


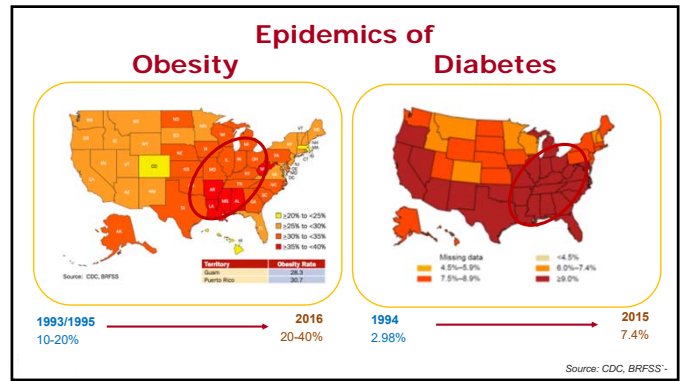
Sleep, Circadian Rhythms, and Health



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OSHER COLLABORATIVE
FOR THE FUTURE OF HEALTH

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Are there additional modern lifestyle factors beyond diet and physical activity to consider?

Time for an updated view?

Modern lifestyle: Increasing prevalence of shift work, late eating, artificial light at night, sleep disturbances, (social) jet lag, etc.







Common factor: *sleep and circadian disruption*

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Sleep ...as Superpower

"I love sleep because its like a time machine to breakfast"
 – Bill Murray



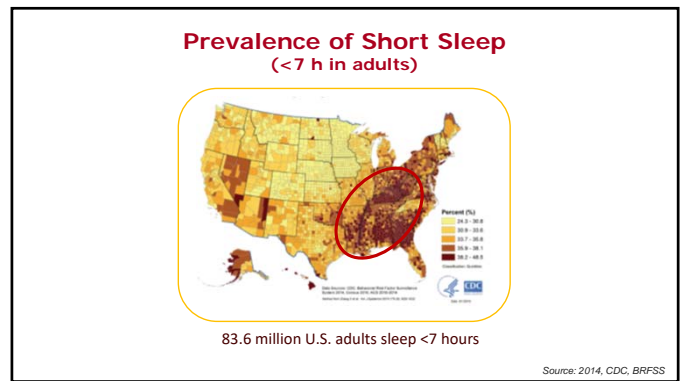
Bill Murray (@BillMurray) | Twitter

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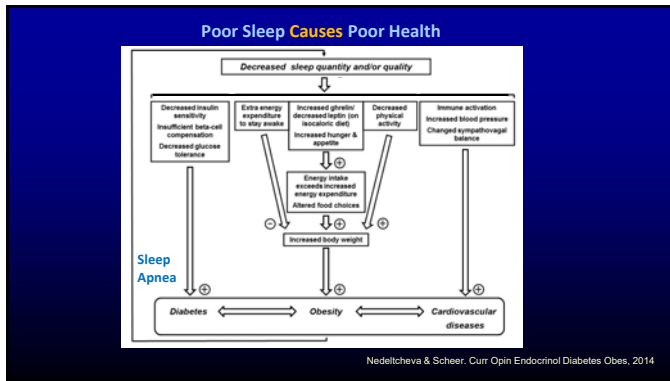
"If sleep does not serve an absolutely vital function, then it is the biggest mistake the evolutionary process has ever made"

–Alan Rechtschaffen, 1971

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Short or Disrupted Sleep

- Impaired memory & cognitive performance
- Poor blood sugar control
- Increased hunger
- Increased high-density food intake
- Decreased physical activity
- During low-calorie diets, decreased fat loss
- Increased blood pressure
- Less effective vaccination

Sleep: Not just for the Brain
Also for the Body!

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Sleep Is As Important As Diet And Exercise (Only Easier!)

NATIONAL SLEEP FOUNDATION
Sleep is essential to the enjoyment of life.

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Sleep is not easy for those with sleep disorders, e.g., Obstructive Sleep Apnea

Characterized by:

- Intermittent hypoxemia
- Sleep fragmentation
- Negative intrathoracic pressure
- Sympathetic surges
- Etc.

Prevalence:

- Increasing with advancing age, male sex, and higher BMI

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Since the beginning

Internal clock... Where and how?

de Mairan experiment ~300 years ago

First life ~3.5 billion years ago (3,500,000,000 years)

atmospheric-phenomena-ap.com

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Circadian system: Central clock and peripheral clocks

Suprachiasmatic nucleus (SCN)

Time-lapse video: Each cycle ~24h

Multi-oscillator system

Hormones, Nervous system, Body temperature

Peripheral clocks

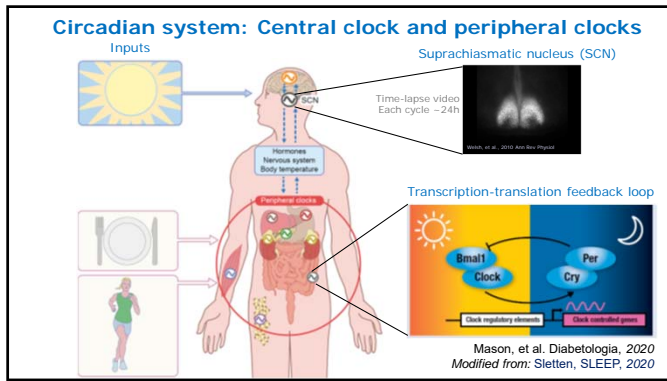
Transcription-translation feedback loop

Small Clock, Per, Cry

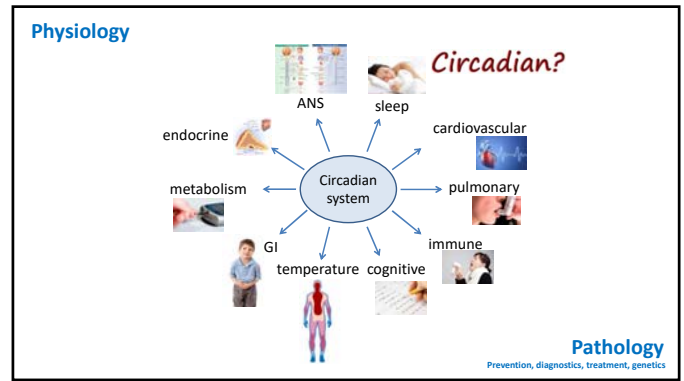
Clock regulatory elements, Clock controlled genes

Mason, et al. Diabetologia, 2020
Modified from: Sletten, SLEEP, 2020

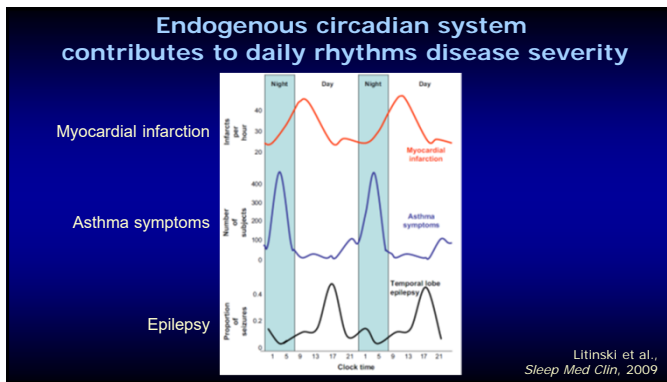
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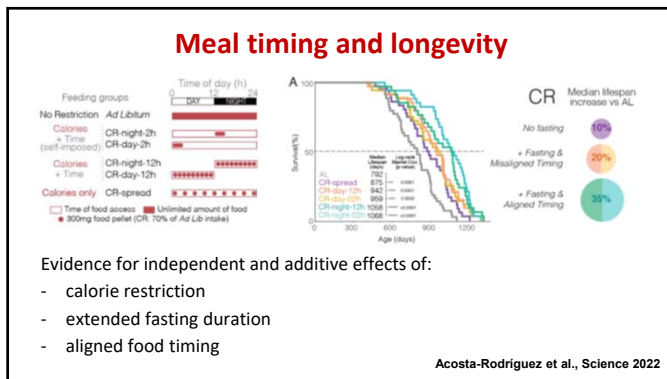
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Adverse health consequences of circadian disruption

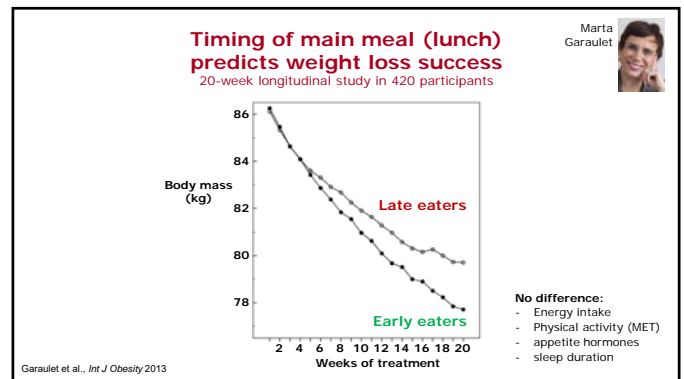
- Genetic
- Anatomical - damage to the central clock
- Behavioral - Mismatched food intake
- Shift work and circadian misalignment

Consequences: Obesity, diabetes, hypertension, cardiovascular disease, increased inflammatory markers, depressive mood, etc.

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Meal Timing



- Later (circadian) eating - worse weight loss with dietary and surgical weight-loss interventions, and higher BMI and adiposity
- Late eating causes increased hunger, decreased energy expenditure, and molecular changes in fat tissue towards fat growth
- Eating when melatonin concentrations are elevated (eating late in the evening and at night or after oral intake of melatonin pill) impairs glucose tolerance (especially in *MTNR1B* risk carriers)
- Daytime eating is a promising countermeasure against the adverse cardiometabolic effects of circadian misalignment/shift work

Garaulet et al., *Int J Obesity* 2013; Ruiz-Lezano et al., *Clinical Nutrition* 2016; McHill et al., *Am J Clin Nutr* 2017; Jakubowicz et al., *Obesity* 2013; Morris et al., *PNAS* 2015; Lopez-Minguez et al., *Clin Nutr* 2017; Chellappa et al., *Science Adv* 2021; Garaulet et al., *Diabetes Care* 2022; Vujovic et al., *Cell Metab* 2022

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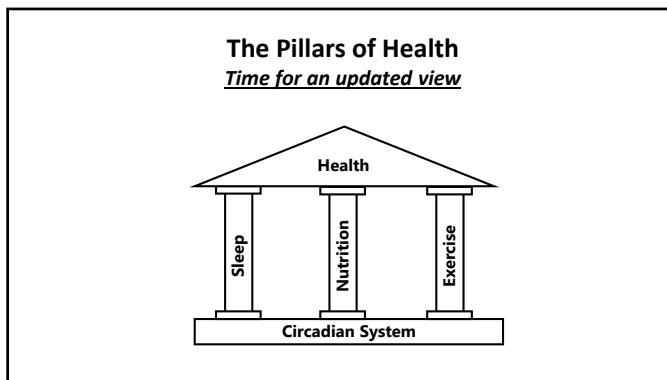
Take Home Messages

In addition to physical activity and *what* we eat, consider:

- Quantity and quality of sleep
- Circadian disturbances, e.g., shift work, (social) jet lag, night eating, light at night
- When you eat

- Circadian time has been mostly overlooked in the prevention, treatment, and diagnosis of disease

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Medical Chronobiology Program



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