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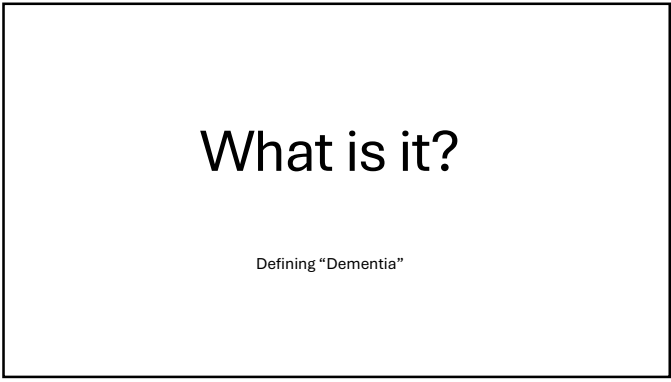
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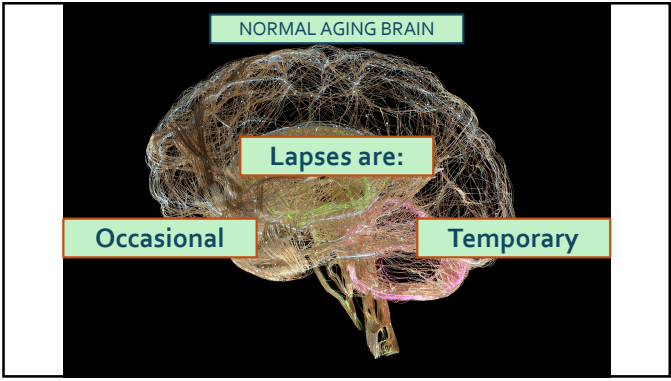
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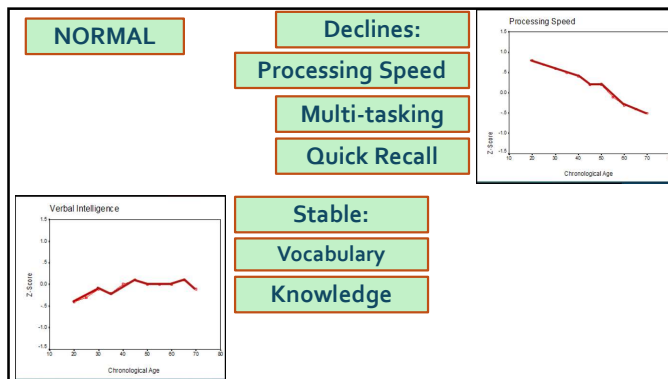
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### Cognitive ability changes

- “Crystallized ability” **stays the same**
  - Information/skills gained from experience
- “Fluid intelligence” **declines**
  - Flexible reasoning and novel problem-solving
- Decreased learning efficiency
  - takes longer/more repetition
- “Tip-of-the-tongue” phenomenon
- Slowed reaction speed

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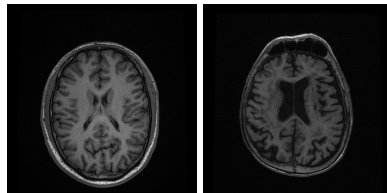
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### Brain changes in aging

- ↓ size
- ↓ blood flow
- Neuron loss
- ↓ connections (synapses)
- **New ones made!**
  - rates of loss > gains



younger patient

older patient

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Not Just Memory	
Immediate Recall	• Very short - within seconds
Delayed Recall	• Longer - minutes
Attention	• Repetitive tasks
Visuospatial/Construction	• Identification and copying
Language	• Repetition, fluency, expression
Executive Function	• Navigation, problem-solving
Orientation	• Self, time, place, etc...

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Major Neurocognitive Disorder	
=	
>2 Areas of cognition impaired	
&	
Impacts day-to-day activities	

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Major Neurocognitive Disorder (DSM)	
Syndrome = cluster of symptoms with no clear cause	
Impairment >2 cognitive domains	
Decline from baseline	
Permanent/Irreversible	
Impaired daily function	
Not explained by other causes	

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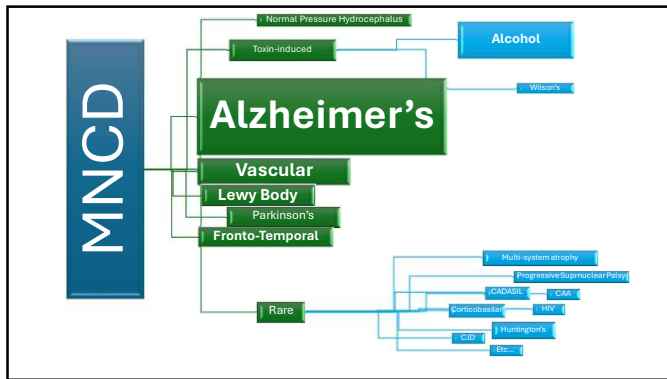
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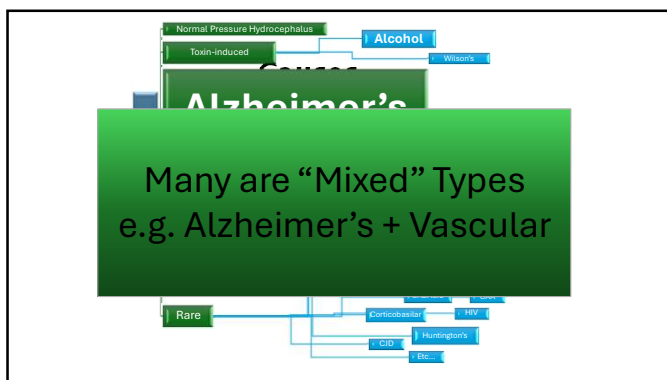
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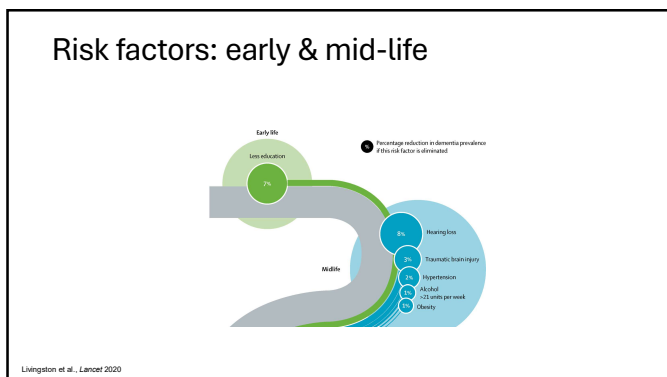
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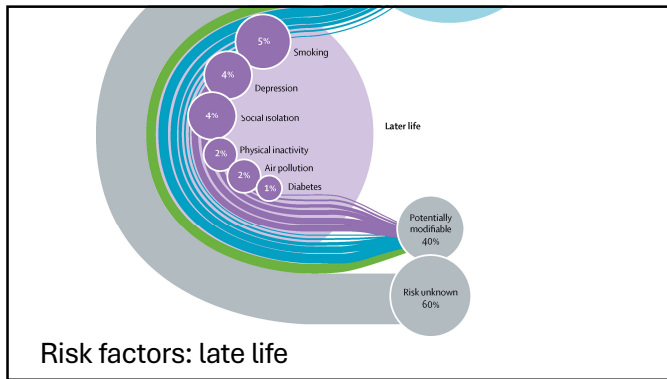
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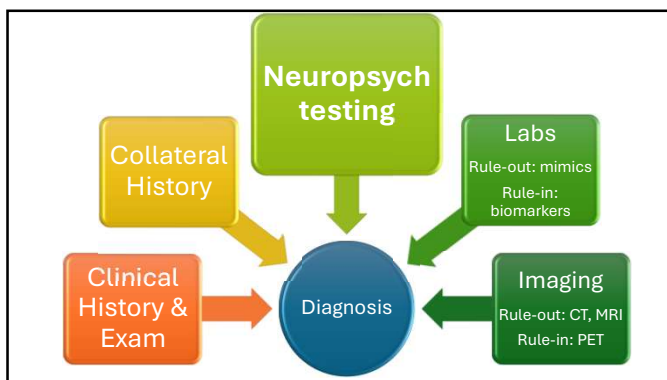
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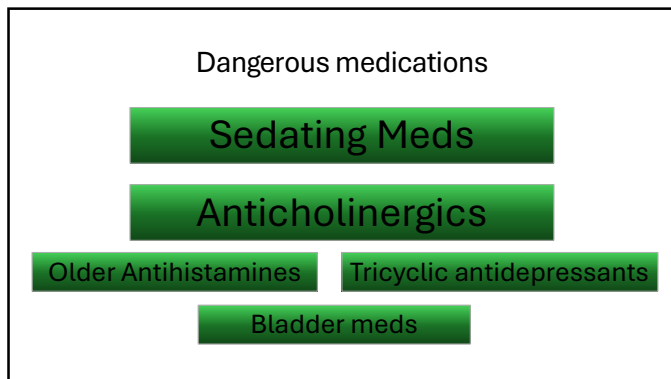
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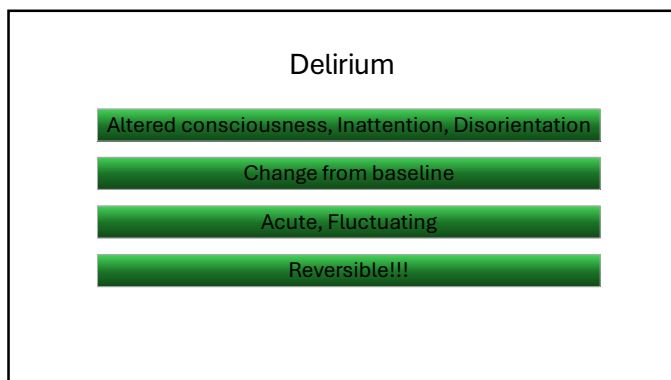
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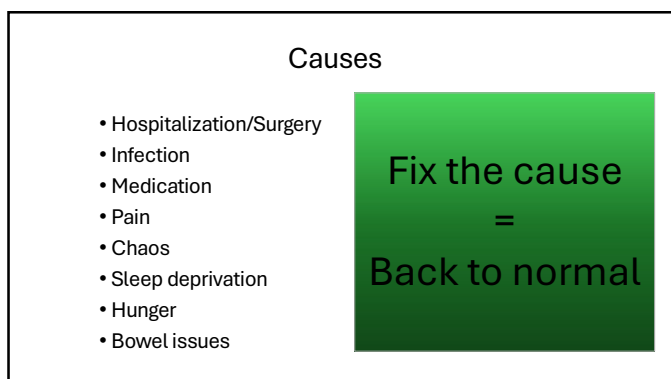
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# What type is it?

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“Probable” Alzheimer’s diagnosis

Meets Criteria for MNCD

Known causative genetic mutation

OR

Memory + 1 other cognitive domain

Steadily progressive, gradual

No evidence of “mixed” etiology

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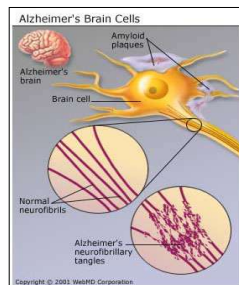
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## Alzheimer’s Neuropathology

- Amyloid beta plaques
  - Neuritic plaques
  - Extracellular
- Neurofibrillary tangles
  - Tau protein
  - Intracellular



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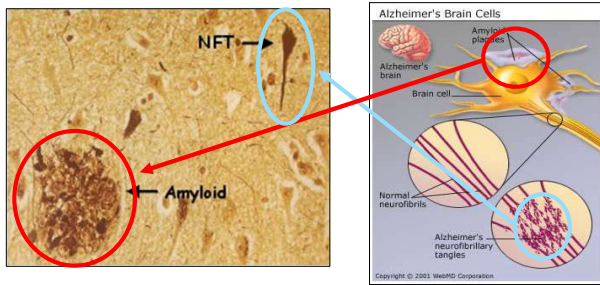
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## Alzheimer's Neuropathology



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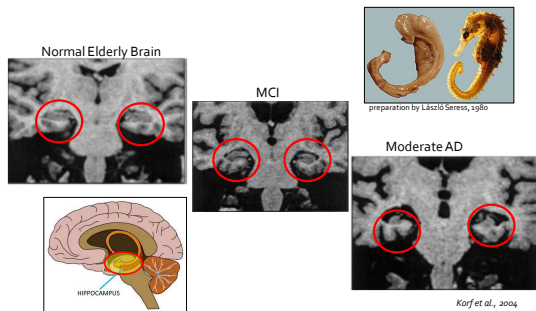
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## Hippocampal atrophy



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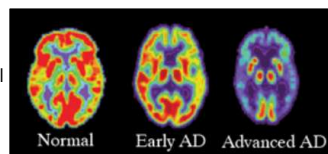
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## Biomarkers

- Cerebrospinal Fluid (CSF) measures
  - Acquired via lumbar puncture (LP)
  - Changes in the levels of tau and beta-amyloid proteins
- Neuroimaging
  - MRI – structural/functional
  - PET – glucose uptake
  - PET – amyloid imaging



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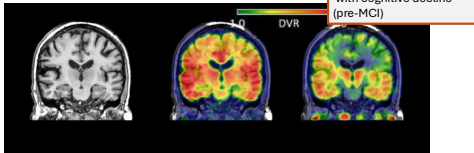
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### New: Amyloid and Tau PET Scans

- Amyloid PET scans
  - Approved, some insurances cover
- Tau PET scans
  - In research



Courtesy: Sterling Johnson, PhD

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### New: Blood-based biomarkers

- Blood tests for Amyloid & Tau
- Detect amyloid- $\beta$  and tau fragments in blood
- Generate a "probability score"
  - E.g. "probable brain amyloid"
- **NOT diagnostic**
  - Supplements clinical evaluation

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### Vascular Dementia

- Forms:
  - Focal infarct
  - Multi-infarct
  - Subcortical ischemia
- Usually coexists with Alzheimer's
  - as a sole cause, only accounts for 10% of cases

Rabin et al., 2009—Clinical Neuropsychology: A Pocket Handbook for Assessment, Hodges & Graham, 2002

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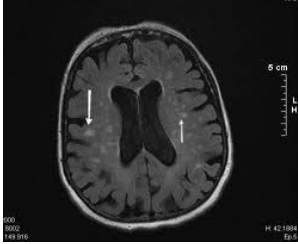
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### Signs

- Cognitive Change:
  - Executive
  - Processing speed
  - Visuospatial
- Evidence of CVD
  - Stroke
  - Stepwise/sudden decline
  - **White matter changes**
  - Physical exam



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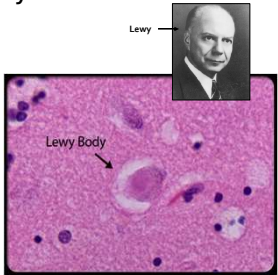
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### Dementia with Lewy Bodies

- Lewy bodies: Abnormal deposits of alpha-synuclein protein inside neurons
- Similar to Parkinson's, but:
  - PD: Lewy bodies mainly in substantia nigra
  - DLB: Lewy bodies distributed throughout cortex



Oda et al., 2009, Psychogeriatrics

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### Dementia with Lewy Bodies

Gradual onset		
>2 = Necessary		
Recurrent hallucinations	Fluctuating Cognition	Parkinsonism
Suggestive		
REM Sleep behavior disorder	Low dopamine uptake on PET/SPECT scan	Neuroleptic sensitivity

DSM-V, 2014

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Frontotemporal Dementia

- 2<sup>nd</sup> most common in age <65
  - 1<sup>st</sup> still Alzheimer's
  - Rare if age>70
- Onset typically between 45-60 years
- Behavioral and Language effects

Weder et al., 2007 Annals of General Psychiatry

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Subtype	Behavioral	Cognitive	Motor
Behavioral Variant (bvFTD) – about half of cases	<ul style="list-style-type: none"><li>• Early behavioral disinhibition</li><li>• Early apathy or inertia</li><li>• Early loss of sympathy or empathy</li><li>• Early perseveration, stereotyped or compulsive/ritualistic behavior</li><li>• Hyperorality/dietary changes</li></ul>	<ul style="list-style-type: none"><li>• Executive/generation deficits</li><li>• Relative sparing of memory/visuospatial function</li><li>• Later: speech deficits</li></ul>	<ul style="list-style-type: none"><li>• Primitive reflexes</li><li>• Eye movement abnormalities</li><li>• Parkinsonism (akinesia, rigidity, tremor)</li></ul>
Language Variants/Primary Progressive Aphasia			
Semantic dementia	<ul style="list-style-type: none"><li>• Loss of sympathy and empathy</li><li>• Mental rigidity/compulsions</li><li>• Dietary changes</li></ul>	<ul style="list-style-type: none"><li>• Confrontation naming</li><li>• Single-word comprehension</li><li>• Object knowledge</li><li>• Surface dyslexia or dysgraphia</li></ul>	<ul style="list-style-type: none"><li>• Normal until late</li></ul>
Progressive non-fluent aphasia	<ul style="list-style-type: none"><li>• Preservation of social skills until late</li></ul>	<ul style="list-style-type: none"><li>• Agrammatism in language production</li><li>• Effortful, halting speech</li><li>• Impaired comprehension of complex sentences</li></ul>	<ul style="list-style-type: none"><li>• Asymmetric parkinsonism</li><li>• Orofacial apraxia</li></ul>

LaForce, 2023

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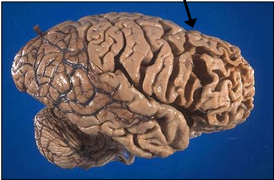
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Frontotemporal Dementia

Frontal/temporal lobe atrophy



**Pick bodies:** spherical cytoplasmic neuronal inclusions ("ballooned neurons") containing deposition of abnormally hyperphosphorylated tau



Talpa et al., 2012 Frontiers in Neurology

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Frontotemporal dementia

- MRI: Frontal & temporal atrophy
  - Parietal lobe less affected – distinguishes from AD
- PET: Hypometabolism in frontal lobe

Brain imaging for a patient with Frontotemporal Dementia

Alzheimer's Dementia

Image copied from: Cleveland Clinic ([my.clevelandclinic.org](http://my.clevelandclinic.org))

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Okay, it's dementia,  
now what?

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Medications

Donepezil

• Increase acetylcholine

Rivastigmine

• Slow down cognitive loss

Galantamine

• Stomach upset, slow heart, anxiety, weird dreams

Memantine

• Alters NMDA activity

• Stomach upset, sedating, weird dreams

Statins

• Improve blood flow to brain

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New = Infusions against Amyloid

Aducanumab	Lecanemab	Donanemab
	Current Treatment	Current Treatment
High brain bleeding	Clears amyloid	Most effective so far?
Some benefit	Lower risk of bleeding	Higher risk of bleeding
Low off market	Some benefit	

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Medication Limits

Designed only for Alzheimer's

Slows disease  
But doesn't stop or reverse

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What else can you do?

Exercise!

Keep your brain active

Support

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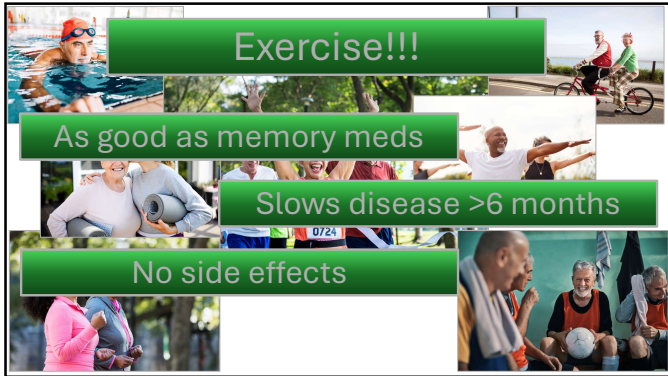
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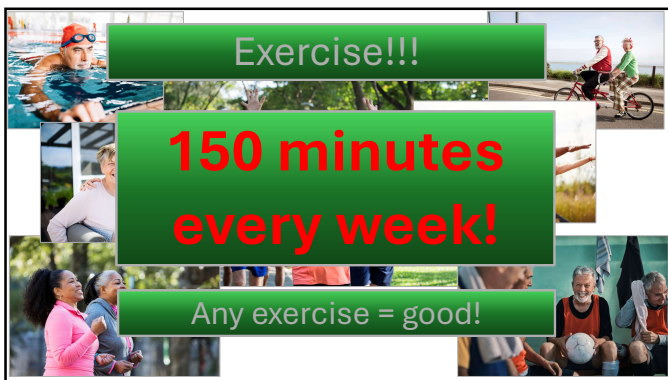
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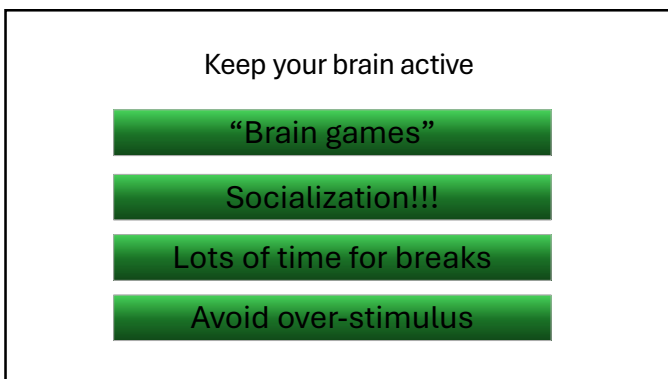
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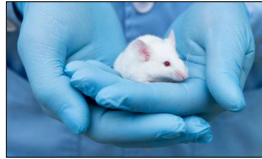
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### Supplements?

- Work great in mice!
- None proven to help in humans



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### How things change

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### Mild Alzheimer's



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### Moderate Alzheimer's

- Can't retain conversation
- Needs frequent reassurance, paranoia
- ↑ Safety issues: cooking, wandering, hoarding
- ↑ Confabulation – **NOT LYING**
- Sleep/wake changes, sun-downing, hallucinations
- No reasoning with them
- ↑ Reliance on Emotion/feeling

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### Mid-Late Alzheimer's

- Tunnel Vision
- Gait small, shuffling, balance poor
- No fine motor skills
- Immediate needs only – demanding, imposing
- Repetition is soothing
- Hypersensitivity to touch, temperature
- Agitation with inability to describe needs

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### Late Alzheimer's

- Cannot recognize or use objects
- Can mimic movement, not follow directions
- Routine is most important
- Reliant on emotional tone for comfort
- ↓ basic bodily functions (swallow, toilet timing)
- ↑ Startle reflex, "living in own world"
- Complete dependence for cares

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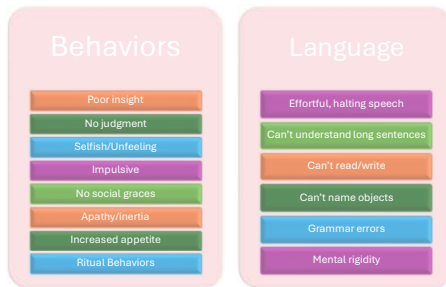
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## Fronto-Temporal Dementia



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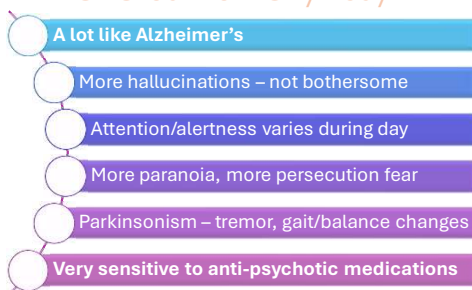
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## Dementia with Lewy Body



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## Vascular Dementia



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### Agitation & Aggression

At least 50% have at some point

15-30% will need medication

>50% on meds need them  
long-term

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### Possible Triggers

New environment

Chaos

Meds

Infection

Pain

Depression

Anything new or  
different

Itching

Strangers

Poor Sleep

Bored/Tired

Constipation

Hunger

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## What do you do?

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Assess the Situation

Dangerous?	• Vs frustrating or uncomfortable
Triggers?	• Time of day? People? Etc...
Body language?	• Do they look afraid? In pain?
Basic needs?	• Bathroom? Food?

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Assess the Situation

What are they really trying to say???	table
Basic needs?	• Bathroom? Food?

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First Steps

Decrease Chaos	• Turn off TV, radio, ↓ glare
Time outs!	• Quiet place to re-set
Stability	• Routines, habitual activities
Don't ask Why	• Stick to who, what, how
Validate feelings	• Reassurance of safety/care
Don't argue	• Hard!!!
Body Language/Tone	• Emotions >>> Words!

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Daily Tasks	
Time	• Will always take longer
Instructions	• One step at a time
Timing	• Calm tasks in late afternoon
Pick your Battles	• Okay to change topics
Two-step choices	• Yes/no, red/blue, etc...
Hallucinations	• Don't argue, okay to not see them
Therapeutic lies	• "Oh, it's not ready today"

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Sometimes medications are Necessary	
Keeping you and them safe	
Keeping them comfortable	
Keeping others safe	

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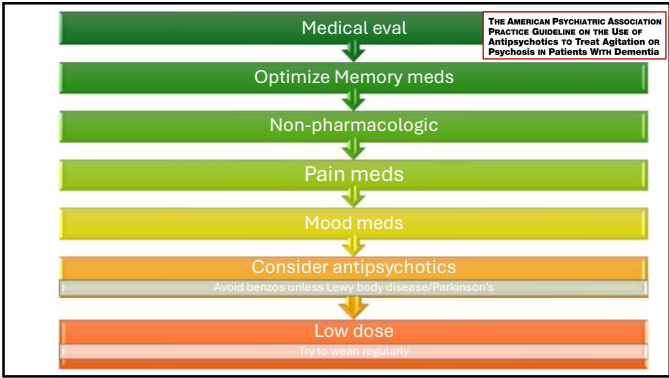
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All medications have side effects

Increased falls

Sedation

Weight gain

Increased mortality

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Use the lowest dose

Always ask: when can we  
decrease/stop?

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Now you know...

More than just memory

Watch for signs!

Rule out mimics

Get tested early

Medications can help

Exercise!!!

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Questions?

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