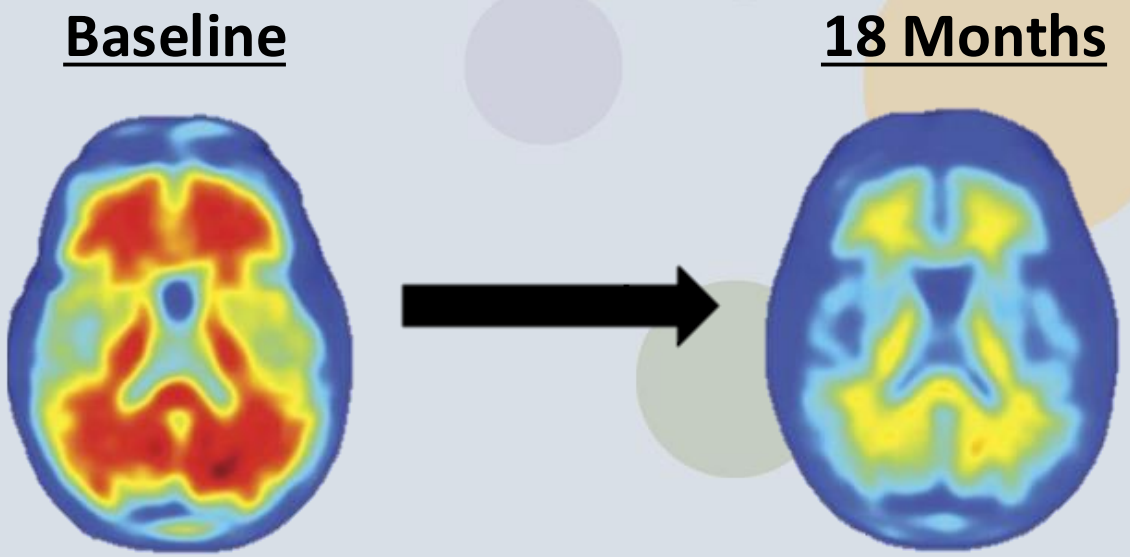
- Generally, well tolerated. Most common side effect is dizziness.
- Uncommonly worsens confusion and hallucinations.

Disease-Modifying Treatments for Alzheimer's

Lecanemab (Leqembi) & Donanemab (Kisunla)

- Lecanemab and donanemab are antibodies that bind to amyloid plaques and trigger an immune response to remove them.
- They do not stop or reverse memory and thinking changes, but rather modestly slow down the progression.
- In clinical trials, these drugs slowed decline on average by about ~25–35% over ~18 months
- Lecanemab & Donanemab can cause swelling and bleeding in the brain.

Amyloid PET Brain Scan



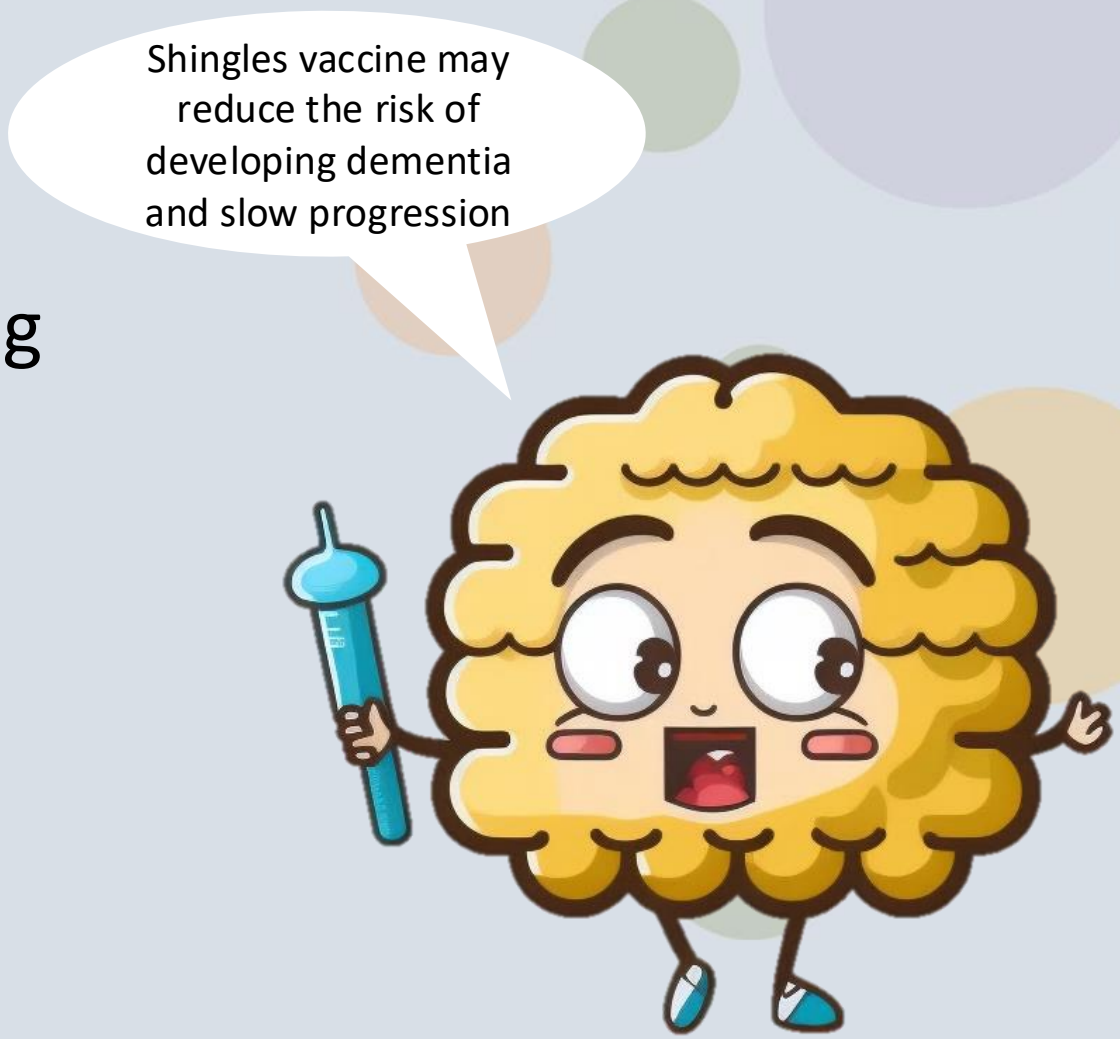
Infections & Vaccinations

Some infections are associated with higher later dementia risk.

- These include common, life-long viral infections like:

  Herpes Simplex Virus & Varicella/Shingles

- There is also evidence that influenza, COVID, and bacterial pneumonia can increase risk.



Levine, K.S., et al. "Virus Exposure and Neurodegenerative Disease Risk across National Biobanks." *Neuron*, January 2023. https://doi.org/10.1016/j.neuron.2022.12.029
Wu, X., et al. "Adult Vaccination as a Protective Factor for Dementia: A Meta-Analysis and Systematic Review of Population-Based Observational Studies." *Frontiers in Immunology* 13 (May 3, 2022): 872542. https://doi.org/10.3389/fimmu.2022.872542.

Hearing & Vision

- Hearing loss is a major risk factor for dementia. Using hearing aids reduces this risk.
- Over the counter amplification devices or hearing aids are less expensive.
- Older adults with severe hearing loss may be eligible for cochlear implants or bone anchored hearing implants.
- Some evidence suggest treating cataracts may also reduce the risk of dementia.

Yoshida, Y., Ono, K., Sekimoto, S., Umeya, R. & Hiratsuka, Y. Impact of cataract surgery on cognitive impairment in older people. *Acta Ophthalmol.* (2024) doi:10.1111/aos.16607.

Healthy Brain Diet

- Best evidence is for the Mediterranean/MIND diet.
- Leafy green and other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil.
- Aim for vegetables daily; fish weekly; olive oil as main fat; minimize ultra-processed foods.

Move it or lose it?

Daily Step Count & Dementia Risk

- 10,000 Daily Steps

  50% lower risk of developing dementia over the next 7 years.

- 3,800 Daily Steps

  25% lower risk of developing dementia over the next 7 years

- Fewer steps at a higher intensity (faster pace) was also protective!

Gardening and housework count as physical activity too!

Pozo Cruz, B., et al. "Association of Daily Step Count and Intensity With Incident Dementia in 78 430 Adults Living in the UK." *JAMA Neurology* 79, no. 10 (October 1, 2022): 1059. https://doi.org/10.1001/jamaneurol.2022.2672.

Cardiometabolic Health

- Cardiometabolic Health:
  - Blood pressure, blood sugar, and cholesterol.
- For some people:
  - Exercise + Diet = ↓BP + ↓Sugar + ↓Cholesterol
- For the rest of us:
  - We have safe, effective medications.
- Treat high blood pressure, diabetes, and high cholesterol

Summary

- MCI and dementia are “umbrella” terms that describe changes in memory and thinking and how they affect function. If symptoms are mild and don’t affect function, we often call it MCI. Once symptoms affect independent function, we call it dementia.
- MCI/dementia are caused by different diseases, most commonly Alzheimer’s disease. We can test for Alzheimer’s disease and some other causes of dementia.
- Some cases of dementia may be preventable. There are many factors within our control that can affect our brain health and may slow down progression of cognitive change.
- We have treatments to help with symptoms for people living with dementia and two disease-modifying treatments for people with Alzheimer’s disease.

Caregiver Connections

An Educational Webinar Series with the Experts

Thank you for joining us today!

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