Introduction to Memory Disorders and How to Treat Them

Jennifer Pauldurai, MD, MS
Inova Cognitive Neurology
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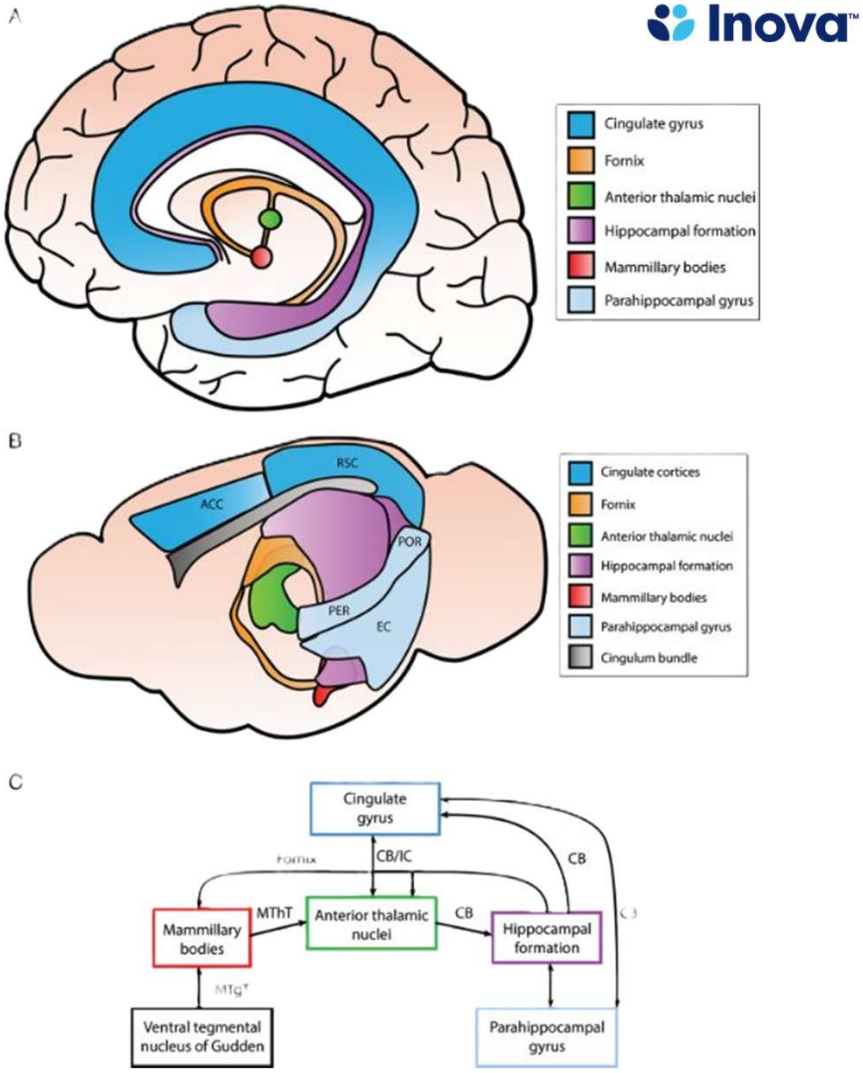
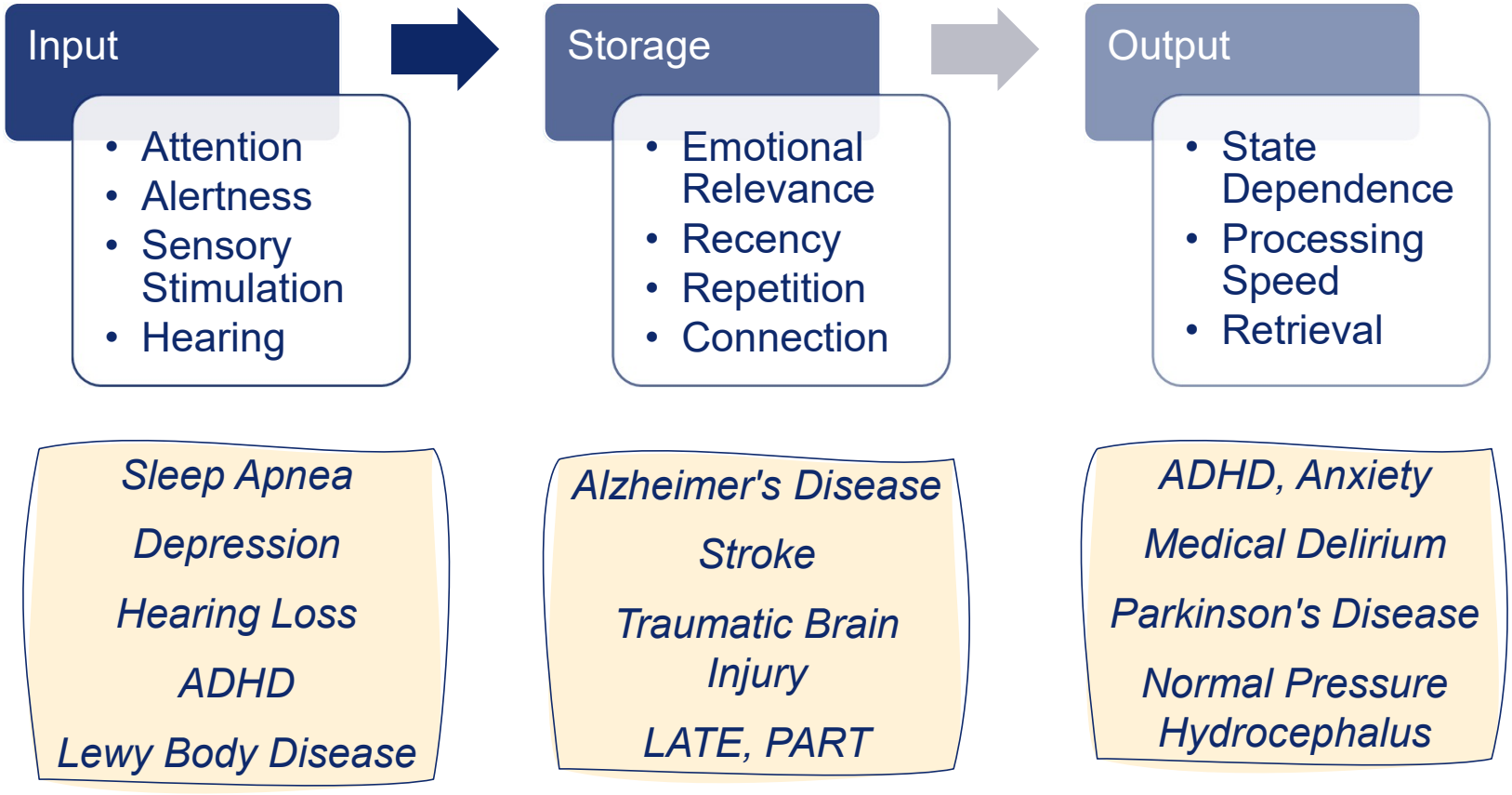
Our brain is a complex network of electrical and chemical signals; this is how we think and behave.

The memory network is called the **Papez Circuit:**

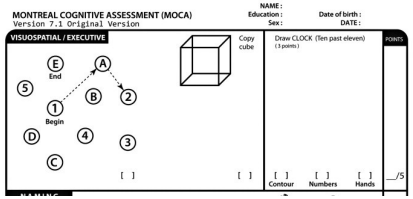
- hippocampus (memory)
- thalamus (perception)
- hypothalamus (regulation)
- amygdala (emotion)
- frontal lobes (decisions)

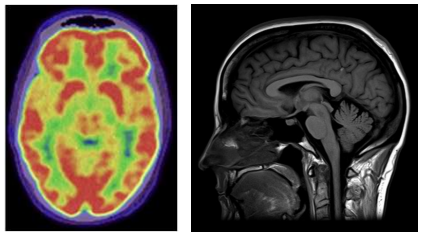


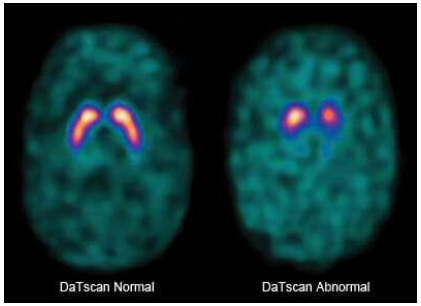
What causes failure in this memory circuit?



Doctors use various tools to figure out the type of memory disorder someone has; often there are overlapping variables.







1. History and Physical: Cognitive Screen or Neuropsych

2. Structural and Chemical Baseline:

- ❑ MRI Brain (Neuroquant) (or CT Head if over age 85)
- ❑ Basic Screening Labs: CBC, CMP, TSH, Vit D, Vit B12

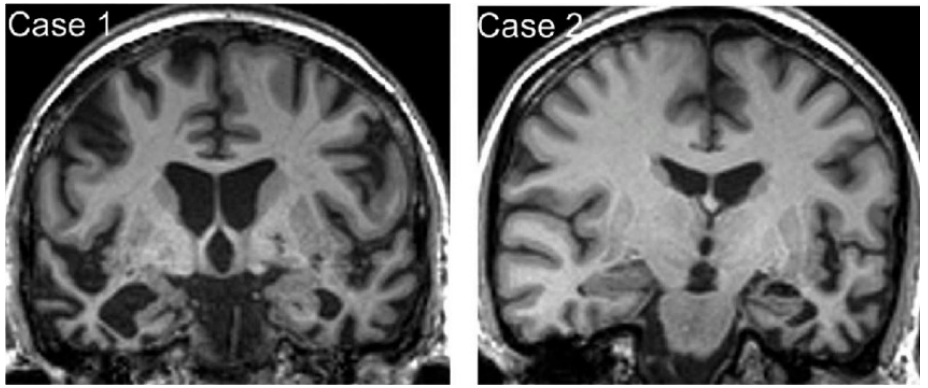
3. Advanced testing, if needed:

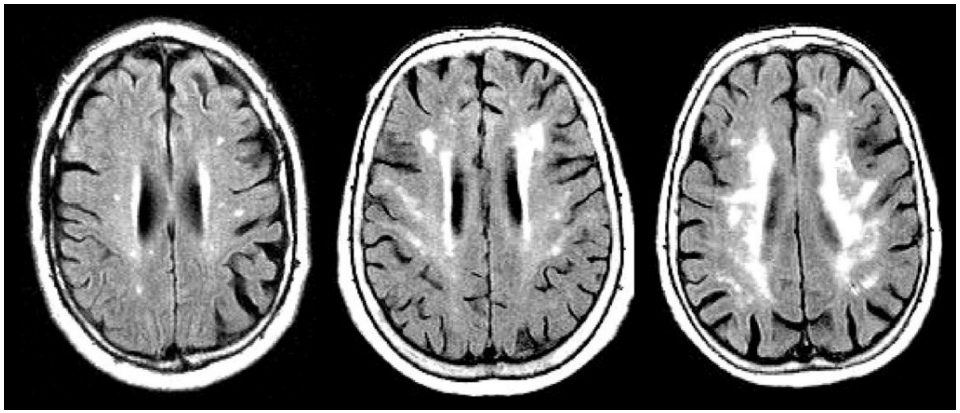
- ❑ Alzheimer's Syndrome:
  - *Amyloid can be confirmed with PET, CSF, serum ATN (suggestive)*
  - *There are other biomarkers: APOE, NFL, pTau, GFAP, ATN profile*
- ❑ Movement Syndrome:
  - *Consider doing a DATscan, skin biopsy for synuclein, or having movement clinic eval*
- ❑ Frontotemporal Syndrome:
  - *PET-Amyloid, FDG-PET*
  - *Genetic panels, CSF panels, autoimmune panels*

Dementia is a **state of function** where the brain needs help to function independently.

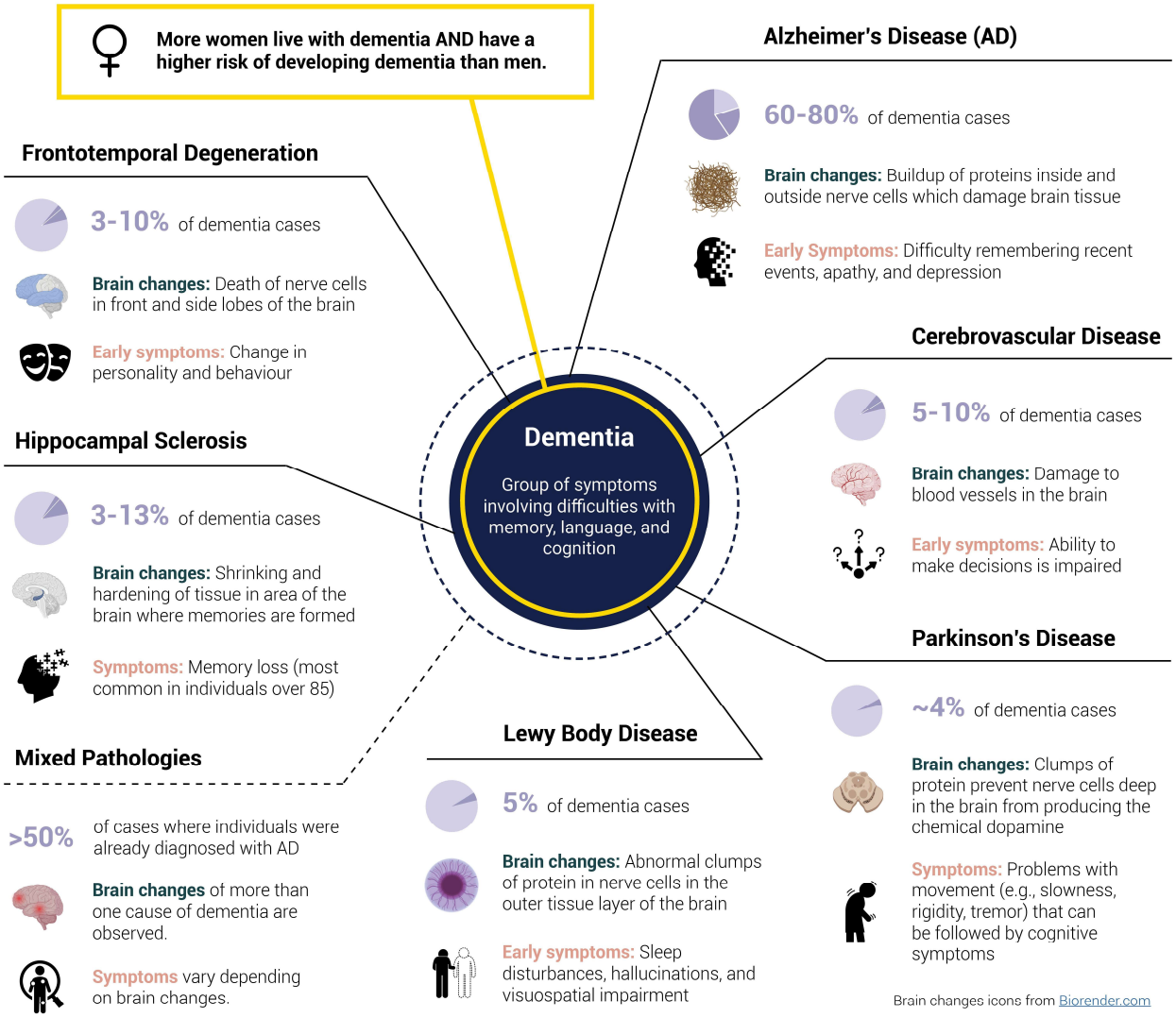
Some diseases can change the brain structurally and chemically, so dementia can be associated with symptoms that are more than just forgetfulness.

memory	concentration	language
behavior	sleep	decisions
appetite	activity levels	alertness
personality	judgement	mood





Data taken from the 2023 Alzheimer's Disease Facts and Figures Special Report: The Patient Journey in an Era of New Treatments



Brain changes icons from Biorender.com

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Treating Dementia Requires a Diagnosis First

We may be able to fix the cause of the dementia if it is reversible, or we manage the symptoms of the dementia if it is a progressive pathology.

Clarifying the dementia diagnosis is very important.

Dementias are a major cause of health care burden on society and on the caregiver.

Caregiving burden on families

Increasing hospitalizations

Increasing availability of disease modifying therapies

Nursing facilities with high staff turnover

Poor access to social work resources

Treatment of dementia can vary depending on the cause, but in general follow three patterns

SYMPTOM BASED THERAPIES

BEHAVIORAL THERAPIES

DISEASE MODIFYING THERAPIES

SYMPTOM- BASED THERAPIES focus on improving **quality of life and reducing distressing symptoms.**

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Treatments for Cognition

- Forgetfulness, Confusion
- Name finding difficulties
- Disorientation
- Navigation issues
- Problem solving difficulties
- Poor concentration and processing

- Donepezil = Aricept
- Rivastigmine = Exelon
- Galantamine = Razadyne
- Memantine = Namenda

Treatments for Stress

- Anxiety, Stress
- Apathy, Depression
  - Duloxetine, venlafaxine
  - Lexapro, Zoloft, Prozac
  - Wellbutrin

- Paranoia, Delusions
- Capgras Syndrome, Fregoli Syndrome
- Hallucinations, Agitation
  - Seroquel
  - Abilify, Risperdal, Olanzapine
  - Rexulti, Neudexta, Nuplazid

Treatments for Sleep/Wake

- Insomnia
  - Melatonin
  - Trazodone, Seroquel
- Sleep-wake disturbance
- Sundowning

- Hypersomnia
- Decreased Alertness
  - Amantadine
  - Modafinil/Armodafinil
  - Adderall, Ritalin, Vyvanse

Treatments for Appetite

- Increased Appetite
- Low Appetite, No Appetite
- Inability to taste or smell food
- Loss of control when eating
  - Binge eating
  - Binge drinking
  - Binge habits

  - SSRIs: Lexapro, Zoloft, Prozac
  - Wellbutrin
  - Mirtazapine
  - Topiramate

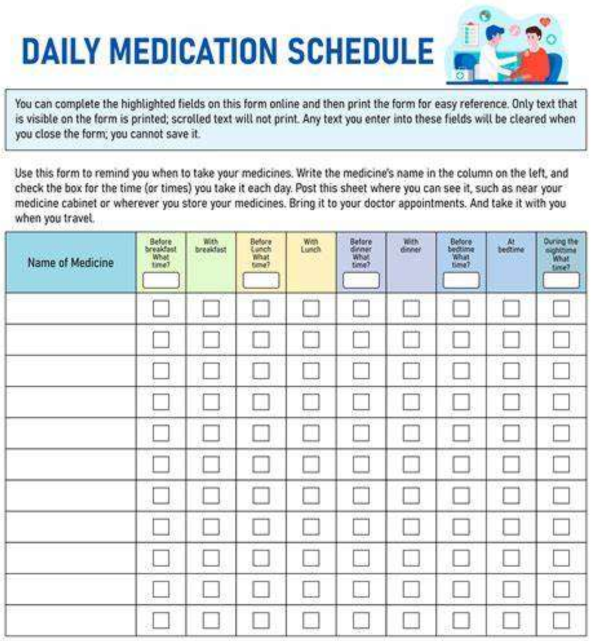
Neurorehabilitation is pivotal for management of cognitive change, physical change, and functional change.

physical therapy
occupational therapy
speech therapy
cognitive therapy

Rehabilitation specialists help achieve goals in function, like:

I want to remember to take my pills on time.

They can also evaluate for changes in function like, I am having trouble swallowing my pills.



DAILY MEDICATION SCHEDULE

You can complete the highlighted fields on this form online and then print the form for easy reference. Only text that is visible on the form is printed; scrolled text will not print. Any text you enter into these fields will be cleared when you close the form; you cannot save it.

Use this form to remind you when to take your medicines. Write the medicine's name in the column on the left, and check the box for the time (or times) you take it each day. Post this sheet where you can see it, such as near your medicine cabinet or wherever you store your medicines. Bring it to your doctor appointments. And take it with you when you travel.

Name of Medicine	Before breakfast What time?	With breakfast	Before Lunch What time?	With Lunch	Before dinner What time?	With dinner	Before bedtime What time?	At bedtime	During the nighttime What time?
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BEHAVIORAL THERAPIES focus on **reducing challenging behaviors** and improving **quality of life.**

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The brain is responsible for survival.

With dementia, "the CEO" is now threatened, because of the structural and chemical changes happening in "headquarters"

The brain is in constant **SURVIVAL MODE.**

- Loss of decision making
- Inability to remember or process data to survive
- Not realizing the severity of dysfunction or debility
- Loss of control and autonomy

Is the doctor going to take away my driving license? Put me in a nursing home?

Step Into Their World:

Recognizing and Addressing Stressors

What just happened?

Did somebody new enter the room?

Was there a loud or unexpected sound?

Is the conversation confusing?

Did this remind them of something?

Is the light too bright?

Is this a difficult task?

Pain or discomfort

Fear or frustration

Loss of control or autonomy

New people or places

Confusing conversation or tasks

Overstimulation or under-stimulation

Lack of information

Is the water too hot or cold?

Are they comfortable in their clothes?

Does their stomach hurt?

Did they not sleep well?

Is something bothering them?

Have they eaten and taken their meds?

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In their world, they are just trying to survive, **so we help them survive.**

5 Rs of De-Escalation:

Reassure

Reorient

Redirect

Repeat

Respect

Usually telling someone with a brain problem, that they have a problem increases the stress response

- Try not to emphasize weakness or inability
  - You get to be a passenger!
- Focus on finding a common ground
  - I also like my food cut up, let me help you
- Reassure and respect
  - I love how you care about my safety, let's check together to make sure we are safe

DISEASE-MODIFYING THERAPIES focus on changing the pathology or trigger of brain dysfunction.

Beginning in 2021, the FDA has approved **amyloid-removing infusion** medications for Alzheimer's Disease. There are not many disease-modifying therapies for dementia.

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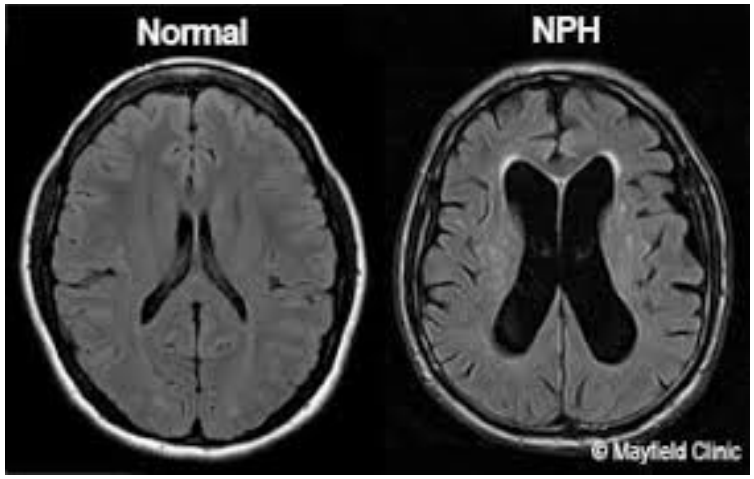
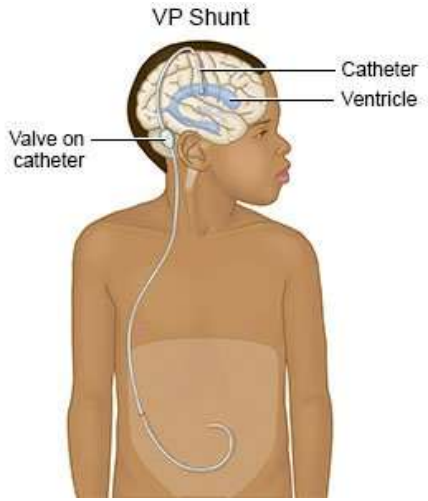
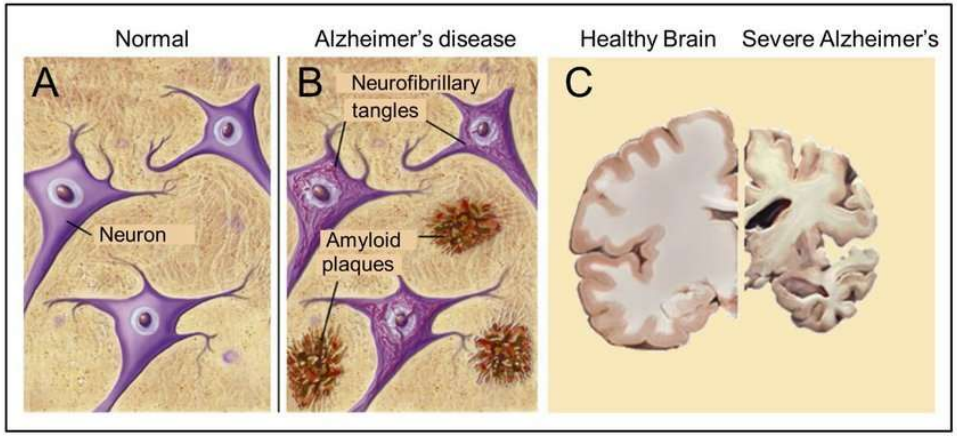
Normal Pressure Hydrocephalus is caused by a buildup of fluid in the brain. It causes **changes in walking, memory loss, and urinary control.**

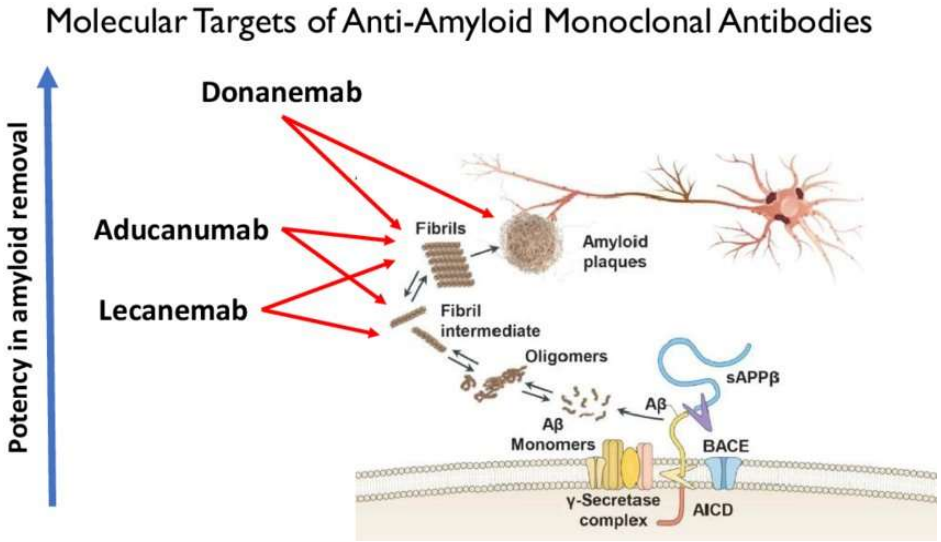


If caught early (before too much ballooning into the brain), a **ventriculoperitoneal shunt (small brain surgery)** can divert the fluid and stop the progression of dementia.



Alzheimer's Disease is defined pathologically by the presence of amyloid plaques and tau tangles.



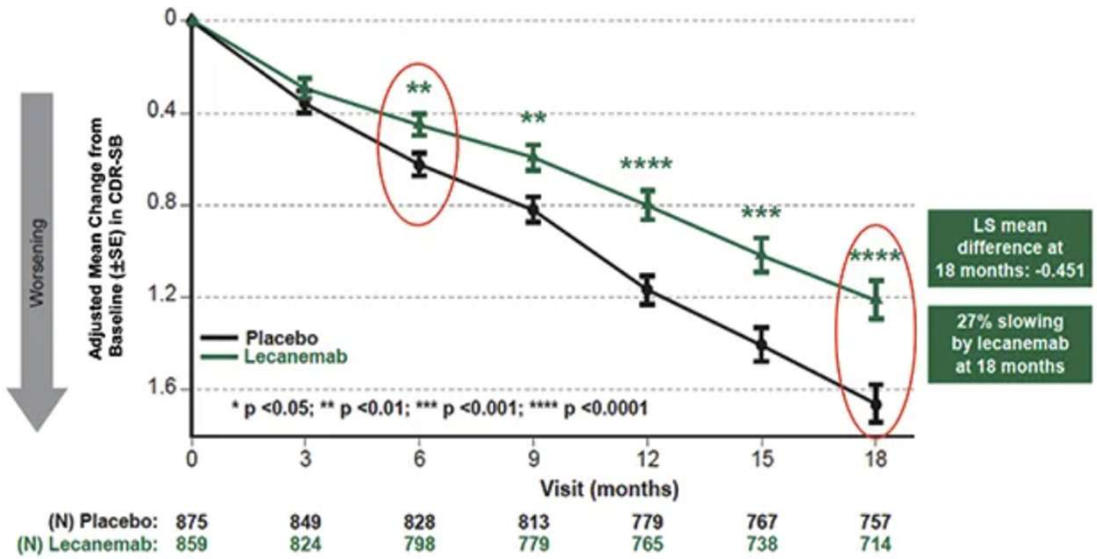


There are new monoclonal antibody medications that tag the amyloid plaques and alert the immune system to remove the toxic agents; thus, reducing further damage to the brain.

Lecanemab = Leqembi

Approved in July 2023

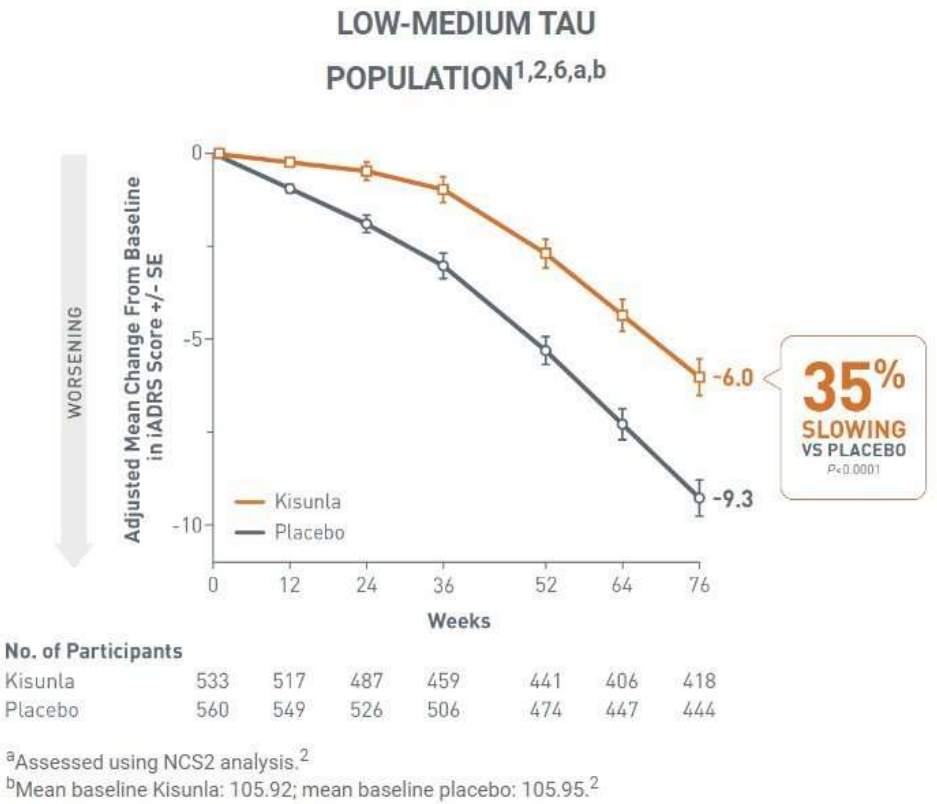
- Lecanemab has demonstrated 27% slowing of baseline cognitive progression over 18 months
  - Bimonthly infusions
  - ~$26,000/year
  - $3k-5k/infusion costs
  - Currently covered by Medicare and many other commercial payers
- Recently approved for maintenance monthly infusions



Donanemab = Kisunla

Approved in July 2024

- Donanemab has demonstrated ~35% slowing of baseline cognitive progression over 18 months
  - Monthly infusions
  - ~$32,000/year
  - $3k-5k/infusion costs
  - Currently covered by Medicare and many other commercial payers
- Can stop treatment in 6-12 months
  - Guided by PET imaging clearance of amyloid plaques



[a]Assessed using NCS2 analysis.[2]
[b]Mean baseline Kisunla: 105.92; mean baseline placebo: 105.95.[2]

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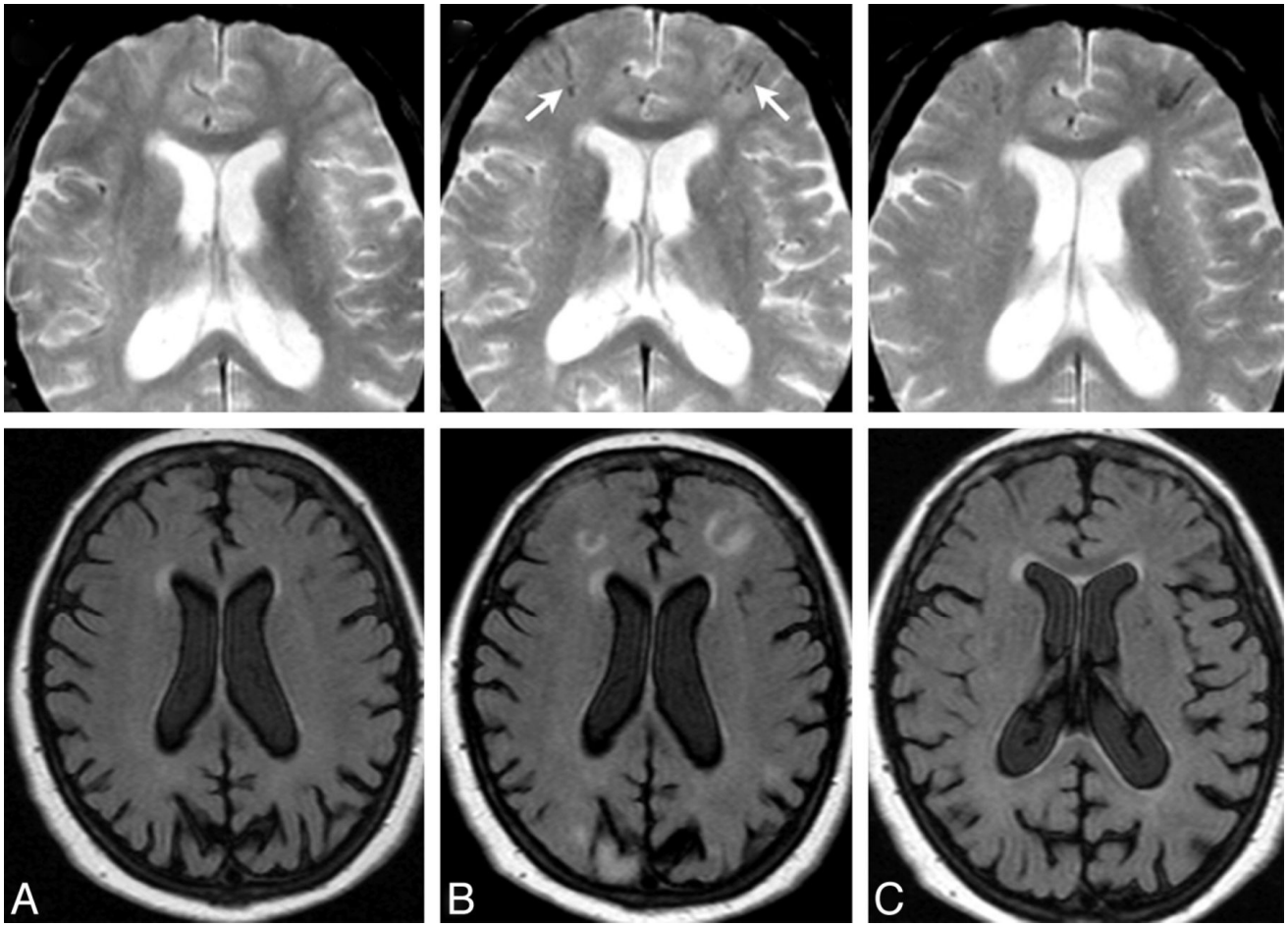
Amyloid-targeting medications are associated with a serious side effect called ARIA: amyloid related imaging abnormalities

ARIA can show up on MRI Brain imaging as swelling or bleeding spots in the brain. ARIA can cause symptoms of headache, dizziness, vision change, seizures, strokes, and even death if not treated.



ARIA can occur 15-30% of the time while on these drugs, but usually this is asymptomatic.

There are specific factors that increase the risk of ARIA, and a thorough risks and benefits discussion is important before beginning anti-amyloid therapy.

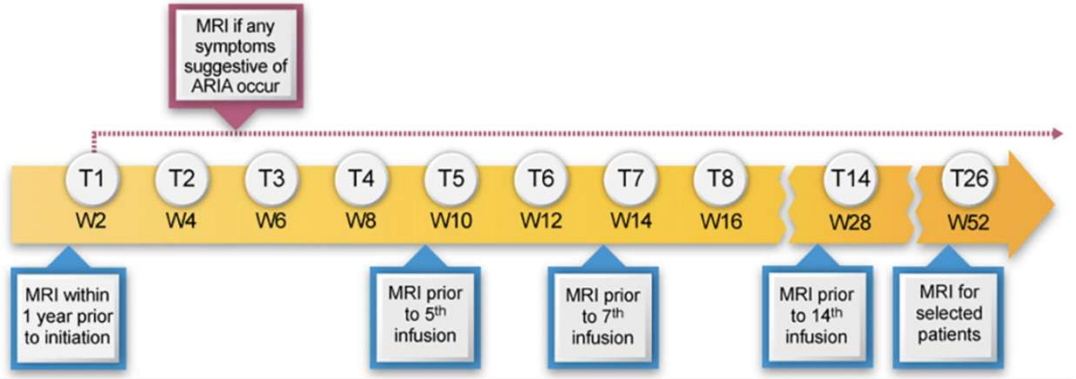


Figure 1. MRI monitoring for lecanemab

ARIA Risk Factors Include:

- *APOE e4/e4*
- *Bleeding disorders*
- *Use of anticoagulants*
- *Recent major stroke or severe vascular disease*

Anti-amyloid infusions are for early stages of dementia and mild cognitive impairment due to underlying **Alzheimer's Disease** only.

These strong monoclonal antibody infusions are not a good fit for someone more advanced in their disease (detailed schedule of MRIs, infusions, doctor appointments).

Infusions can slow down progression of dementia but are not cures, so it is important to assess if this is worth the risk before considering this for a patient.

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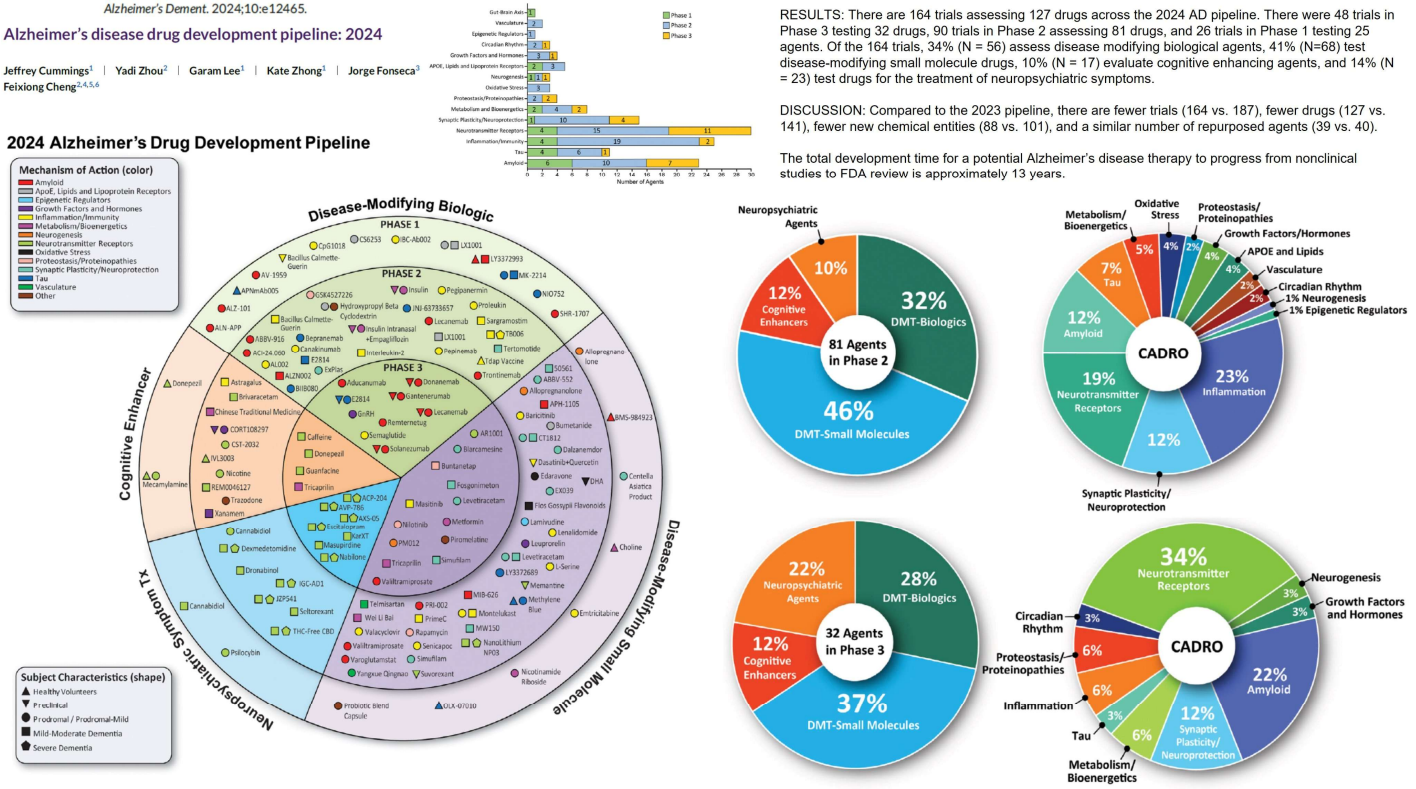
There are many targets being studied to combat AD, and **amyloid is just one target**. Other treatments focus on glucose control, reducing inflammation, removing tau, or controlling the symptoms.



We also have hundreds of research trials demonstrating that keeping the brain healthy throughout life is an effective way to prevent and treat the onset of dementia symptoms.

1. Keep your body physically fit
   Aim for at least 30 minutes of daily moderate exercise
2. Eat nutritious brain healthy foods
   Low in processing, high in fruits, vegetables and antioxidants, MIND diet
3. Treat your medical risk factors
   Tight control of glucose, blood pressure, cholesterol
4. Get enough rest and sleep
   Aim for at least 7-8 hours of uninterrupted sleep, at night
5. Keep your brain sharp and engaged
   Find challenging tasks and hobbies that interest you
6. Keep socially connected
   Be part of a community, reduce stress, be happy

It is exciting to have these advanced diagnostics and therapeutics for memory disorders, but dementia is usually not an emergency.

Many symptoms of dementia can be managed at the primary care level, but it is important to clarify if the patient may need more help.

SYMPTOM BASED THERAPIES

BEHAVIORAL THERAPIES

DISEASE MODIFYING THERAPIES

1. **History and Physical:** Cognitive Screen or Neuropsych
2. **Structural and Chemical Baseline:**
   - ❑ MRI Brain (Neuroquant) (or CT Head if over age 85)
   - ❑ Basic Screening Labs: CBC, CMP, TSH, Vit D, Vit B12

Here is an opportunity to connect the patient with resources based on the initial evaluation

As you know, specialists that can help guide advanced therapeutics often have a 6-9 month waitlist.

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Any Questions?

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