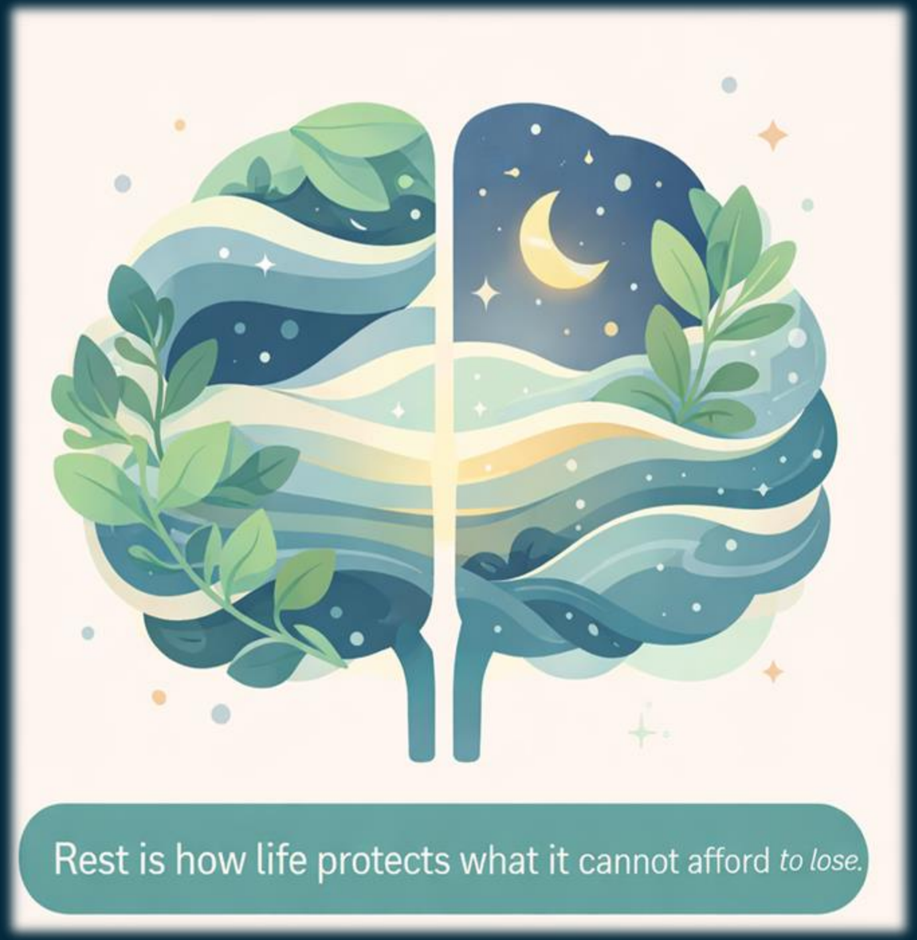
BEACON 2026

Brain Restoration

How the Brain Rejuvenates Itself, and What We Can Do to Protect It

A PRESENTATION BY
JAMES RINI, MD, MPH



Law of Conservation is Restoration

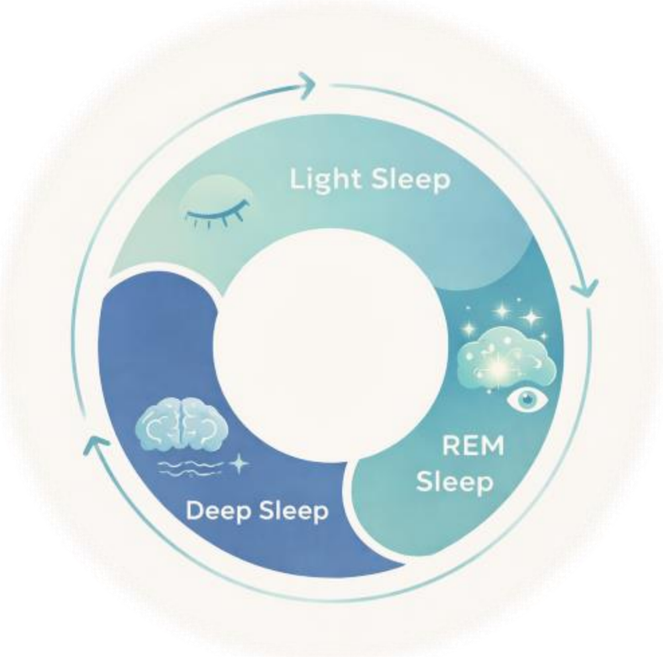
- Energy conservation is basic to all life and complex brains are energy expensive
- Without restoration, neural stimulation creates noise not strength
- The inability to fully restore the brain results eventually results in neural damage

Sleep evolved as a protected state for **restoration**, **recalibration**, and **repair**

Human Sleep is a Cycle

Brain Restoration

Sleep is not a 'OFF' switch— it unfolds in repeating stages through the night



90 mins Cycle
4-6 Cycles per night
Early night Heavy N3
Middle night Heavy N2
Late night Heavy REM

LIGHT SLEEP (N1/N2): 50-60% of sleep
- Disconnect from the outside world
- Settle into protected rest
- Decrease metabolic demands

DEEP SLEEP (N3-N4): 15-25 % of sleep
- Deep physical restoration
- Energy conservation
- Physiologic reset
- Clearence of Brain inflammation

REM SLEEP: 20-25% of sleep
- Supports memory
- Emotional processing
- Internal integration

- A healthy night of sleep depends on **number of full cycle**, not just time spent asleep
- Different stages of sleep **do different jobs** — together they restore and protect the brain.

The best way to understand these jobs, is to understand why they were built in the first place

The Evolution of Sleep

Before Sleep, There Was Rest

- Life could not remain active all the time
- Early organisms developed cycles of engagement and quiescence
- Restoration began as **rhythmic inactivity** before complex brains existed

Rest began as stillness—sleep evolved when **stillness was no longer sufficient**.

Precursor to N1

- **Why it emerged:** Even simple systems **required periodic disengagement** to prevent depletion
- **What it enabled:** Energy conservation
- Reduced environmental reactivity, Baseline restoration without internal processing

“Periodic Disengagement Prevents Depletion”

The Evolution of Sleep

The Brain Learned to Filter Itself

- As sensory complexity increased, rest required active filtering—not just disengagement

- The brain began:
  - Gating external input → protected internal processing
  - Generating sleep spindles = plasticity pulses
  - Stabilizing fragile learning traces
  - Refining motor and cognitive patterns

Rest became an **active process of selection**—keeping what matters, suppressing what doesn't

Precursor to N2

- **Why it emerged:** Increasing complexity required low-noise internal processing
- **What it enabled** low-reactivity states, thalamocortical gating, controlled passive rest → controlled neural filtering

"Complex Sensation Requires Stable Deactivation And Filtering"

The Evolution of Sleep

Deeper Rhythmic Recovery

- Simple disengagement was no longer sufficient
- A fundamental tradeoff emerged: **restoration vs. vulnerability**
- The solution: rhythmic cycling between disconnection and intermittent awareness
- This architecture enabled deep restoration without sustained helplessness

Deep restoration became possible **without continuous vulnerability**

Proto-NREM Architecture (N1-N2-N3)

- **Why it emerged:** Need for true metabolic and structural reset
- **What it looked like:** : Global synchronization, profound downscaling, minimal responsiveness

"Deep Recovery Became Possible Without Total Shutdown"

The Evolution of Sleep

Sleep Began Serving the Mind

- Rest was no longer just about restoring depleted energy
- More developed brains likely used off-line states to sort, reinforce, and rehearse information
- In some predators, sleep-like offline states may have helped process sensory experience and prepare future behavior — an early step toward REM-like activity

Precursor to REM

- **Why it emerged:** Brains needed a more stable buffer from the outside world
- **What it looked like:** lighter but structured disengagement, sensory gating, reduced reactivity

"Sleep Became An Offline Mode For Rehearsal, And Adaptation"

The Evolution of Sleep

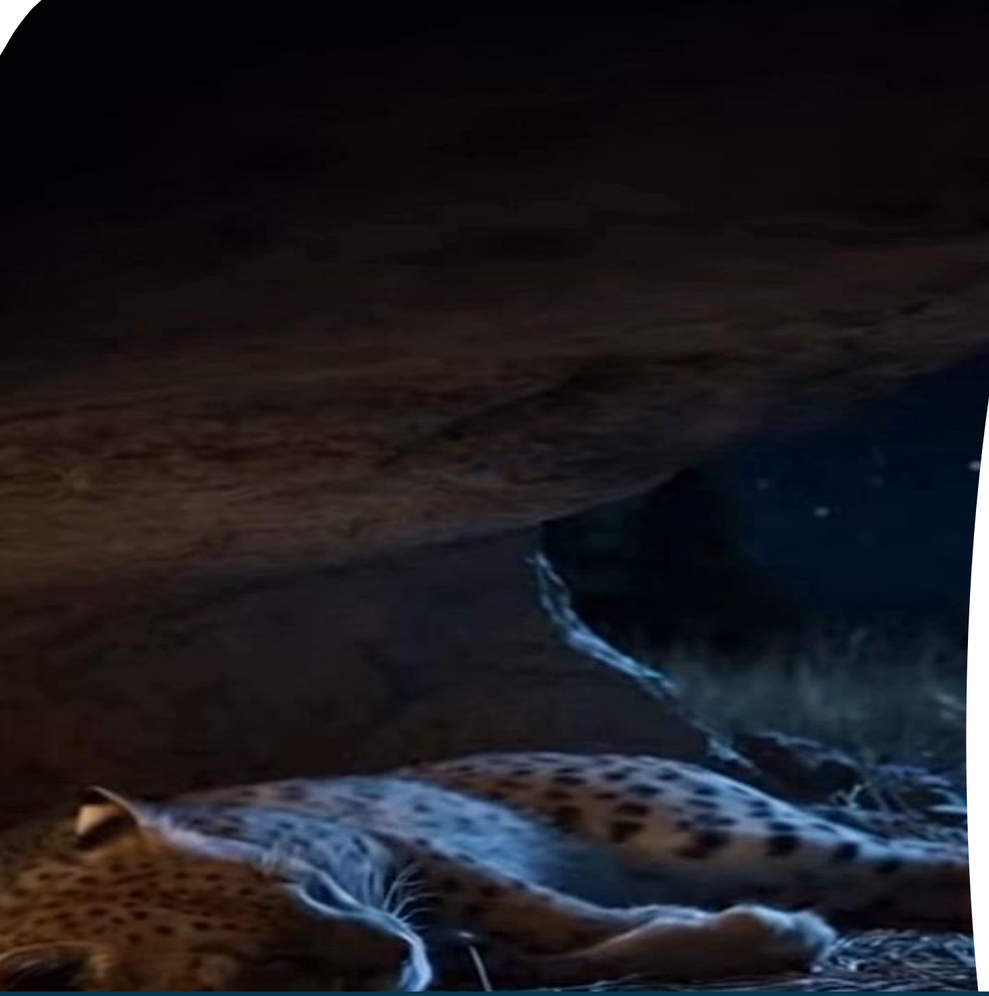
Warm Brains need Deeper Sleep

- Early mammals were **social**, **nocturnal**, and sheltered in **cool** underground burrows, where longer immobility became safer
- Endothermy (warm-blooded) allowed longer, more reliable brain activity but required more energy and tighter physiologic control
- Preserved deeper sleep allowed restoration despite environmental pressures and repeated intermittent social arousals

Toward deeper N3-NREM

- **Why it emerged:** Endothermic animals need to conserve heat and remain safe longer
- **What it looked like:** Deeper atonic sleep, brief arousals, and stronger suppression of wakefulness

"Cooler environments need deeper more protected sleep"



The Evolution of Sleep

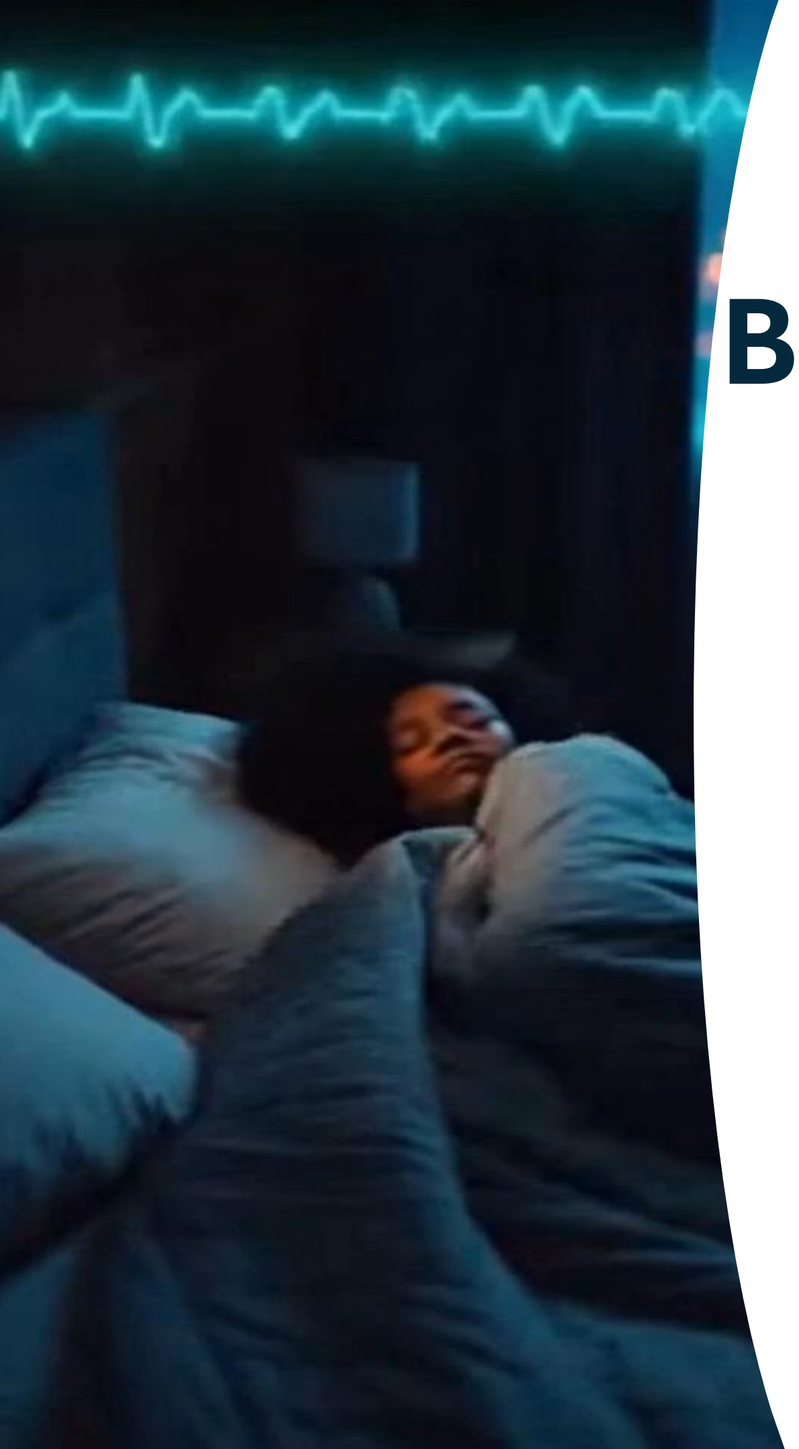
REM Became Active-Rest

- Proto-REM-like predator behavior, likely evolved as an active sleep state for internal rehearsal and processing
- It reduced movement and thermoregulation while preserving brain activity
- Supported memory, emotion, and adaptive prediction

Consolidated REM

- **Why it emerged: C**omplex endothermic brains could shift energy away from thermoregulation toward complex neural processing
- **What it looked like:** Muscle atonia, vivid internal activation, and recurring cycles through the night

“Deeper Sleep Allowed For More Complex Brain Activity”



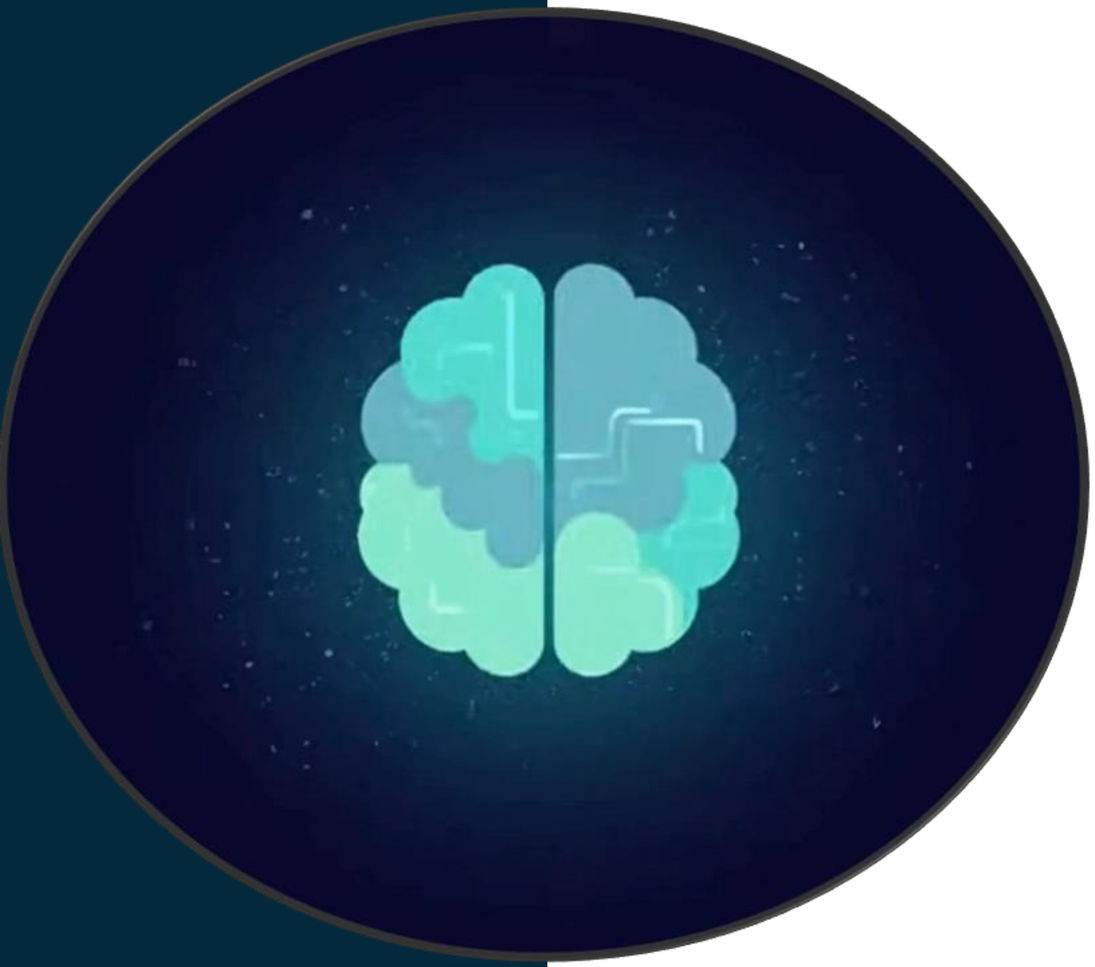
Better Rest, Better Brain

Sleep Was Never Just About Fatigue

- Complex brains require active sequence to maintain **deep physiological recovery** to preserves neural systems that would otherwise degrade under constant use

- Sleep was built over eons of evolution to
  - Protects **energy balance**
  - Protect the nervous system from **overactivity**
  - Balance **safety** with deactivation
  - Improve **cognitive processing**

Restoration is an active biologic process
***not* a passive process**



What restoration means on the neural level

- Neural reset (sleep)
- Physiologic downshift (autonomic)
- Environmental quieting (low demand states)

Majority of this occurs during **deep sleep**

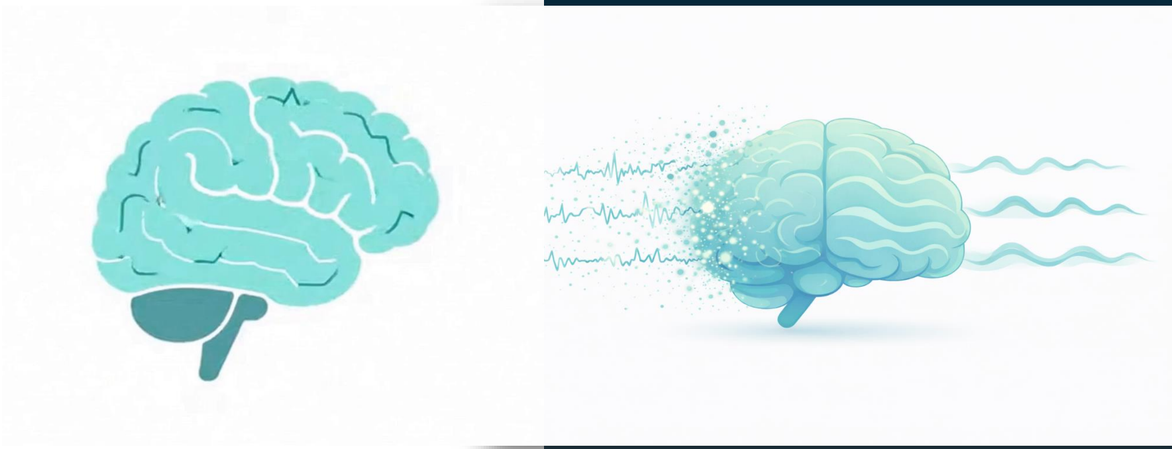
Deep Sleep and the Global Brain Activity

Deep sleep is the brain's **lowest-noise state**.

- Lower noradrenergic tone →
- Decreased fragmented firing → Less background noise

Deep sleep **resets** the brain's electrical activity .

- More synchronized slow wave activity →
- Reset overactive circuits → Reduces complexity



Deep sleep does not simply turn the brain off — it reorganizes brain activity into a **quieter** and **coordinated state** that may support restoration.

So, then what is **single neuron recovery**?

Krause et al., 2017;
Mander et al., 2017;
Bishir et al., 2020;
Himali et al., 2023;

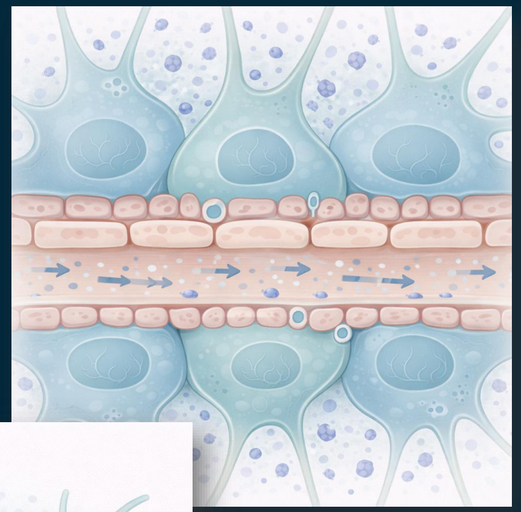
Deep Sleep and the Glymphatic System

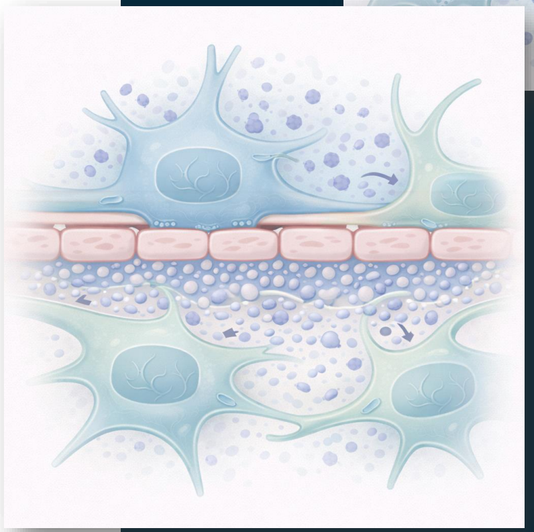
Brain Restoration

Deep sleep is the brain's **most <u>permeable</u> state**.

- Lower noradrenergic tone →
- Decrease Astrocytes swelling →
- More interstitial space = More flow of CSF →
- Enables Aquaporin-4–dependent glymphatic exchange to **clear waste**

DAY





NIGHT

Deep Sleep opens a **Window for Cleanup and Repair**

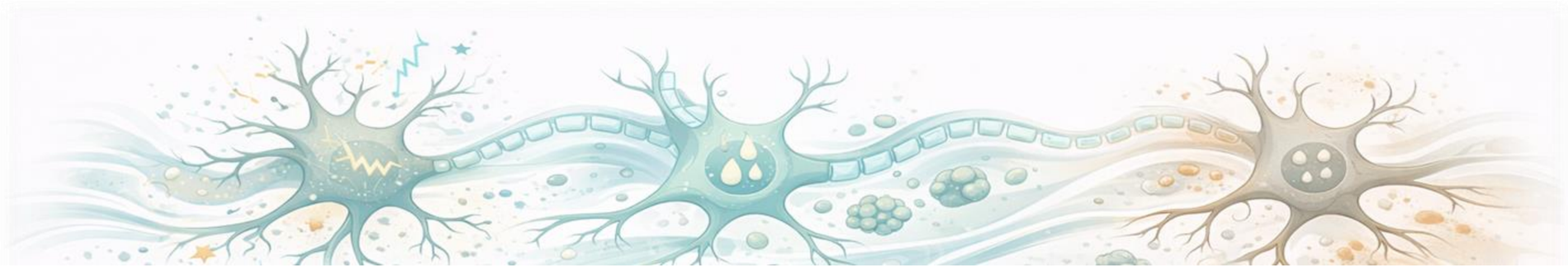
- Helps reset **excess chemical** signaling in the brain
- Reduces **inflammatory stress**
- Helps clearance of byproducts, e.g. **amyloid and tau**
- Helps restore cellular energy balance i.e. **creatine**

When the brain becomes quieter and more synchronized, **cleanup**, **reset**, and **repair** become easier.

Xie et al., 2013;
Mander et al., 2017;
Garbarino et al., 2021;
Himali et al., 2023;
Zamore et al., 2024

When Restoration Is Lost, the Brain Pays a Price

Less restorative sleep	Short-term brain effects	Long-term vulnerability
Less efficient chemical reset	Brain fog	Chronic Fatigue
Less efficient neural signal	Irritability/low mood	Chronic Mood Disorders
Less cellular energy reserves	Worse attention/memory	Cognitive Impairment
less efficient clearance of amyloid, tau, and waste		Higher risk of dementia



Mander et al., 20
Mander et al., 20
Dominguez et al., 2

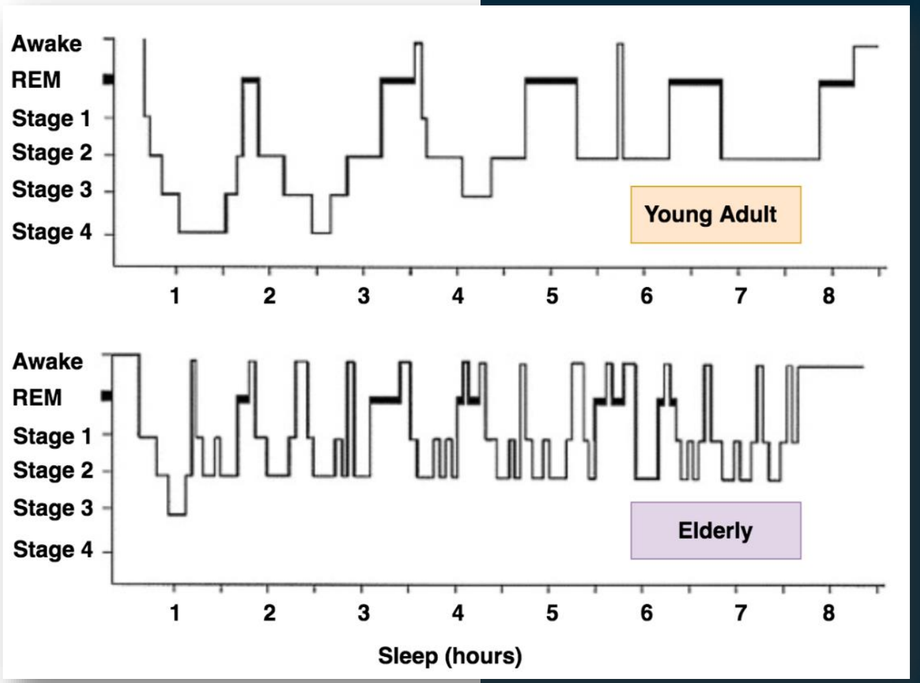
Reasons Sleep Becomes Fragmented - Age

Across adulthood, sleep architecture gradually changes:

- Deep sleep declines
- Sleep becomes lighter
- Nighttime awakenings become more common

What studies show

- Deep sleep drops 2% per decade through around age 60
- Total sleep time falls by about 10 minutes per decade
- Wake time after falling asleep tends to rise with age



Aging reduces access to deep, restorative sleep.

Scullin and Bliwise, 2015;
Varga et al., 2016;
Mander et al., 2017;
Li et al., 2018;
Tatineny et al., 2020;
Jaqua and Wisbey, 2022

Reasons Sleep Becomes Fragmented - Medical

Poor sleep is not always “just getting older.”

Common medical causes include:

- **Obstructive sleep apnea (OSA)**
- **Restless legs syndrome**
- **Chronic pain**
- **Nocturia**
- **Depression/anxiety**
- **Circadian rhythm changes**
- **Medication effects** e.g. Benadryl, Prozac, Sudafed, etc..

Most common and most treatable: Obstructive Sleep Apnea

- **Short term:** sleep quality, daytime alertness, attention, and mood
- **Long term:** physiologic stress (HTN, Afib, MDD), and risk trajectories related to dementia

Himali et al., 2023;
Kinugawa et al., 2023;
Pase et al., 2023;
Marchi et al., 2024;
Livingston et al., 2024

Chronic Sleep Disruption and Dementia Risk

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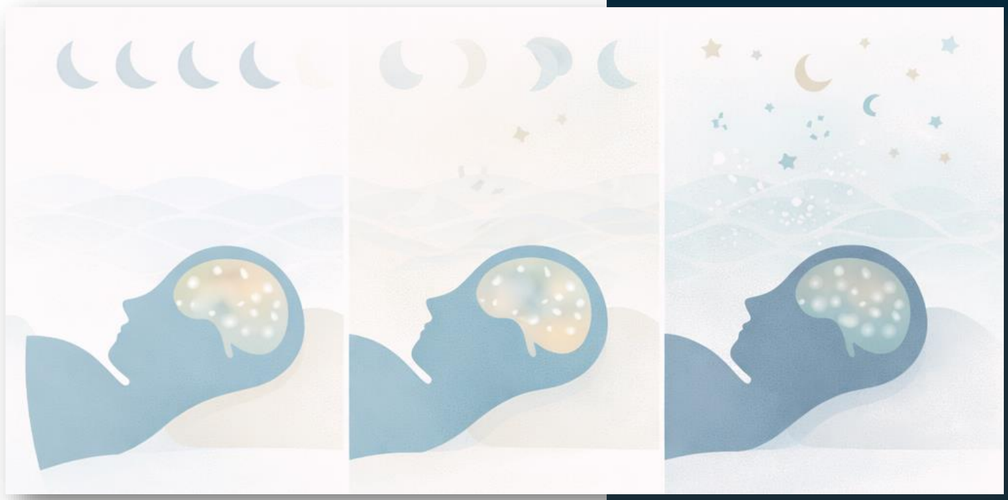
Chronic, <u>not</u> Acute, Poor sleep is associated with **higher dementia risk**

- **Less deep sleep** associated with higher risk
  - Framingham study suggest 27% higher risk of dementia
- **Sleep apnea** associated with higher risk
  - Meta-analysis suggest 43% higher risk of neurocognitive disorder
- Neurodegenerative disease also increase the risk of insomnia?

...so chicken or the egg?



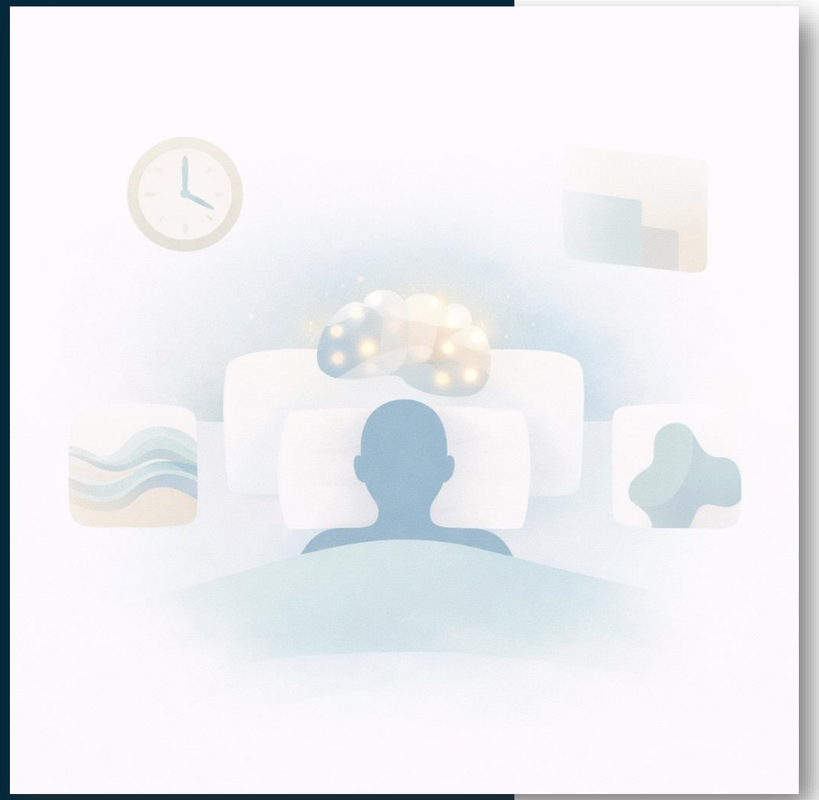
Treatment is promising, but still evolving

- **OSA/CPAP** - strongest evidence for reducing long-term cognitive risk
- **Dual Orexin Receptor Antagonists (DORAs)** - early promise, but dementia-risk still preliminary
- **Melatonin** - limited evidence for reducing dementia risk

Sleep is both a **warning sign** and a **modifiable treatment target.**

Mander et al., 2017;
Himali et al., 2023;
Gottesman et al., 2024

So, What Can We Actually Do?



- Sleep is the most powerful form of brain restoration—but it is not automatic.
- Restoration **evolved** to depend on:
  - Timing
  - Environment
  - Physiology
  - Underlying health

If we want better brain function,

we have to build better sleep conditions

Better Sleep Starts with Rhythm

Before pills, before gadgets, before complicated routines — the brain needs **timing cues.**

- Keep a **regular wake time**, even on weekends
- Get **morning light** soon after waking
- **Avoid bright light late at night** when possible
- Sleep and meals should be **reasonably predictable**

The brain sleeps best when time is predictable.

Life evolved around cycles of activity and quiescence. The brain still depends on those timing signals.

Better Sleep =

Better Sleep Drive

- Sleep systems evolved to **balance activation and restoration**.

- **Build sleep drive (Daytime)**
  - Physical activity increases need for deep sleep
  - Daylight anchors circadian rhythm
  - Consistent timing lowers the energy required for sleep

- **Allow the brain to disengage (Evening)**
  - **Reduce stimulation** (screens, caffeine, conflict)
  - Quiet routines signal safety
  - Breathing, mindfulness, gentle stretching
  - Heat → **cooling** (bath/sauna) supports physiologic transition

A good night of sleep begins with a good day's work

Better Sleep with a Protect Environment

As brains became more complex, deep sleep required true disengagement, but disengagement **increases vulnerability**.

Mammals need protected environments to fully power down.

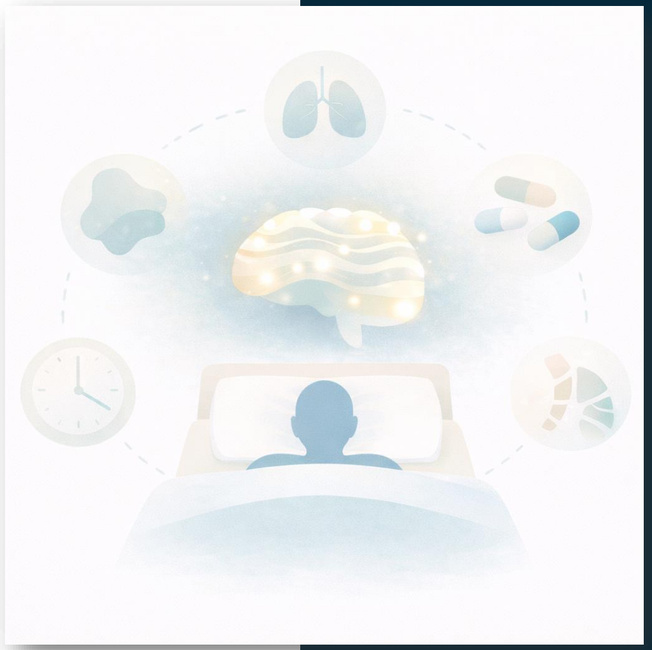
- **Dedicated space:** Reserve the bed for sleep
- **Cool environment**: Drop in core body temperature drives sleep
- **Darkness**: Enables circadian alignment
- **Reduced sensory input**: Limits micro-arousals
- **Limit late stimulation:** Caffeine, screens, “alert mode”
- **Physical containment**: Supportive mattress, weighted blanket

Deep sleep needs shelter from interruption.

When Sleep Doesn’t Improve — Look Deeper

- Sleep that stays fragmented is rarely just “bad sleep.”

It is often a signal.



- **Common hidden drivers:**
  - Breathing (sleep apnea)
  - Medications
  - Mood / stress
  - Pain
  - Circadian timing

If sleep isn’t improving → ask why.

Don’t just treat the symptom.

Talk to your doctor about underlying causes.

Pharmaceutical Sleep Aids: Use Thoughtfully

Brain Restoration

Sedation ≠ Restoration.

- Avoid chasing unconsciousness
- The goal is biologically **organized sleep.**
- Some medications help but most aids just sedate, don't improve sleep architecture

Some sleep medication may make things worse

- Alcohol/Anticholinergic/Antihistamine aides increase the **risk of cognitive impairment**
- Oversedation increases the risk for **falls, hypoxia, and next-day cognitive impairment**
- Untreated medical conditions e.g. OSA + sedatives **accelerate cognitive impairment**

The target is restorative architecture, not just sedation.

**If you feel the need for a sleep aide, talk to your doctor about safe options

Sleep Aides to review with your physician that can help with deep sleep

- Melatonin
- Ramelteon
- DORAs (Belsomra, Dayviyo, Quviviq)

Situational
Trazodone/Gabapentin/Doxepin

Protect Rest, Protect the Brain

Longevity is not possible without restoration

- **Core Repair**
  - Sleep
  - Glymphatic clearance
- **Entry Into Restoration**
  - Breathing
  - Heat
  - Relaxation
- **Supportive States**
  - Quiet wakefulness
  - Low-demand engagement

If we want to preserve the brain, we have to protect its time to recover.

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Brain Restoration

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