“Sleep is the golden chain that ties health and our bodies together.”

Thomas Dekker

Mary ET Boyle, Ph. D.
Department of Cognitive Science, University of California, San Diego
First, then, this much is clear, that waking and sleep appertain to the same part of an animal, inasmuch as they are opposites, and sleep is evidently a privation of waking.

Aristotle

Think in the morning.
Act in the noon.
Eat in the evening.
Sleep in the night.

William Blake
"We are always hearing people talk about 'loss of sleep' as a calamity. They better call it loss of time, vitality and opportunities."

Thomas Edison

Photos: Henry Ford Museum

1800’s

“Sleep is a criminal waste of time and a heritage from our cave days.”
Margaret Thatcher

“Sleep is for wimps!”

1980’s
Bill Clinton

"Every important mistake I've made in my life, I've made because I was too tired."
Sleep deprived bees cannot communicate the direction of the food source when they are sleep deprived.

Sleep deprivation impairs precision of waggle dance signaling in honey bees

Barrett A. Klein, Arno Klein, Margaret K. Wray, Ulrich G. Mueller, and Thomas D. Seeley
Sleep deprivation has been indicated as a cause in 78 percent of all the Air Force's Class A mishaps (Lund, 2003). Disasters such as Chernobyl, Three Mile Island, the Shuttle Challenger disaster (Presidential Commission on Space Shuttle Challenger Accident, 1986) are perfect examples of how sleep deprivation affects decision-making processes.

Furthermore, sleep loss was specifically cited as a factor that contributed to the collective human error and poor judgment related to the Space Shuttle Challenger disaster (Presidential Commission on Space Shuttle Challenger Accident, 1986).

When sleep deprivation effects are especially powerful, and all involved errors made by people working in groups (Harrison & Horne, 2000).
One Silicon Valley startup that encouraged its employees to think about work 24/7 found they missed market signals, tanked deals and became too irritable to build crucial working relationships.
What happens when we don't sleep?

1. Cognitive & Behavioral changes
2. ↓↓ Ability to concentrate
3. ↓↓ Short-term memory
4. Paranoia & hallucinations

The world's record for the longest sleep deprivation period is 11 days!
NO SLEEP $\rightarrow$ COGNITIVE IMPAIRMENT

17-19 HOURS $\rightarrow$ 0.05 BAC

28 HOURS $\rightarrow$ 0.1 BAC

Moderate sleep deprivation produces impairments in cognitive and motor performance equivalent to legally prescribed levels of alcohol intoxication

A M Williamson, Anne-Marie Feyer
New way to think about sleep
Sleep is important; our bodies demand it.
What regulates sleep?
Sleep wake cycle is regulated by the circadian system.

Light & Melatonin are the two most influential external cues that synchronize the circadian rhythm.
Cyanobacteria is a photoautotrophic organism that has a self-sustained circadian rhythm. Sleep-wake cycle is regulated by the circadian system.
Our metabolic clocks are based on the diurnal rhythm – it is in our genes.
Watch brain ticking

7 day timelapse recording

Mouse SCN

Day in the life of a cell 0-24 hours

Genes in cells cycle on and off every 24 hours
Every cell has its own clock!

Data from: David Welsh; Video: J. Takahashi (2013) https://www.youtube.com/watch?v=ocqn3wYTCRM#
One week of insufficient sleep alters gene expression in human blood cells.

Immune and stress response

Intensifies the effects of subsequent total sleep loss on gene expression

Effects of insufficient sleep on circadian rhythmicity and expression amplitude of the human blood transcriptome


Insufficient sleep and circadian rhythm disruption are associated with negative health outcomes, but the mechanisms involved remain largely unexplored. We show (pp. E1132–E1141) that one wk of insufficient sleep alters gene expression in human blood cells, reduces the amplitude of circadian rhythms in gene expression, and intensifies the effects of subsequent acute total sleep loss on gene expression. The affected genes are involved in chromatin remodeling, regulation of gene expression, and immune and stress responses. The data imply molecular mechanisms mediating the effects of sleep loss on health and highlight the interrelationships between sleep homeostasis, circadian rhythmicity, and metabolism.
Shift workers are more prone to developing metabolic disorders

- Higher incidence of cardiovascular disease
- 40% more likely to have Diabetes Type II
- Higher risk of cancer — melatonin disruption


The Health Survey for England (2013);
Davis S, Mirick DK. Cancer Causes Control. 2006 May; 17(4):539-45.
SCN is not the only clock in the body

Food can be a zeitgeber for the gut.

intestinal activity and its ability to absorb nutrients are dependent on the time of day.
Time of eating has a huge effect on the liver and insulin efficacy.

Cellular response to INSULIN is dependent on the circadian cycle.

Insulin-sensitivity is dependent on the peripheral clock in muscle cells.

Glucose uptake in muscle is dependent on the circadian rhythm.

High blood glucose

Beta cells release **INSULIN**

Insulin stimulates the liver to remove glucose from the blood and stores it as glycogen

Tissues take up glucose from blood

Lowers glucose levels in blood

*Figure adapted from Kaidanovich-Beilin, O. et al 2012*
Glucagon stimulates the conversion of stored glycogen in the liver into glucose.

Increases glucose levels in blood

Alpha cells release GLUCAGON

low blood glucose

Figure adapted from Kaidanovich-Beilin, O. et al. 2012
When you eat sugar determines how your body will respond

EATING SUGAR AT NIGHT → HIGHER BLOOD SUGAR
Insulin activates insulin receptors in the brain → affects feeding behaviors, reward, body metabolism, normal emotion & cognitive behaviors.

Insulin receptors are found throughout the brain – cortex, midbrain and hypothalamus.
The risk of developing Alzheimer's disease is increased by 50 percent in people with diabetes.

Craft, S. Nat. Rev. Neurol. 8, 360–362 (2012);
• 5 – 20 years before diagnosis of Alzheimer's dementia
• damages synapses

• 1 – 5 years before diagnosis
• Tau protein detaches from the microtubules

• 1 – 3 years before diagnosis
• Cell death shrinks the brain.
Amyloid Accretion
5–20 years before diagnosis of Alzheimer’s dementia

Scientific American (June 2010)
Alzheimer’s: Forestalling the Darkness
Amyloid blocks neurotransmitters from reaching the post-synaptic receptors.
PET scans show increasing retention in the brain’s frontal lobes of the amyloid-beta tracer Pittsburg imaging compound-B (PIB) over the course of two years in a 74-year-old, even while the subject remained cognitively normal.

Scientific American (June 2010)
Alzheimer’s: Forestalling the Darkness
Disintegrating microtubule

Enzyme adding phosphate groups to tau

Toxic tangles formed by tau

Microtubules held together by tau proteins

Neuron
Alzheimer’s: Forestalling the Darkness

Healthy brain vs. Alzheimer’s brain

Hippocampus

Extreme shrinkage of hippocampus

Scientific American (June 2010)
Alzheimer’s: Forestalling the Darkness
High carbohydrate intake worsens cognitive performance and behavior in patients with Alzheimer’s disease.

Henderson, 2004
Hypometabolism: Decline in glucose metabolism

- Early feature of AD – region specific decline in glucose metabolism
- Reduction of glucose metabolism → reduction in function
The circadian clock has a profound effect on the physiology and behavior of organisms.
The circadian clock has a profound effect on the physiology and behavior of organisms.
A Single Night of Partial Sleep Deprivation Induces Insulin Resistance in Multiple Metabolic Pathways in Healthy Subjects

Esther Donga, Marieke van Dijk, J. Gert van Dijk, Nienke R. Biermasz, Gert-Jan Lammers, Klaas W. van Kralingen, Eleonara P. M. Corssmit, and Johannes A. Romijn

Departments of Endocrinology and Metabolic Diseases (E.D., M.v.D., N.R.B., E.P.M.C., J.A.R.), Neurology (J.G.v.D., G.-J.L.), and Pulmonology (K.W.v.K.), Leiden University Medical Center, 2300 RC Leiden, The Netherlands

the effect of a single night of partial sleep on insulin sensitivity

This is what really happens in your brain when you sleep.

Figure: Eiko Ojala, NYT
Sleep Drives Metabolite Clearance from the Adult Brain

Lulu Xie,1,2 Hongyi Kang,1,2 Qiwu Xu,2 Michael J. Chen,2 Yonghong Liao,2 Meenakshisundaram Thiagarajan,2 John O'Donnell,3 Daniel J. Christensen,4 Charles Nicholson,2 Jeffrey J. Blitt,3 Takahiro Takano,3 Rashid Deane,1 Maiken Nederhaard1

The conservation of sleep across all animal species suggests that sleep serves a vital function. We here report that sleep has a critical function in ensuring metabolic homeostasis. Using real-time assessments of tetramethylammonium diffusion and two-photon imaging in live mice, we show that natural sleep or anesthesia is associated with a 60% increase in the interstitial space, resulting in a striking increase in convective exchange of cerebrospinal fluid with interstitial fluid. In turn, convective fluxes of interstitial fluid increased the rate of β-amyloid clearance fluid. Thus, the restorative function of sleep may be a consequence of the enhanced removal of potentially neurotoxic waste products that accumulate in the awake central nervous system.

https://www.youtube.com/watch?v=ci5NMsCkJws
Average Number of Hours of Sleep per Night

1960: 8+
1995: 7
2004: 6

Are you getting enough sleep?

Adapted from: Nature Neuroscience Reviews
Imagine the benefits that would await you if you got one more hour of sleep?