Please sit with people of a similar chronotype (morningness, intermediate, eveningness)!

From Bench to Bedtime: Entraining Policy to Science

Day 2

Website: bit.ly/mahping

Instructors: Lucy Lai, Ben Finander, Mikaili Abdullah

Course Schedule

Day One

- What are circadian rhythms, and why do they matter?
- Autoinhibitory transcriptional networks allow for temporal gene regulation
- How environmental stimuli like light can “entrain” the circadian clock
- How the brain coordinates circadian rhythms in the periphery

Day Two

- How does circadian biology impact shift workers?
- Shift work as a historical phenomenon
- How to leverage circadian biology to improve health outcomes in shift workers
- Exploring the broad implications of shift work

Day Three

- How our natural rhythms interact with societal demands
- The biological effects of policies such as Daylight Savings Time (DST)
- How future policies be informed by circadian biology
- How to mitigate negative effects of circadian disruption

Learning Objectives

At the end of Day 2, students can ...

- ❏ recall the origins and types of shift work
- ❏ explain the broad implications of non-standard work schedules
- ❏ describe how common circadian rhythm disruptions shift the clock
- ❏ predict how the the content, size, and timing of meals can impact entrainment of peripheral clocks in the gut

But first...

Addressing a few questions from Day 1

- How does the SCN synchronize or communicate with peripheral clock mechanisms?
- Why are medical training institutions still pushing for students/residents to work unhealthy shifts if they know the detrimental impacts on the body?

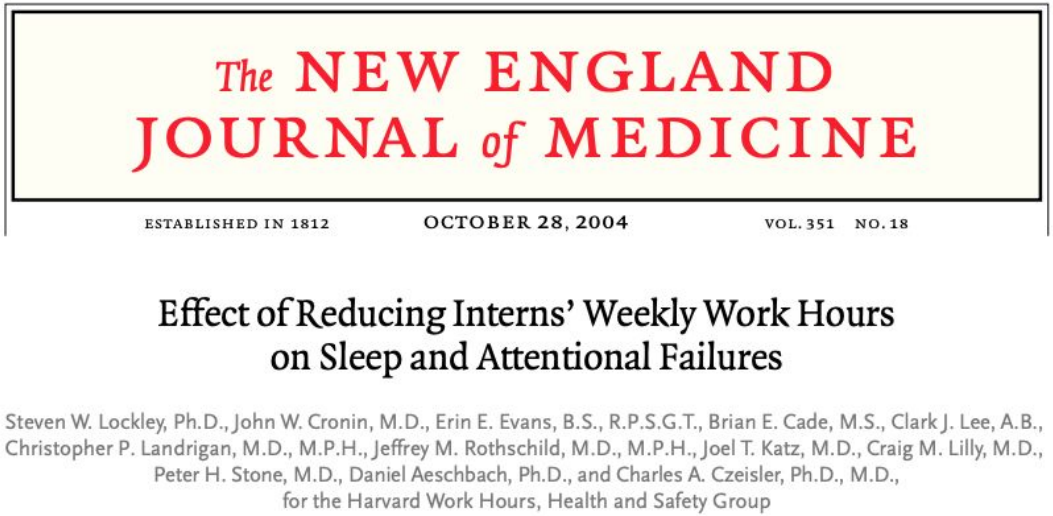
How does the SCN synchronize peripheral clocks?

1. **Glucocorticoids** (corticosterone)
   Secreted rhythmically from the adrenal gland when 'activity' starts
   SCN lesions abolish this rhythmicity - R.Y. Moore and V.B. Eichler (1972) *Brain Research*
   Peripheral tissues have GC receptors and SCN neurons do not
   Treating peripheral tissues with GCs causes a phase shift in peripheral clocks - A. Balsalobre et. al. (2000) *Science*

2. **Body temperature**
   Temperature pulses ($36^{o}C \rightarrow 38.5^{o}C$) reset peripheral clocks
   Dependent on heat shock factor 1 (HSF1) in peripheral tissues
   E.D. Buhr et. al. (2010) *Science*

3. **Food is an exogenous signal that causes phase shifts to peripheral clocks**

Why are medical training institutions still pushing for students/residents to work unhealthy shifts if they know the detrimental impacts on the body?



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 28, 2004 VOL. 351 NO. 18

Effect of Reducing Interns' Weekly Work Hours on Sleep and Attentional Failures

Steven W. Lockley, Ph.D., John W. Cronin, M.D., Erin E. Evans, B.S., R.P.S.G.T., Brian E. Cade, M.S., Clark J. Lee, A.B., Christopher P. Landrigan, M.D., M.P.H., Jeffrey M. Rothschild, M.D., M.P.H., Joel T. Katz, M.D., Craig M. Lilly, M.D., Peter H. Stone, M.D., Daniel Aeschbach, Ph.D., and Charles A. Czeisler, Ph.D., M.D., for the Harvard Work Hours, Health and Safety Group

In 2003, the Accreditation Council for Graduate Medical Education (ACGME) restricted work hours to an **average of 80 per week**, with in-hospital call **capped at 30 hours.**

*Interns made **36 % more serious medical errors**, including **5x as many serious diagnostic errors**, on the **traditional 24 hour schedule** than on an **interventional 16 hours schedule**.*

Why are medical training institutions still pushing for students/residents to work unhealthy shifts if they know the detrimental impacts on the body?

- Standard recommendation: residents should work **no more than 16 consecutive hours without sleep**. **This is very controversial!**
- Numerous studies demonstrate the **adverse consequences of sleep deprivation** in industrial settings, but critics say that the data is **insufficient** to support a radical change in traditional resident scheduling practices.
- **Concerns include:**
    - the potential for “unintended consequences” of reducing work hours on patient safety due to concerns about **inadequate handovers of care**
    - the effects of **work hour reduction on resident education**.
    - data have emerged suggesting that implementing recommendations could cost up to **$1.6 billion dollars** (to make up for lack of staffing)

Why are medical training institutions still pushing for students/residents to work unhealthy shifts if they know the detrimental impacts on the body?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 7, 2019 VOL. 380 NO. 10

Patient Safety Outcomes under Flexible and Standard Resident Duty-Hour Rules

Jeffrey H. Silber, M.D., Ph.D., Lisa M. Bellini, M.D., Judy A. Shea, Ph.D., Sanjay V. Desai, M.D., David F. Dinges, Ph.D., Mathias Basner, M.D., Ph.D., Orit Even-Shoshan, M.S., Alexander S. Hill, B.S., Lauren L. Hochman, B.A., Joel T. Katz, M.D., Richard N. Ross, M.S., David M. Shade, J.D., Dylan S. Small, Ph.D., Alice L. Sternberg, Sc.M., James Tonascia, Ph.D., Kevin G. Volpp, M.D., Ph.D., and David A. Asch, M.D., M.B.A., for the iCOMPARE Research Group*

News Release

Permitting First-Year Doctors to Work Longer Shifts Does Not Create Chronic Sleep Loss or Reduce Patient Safety

Two large national studies show that patient safety was unaffected and residents showed no signs of chronic sleep loss regardless of shift length

March 06, 2019

*When medical residents were permitted to **work shifts longer than 16 hours**, **patient mortality was not affected** and the **doctors themselves did not experience chronic sleep loss***

“Because even if it’s worse for the trainees, it’s still fine for the patients…!”

What is shift work?

- **Shift work refers to a work schedule that *falls outside the hours of 7am to 6pm.***
- *Shift work can include **evening, night, and early morning shifts**, that are on a **fixed** or **rotating** schedule.*

Fixed vs. Rotating Shifts

	Mon	Tues	Wed	Thurs	Fri
5AM					
8AM					
11AM					
2PM					
5PM					
8PM					
11PM					
2AM					

Rotating shift work: shifts that change in time from day to day, may fall in the “normal” work day

	Mon	Tues	Wed	Thurs	Fri
5AM					
8AM					
11AM					
2PM					
5PM					
8PM					
11PM					
2AM					

Fixed shift work: predictable, consistent shifts, even if they are not during “normal” hours

What is shift work?

- **Shift work refers to a work schedule that *falls outside the hours of 7am to 6pm.***
- *Shift work can include **evening, night, and early morning shifts**, that are on a **fixed** or **rotating** schedule.*
- **15 million (**roughly **16% of workers)** American workers work on night or rotating shifts (Bureau of Labor Statistics)
- Result in **misalignments** of the circadian-influenced physiology with the environment → “Shift work disorder”
    - Increased risk for metabolic syndrome, diabetes, cardiovascular disease, and even cancer (Figueiro MG, White RD. Health consequences of shift work and implications for structural design. J Perinatol. 2013 Apr;33 Suppl 1:S17-23. doi: 10.1038/jp.2013.7. PMID: 23536025.)

Why do we have shift work?

Back then...

- Keeping watch / security
- Productivity after the sun goes down
- Emergencies that could happen around the clock

Why do we have shift work?

But now…

- With the advent of artificial lighting, we quickly became a **“24/7”** society
- The **19th century Industrial Revolution**, demanded the expansion of “non-essential” shift work → This is truly a RECENT phenomenon!

However, our changing society doesn’t change the fact that 24/7 life deviates from our natural biological rhythm!

Common shift work jobs

- Late night entertainment (clubs, bars)
- Manufacturing and production

- Construction workers
- Farmers
- Food services
- Retail workers
- Performing artists

- Grad student?!

24/7

- Healthcare workers
- Police officers / security personnel
- Flight and transportation industry

Which are truly essential?

Bring it back to yourself...

- What are some **disturbances (environmental or social factors)** to your own circadian clock during your day?
- What are the **downstream consequences**?
- How do you **address or manage** these factors?

Talk to your neighbors (5 mins), the person with the shortest name will share out!

Circadian Science Should Inform Policy

Why Should Policy Be Informed By Circadian Science?

Healthcare Workers

"Working more than 40 weekly hours is associated with a negative impact on nurses' job satisfaction and performance, including reports of errors and harms to both patients and staff [16]. Long working hours by nurses have been associated with increased mortality [17]."

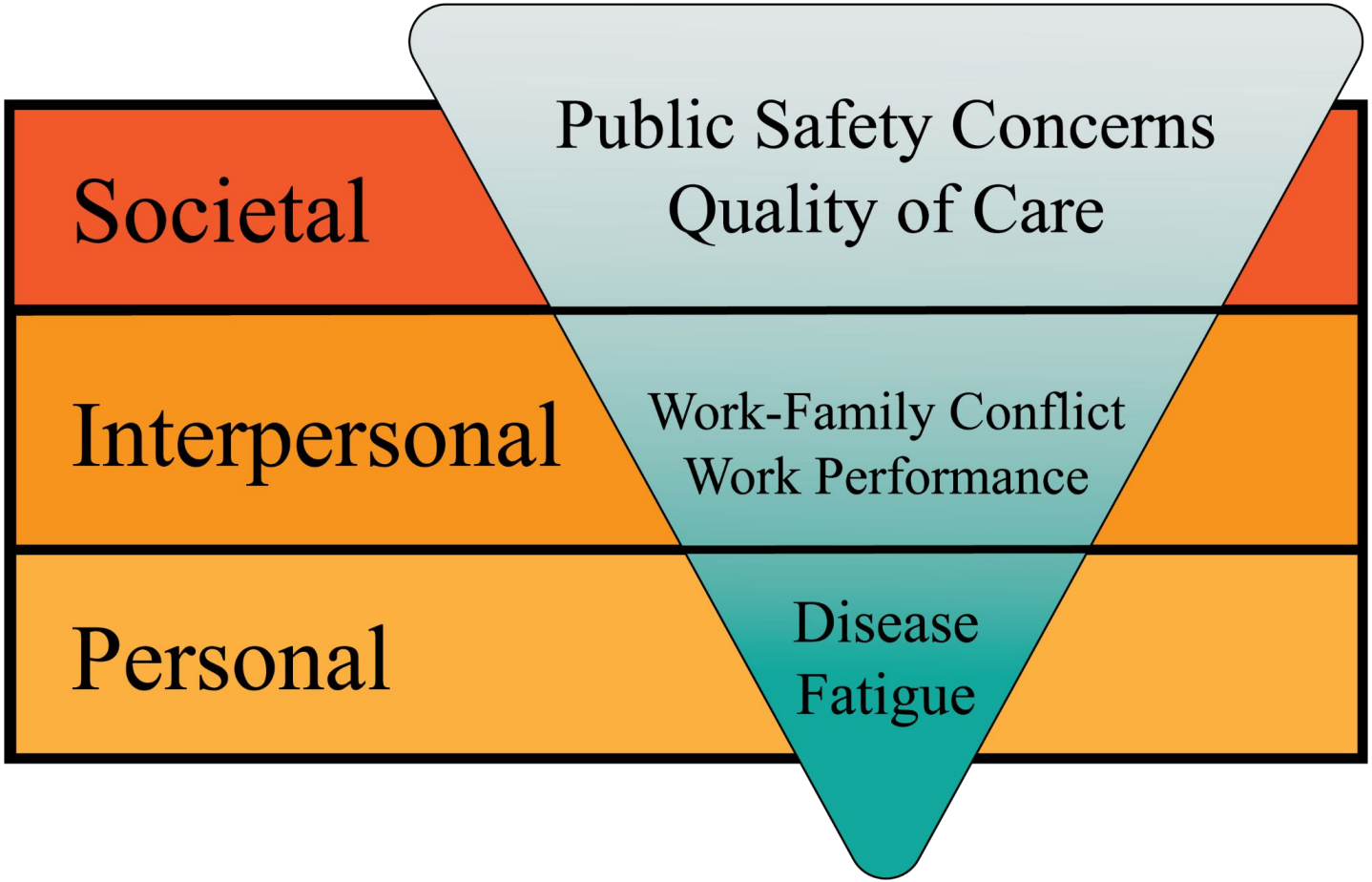
(2017). Shift work in hospitals : what are the effects on patient and employee outcomes ?

"[The] combination of excess work and reduced sleep perilously heightens the risk of officer injury, compromised public safety, and the possibility of significant civil liability damage awards for avoidable accidents."

Anderson, W., et al. "Stress Management for Law Enforcement Officers." *Stress Management for Law Enforcement Officers | Office of Justice Programs*, 1995, https://www.ojp.gov/ncjrs/virtual-library/abstracts/stress-management-law-enforcement-officers.

Police and Public Safety Professionals

The Broad Effects of Circadian Disruption



Work scheduling policies have broad implications for the workforce and society

Why Should Policy Be Informed By Circadian Science?

Healthcare Workers: Working 12(+)hr Shifts Associated with

- Increased Error Rates
- Increased Levels of Omitted Nursing Care
- Reduced Patient Safety

(2017). Shift work in hospitals : what are the effects on patient and employee outcomes ?

Police and Public Safety Professionals: Working 12hr Shifts Associated with

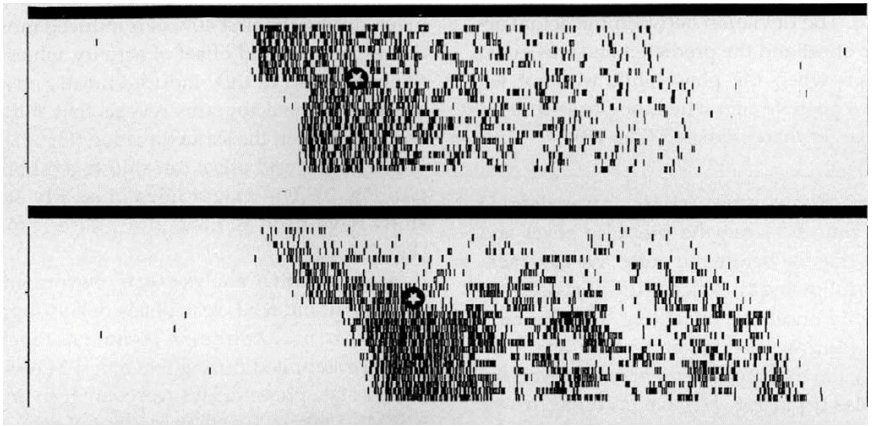
- Increased Fatigue
- Decreased Quality of Sleep
- Decreased Hours of Sleep
- Decreased Quality of Work Life
- Decreased Alertness

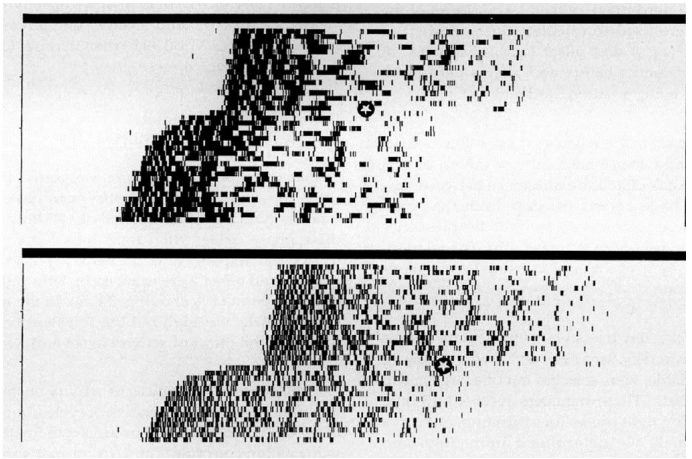
(Amendola et al., 2011) - https://www.ojp.gov/pdffiles1/nij/grants/237330.pdf

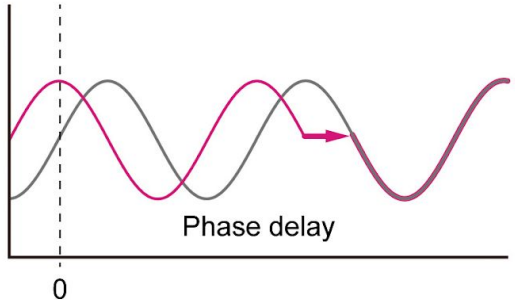
What potential issues come to mind when thinking of fatigued first responders? How do you think circadian science can be used to address these issues?

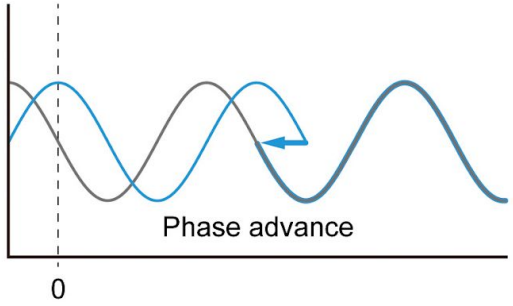
Individually, Interpersonally, and Societally

Review: Light exposure during nighttime shifts can advance/delay circadian phase

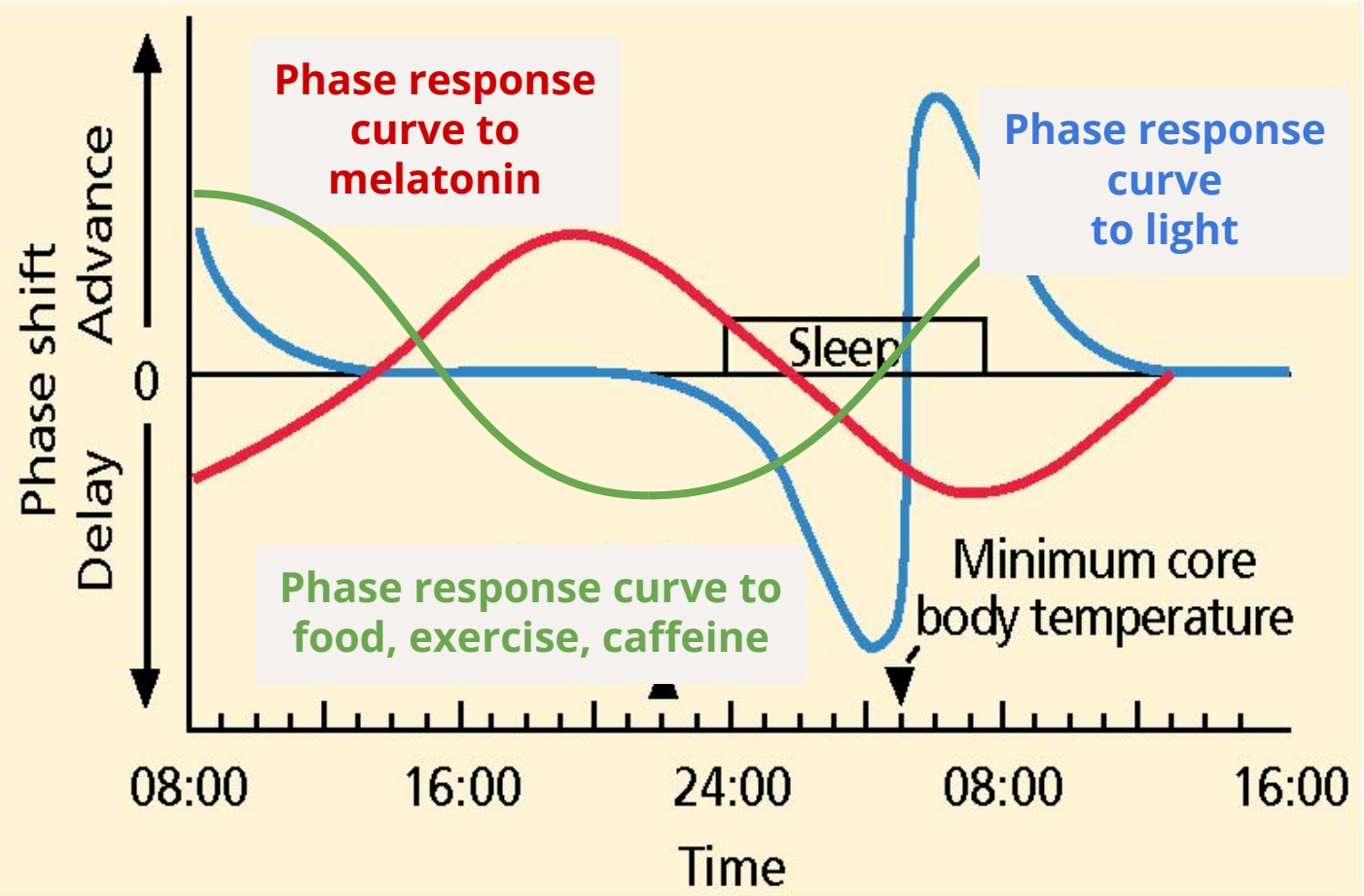








Drugs, food, and exercise can also advance/delay phase



Drugs, food, and exercise can also advance/delay phase

- **Melatonin** advances phase in late daytime, delays in early daytime
- **Exercise, food and caffeine** delay phase in late daytime, advance in early daytime
- **Activity:** Based on the circadian rhythm on your group's worksheet, use drugs, food, and behavioral interventions to optimize the physiological readout

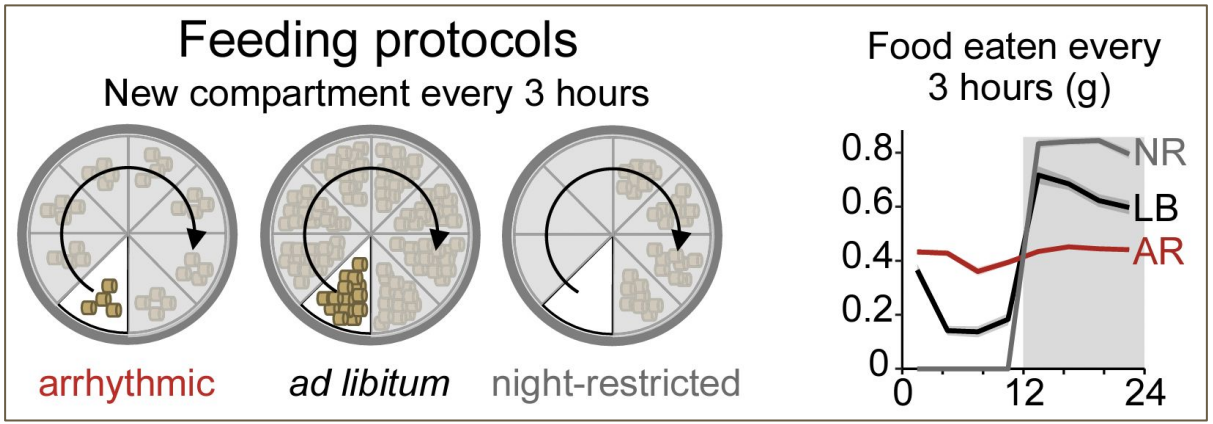
Snacking wisely: Balancing performance and comfort

- Human experiments show that snacks (10% of daily caloric intake) can improve performance of difficult tasks at night, while meals (30% of daily caloric intake) harm performance and cause digestive discomfort
- Ideal snacks should be micronutrient dense but calorie-poor, non-perishable, easily digested, and convenient
- Rate the following shift work snacks using the “thumb scale.” As a scientist, would you recommend this snack to a shift worker?

Shift work snacks

Food Intake can drive rhythmic gene expression

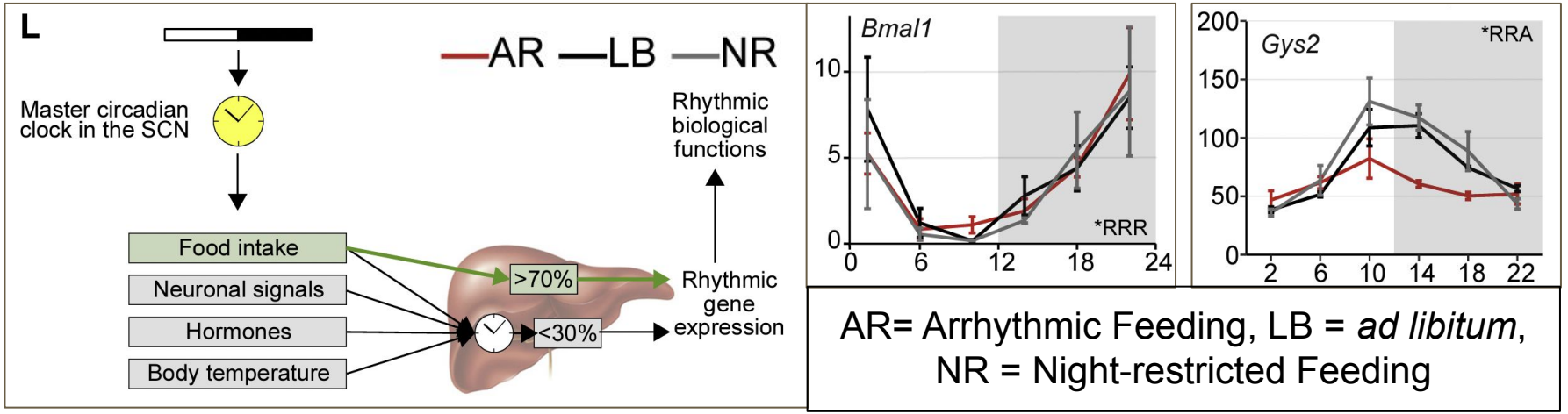
- Three eating conditions tested for effect on rhythmicity of gene expression across the genome in the liver of mice
- Discussion Questions: What percentage of rhythmic genes do you think will change due to feeding protocol? Do you think clock genes will change?
- 2 minutes to think about it, 5 minutes to discuss with a partner



Greenwell et al., 2019

Food Intake can drive rhythmic gene expression

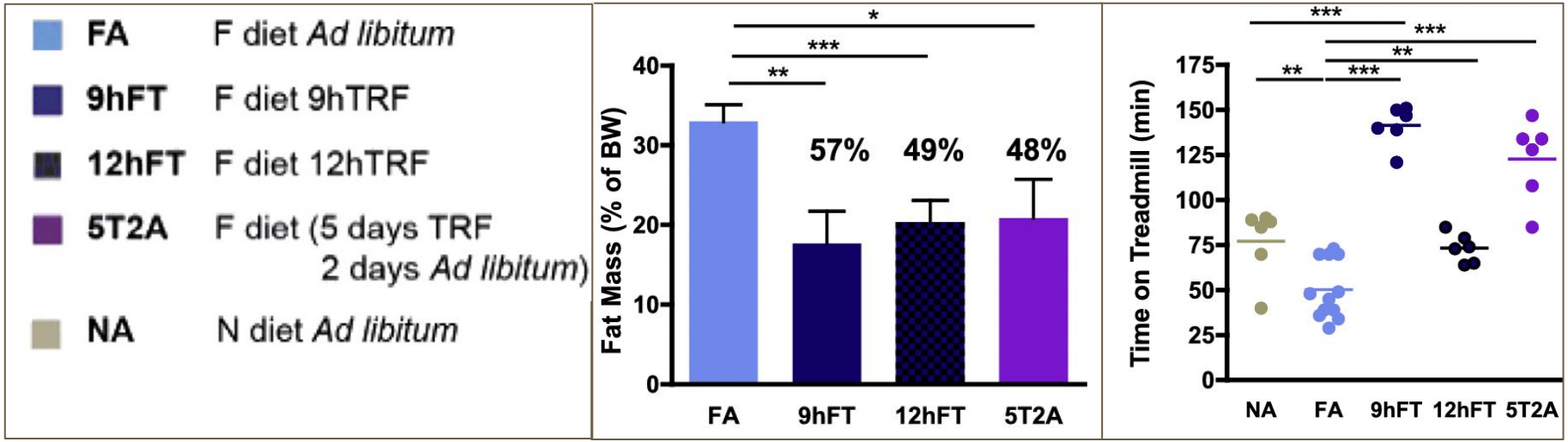
- **70%** of rhythmically expressed genes in Night-restricted Feeding mice are altered in their rhythm in other feeding groups
- Clock genes (like Bmal1) are **not changed**



Greenwell et al., 2019

Time Restricted Feeding Improves Performance and Metabolic Health in Mice

- A high-fat diet causes metabolic health athletic performance deficits in mice, but is alleviated by restricting eating to a shorter time (TRF)



Chaix et al., 2014

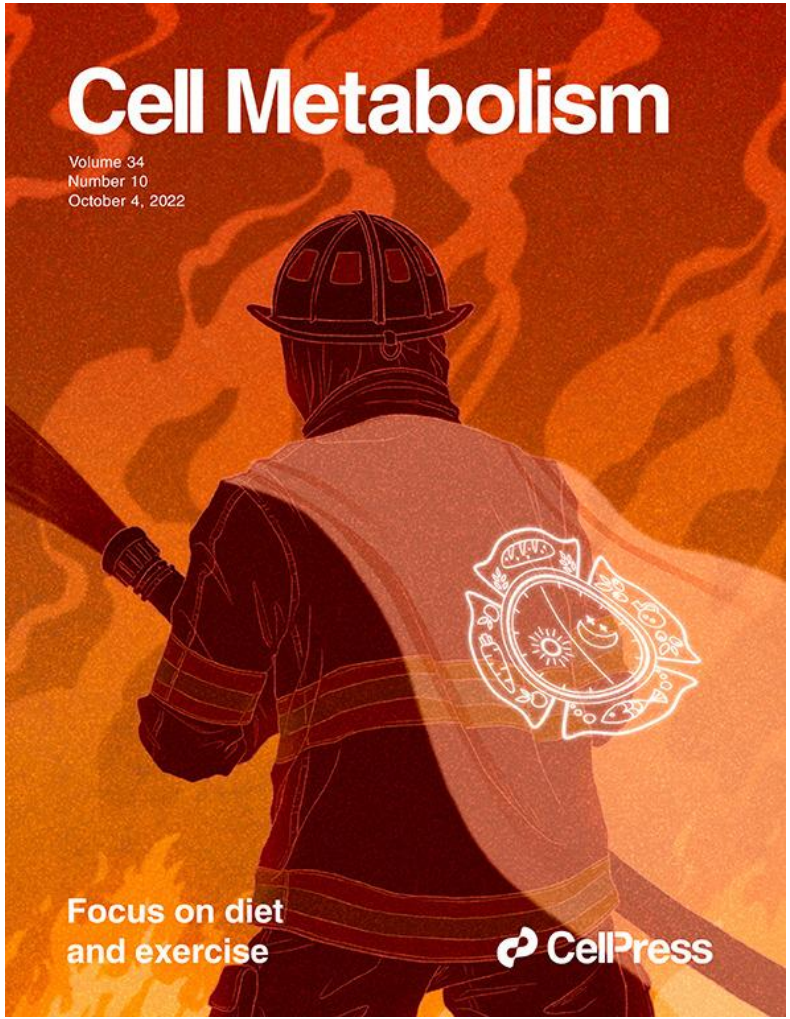
Brainstorm: Benefits of TRE for shift workers

- Based on what we've learned in class so far, why might time-restricted eating (TRE) be especially helpful for shift workers? Name one specific benefit shift workers might receive from TRE and use circadian biology to explain why
- 2 minutes to think about it, 5 minutes to discuss with a partner
- Were your benefits health benefits, or work performance benefits? Were they short-term or long-term?
- Do your proposed benefits apply to both fixed and rotating shift work?

The Healthy Heroes Study

- The first randomized controlled trial (RCT) of the metabolic benefits of TRE in shift workers was published ***just last month***
- Firefighters (on rotating shifts) in the 10-hr TRE group showed decreased VLDL particle size and increased quality-of-life measures
- Why might shift workers typically be excluded from RCTs?

Manoogian et al., 2022



Meet our new revolutionary app for shift workers

The science was missing.
Now, it will be the foundation

Light is the most important time cue for the circadian clock. By providing timed light exposure advice, Timeshifter will finally be able to help shift workers manage their changing schedules effectively.

Quick manual entry

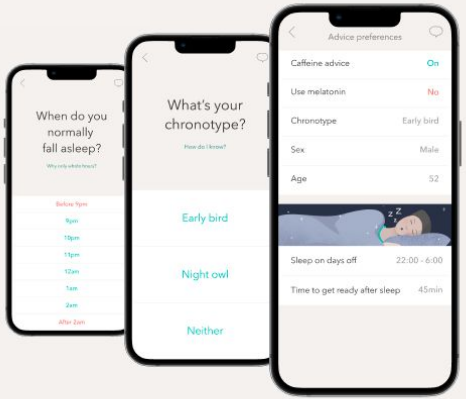
Automatic import

TIMESHIFTER®

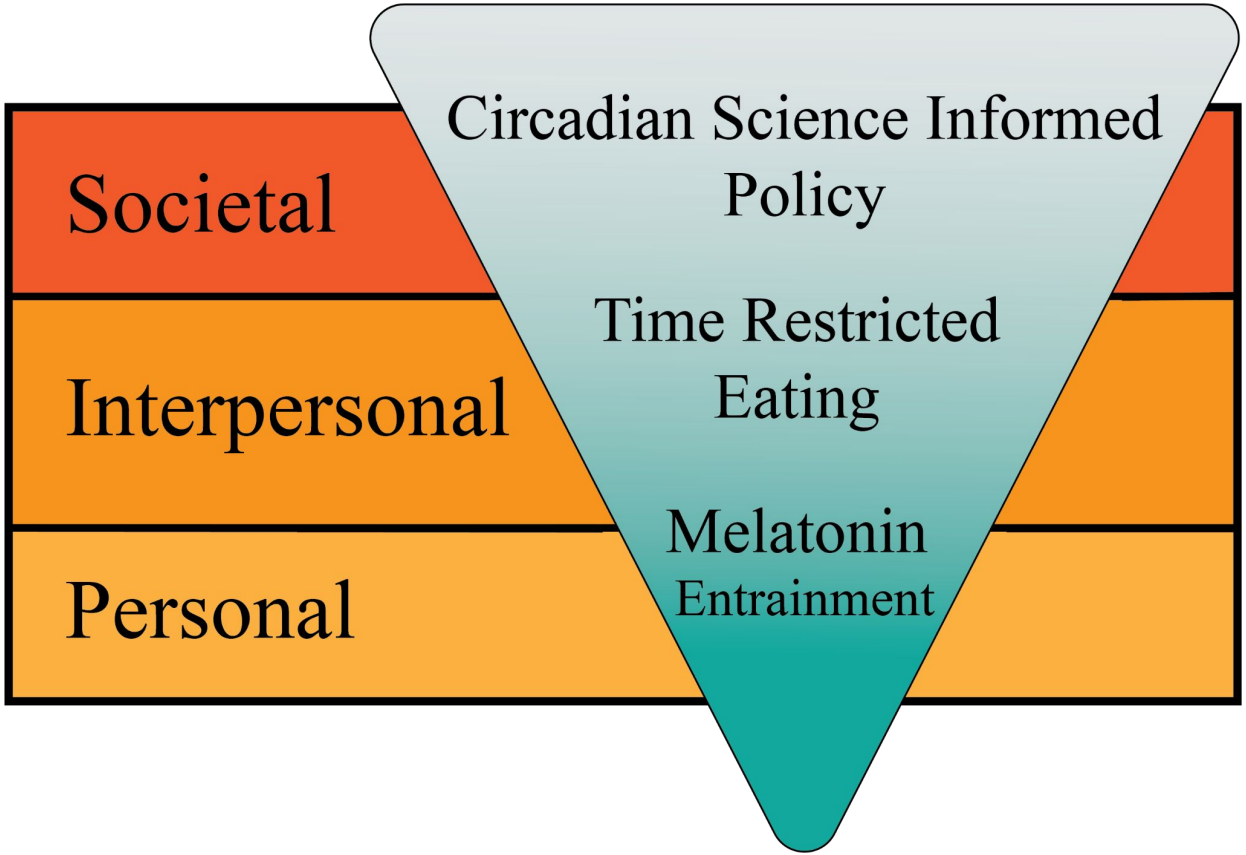
Technologies can also help shift workers adapt by recommending when to sleep, eat, etc.

The app will provide highly personalized advice

No advice is the same. Each shift worker's sleep pattern, chronotype, work schedule, and personal constraints and preferences are the basis for highly personalized advice.



Ways to Mitigate Negative Effects of Circadian Disruption



Many factors must be considered in researching the adoption/adaptation of non-standard work scheduling practices. **What kinds of questions might you ask as a researcher studying shift work optimization?**

When we know the best cue for circadian entrainment in the SCN is light, what else can we do to preserve circadian rhythmicity in people who work when it is dark? (5 minutes)

What is 1 thing you learned today
...and 1 question you still have?