Light’s Effects on Human Health, Alertness, and Sleep

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Presenter

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- Dr. Figueiro is well known for her research on the effects of light on human health, circadian photobiology, and lighting for older adults.
- She is the author of more than 80 scientific articles in her field, and her research is regularly featured in national media.

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Disclosures

- Dr. Mariana G. Figueiro has no relevant financial or non-financial relationships to disclose relating to the content of this activity
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- Commercial support was not received for this activity.

Learning Objectives

At the conclusion of this activity, participants will be able to:

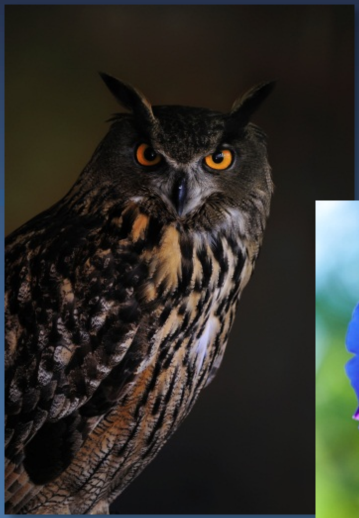
1. Explain basic concepts of light's effects on the circadian system and human health.
2. Comprehend and implement lighting strategies for promoting alertness without adversely affecting the circadian system.
3. Recognize and implement lighting strategies for promoting sleep and general well-being.

Circadian system

- Circadian rhythms are biological processes that display an endogenous (and entrainable) rhythm close to 24 h

circa = approximately; *dies* = day

- Circadian rhythms are generated and regulated by a biological clock in the brain
  - In humans, circadian rhythms free-run with a period slightly greater than 24 hours



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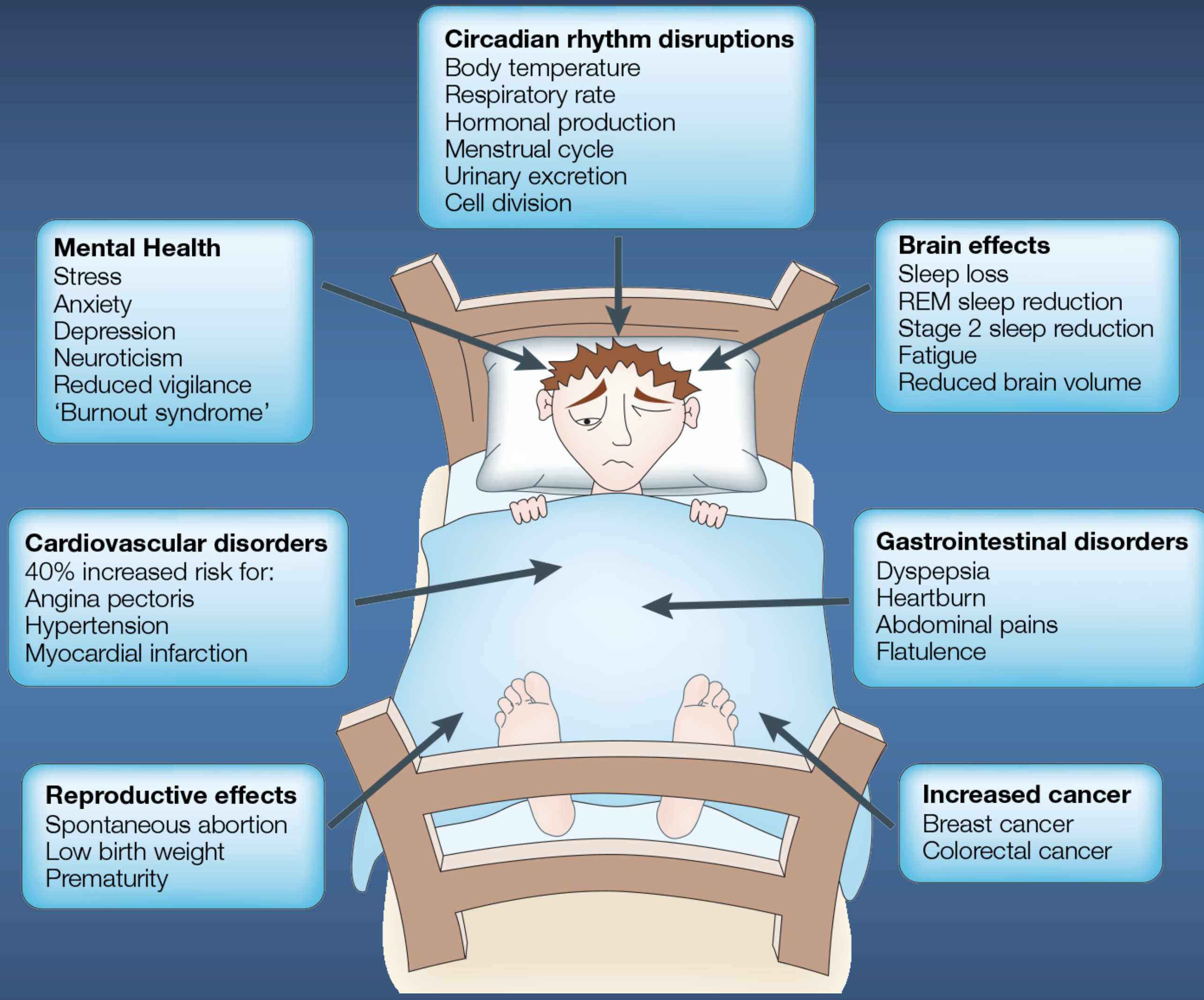

Image: Foster RG and Wulff K. The rhythm of rest and excess. *Nature Reviews Neuroscience*. 2005; 6: 407-414.

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YOUR GUIDE TO SLEEP
What’s your circadian clock got to do with it?

Sleep – wake cycle

Two-process model

- Circadian (C)
- Homeostatic (S)
  - The suprachiasmatic nuclei (SCN) maintain wakefulness, counterbalancing the "homeostatic sleep drive"
  - In both humans and monkeys, the circadian timing system promotes and maintains wakefulness across the subjective day and opposes the accumulating homeostatic sleep drive

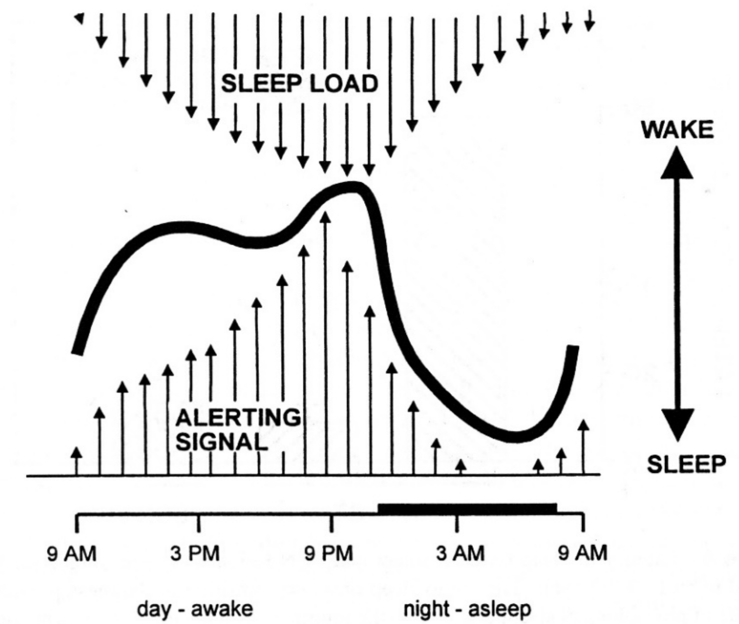

Figure 5 Schematic of the "opponent processes" mediating physiological sleepiness as a function of time of day. Sleep drive increases in response to wakefulness imposed and/or maintained by the suprachiasmatic pacemaker. Increasing levels of SCN-dependent alerting over the subjective day opposes homeostatic sleep drive, both of which peak shortly before the habitual sleep phase. (From Ref. 66.)

Dijk DJ, Edgar DM. Circadian and homeostatic control of wakefulness and sleep. In: Turek FW, Zee PC, editors. *Regulation of Sleep and Circadian Rhythms*. New York: Marcel Dekker Inc; 1999. pp. 111–147.

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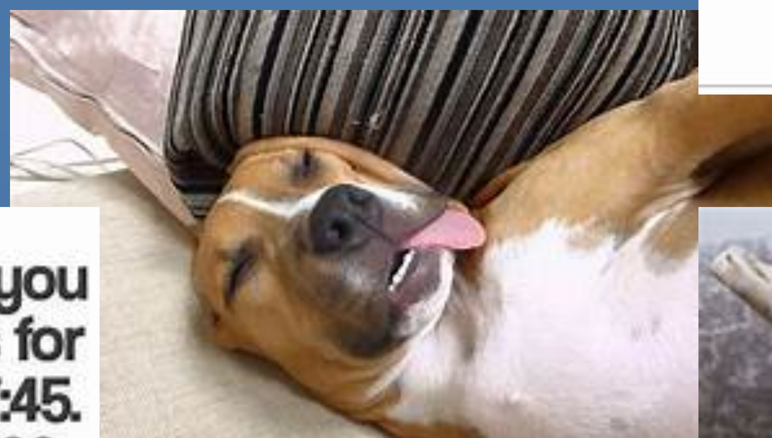
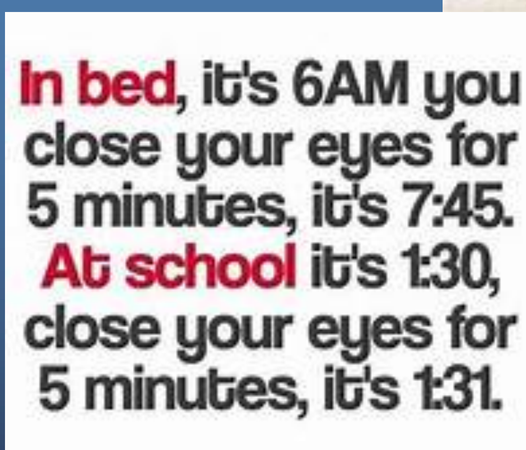
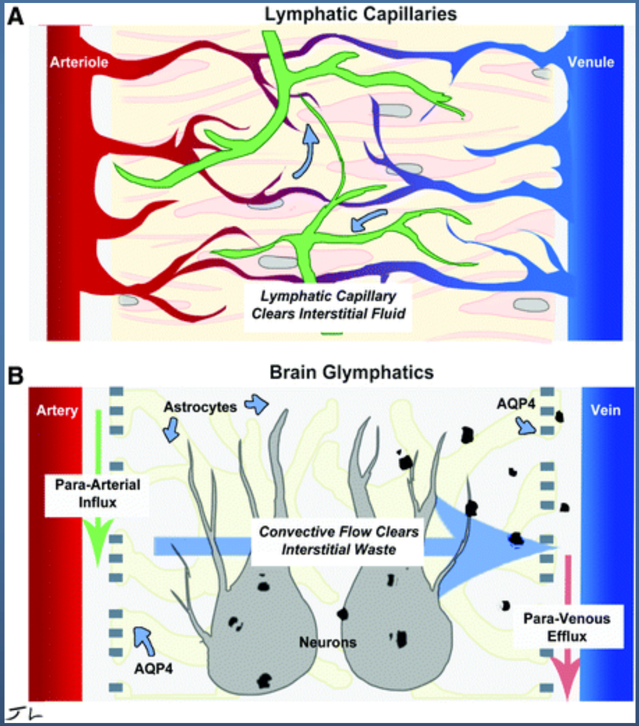
Why do we sleep?

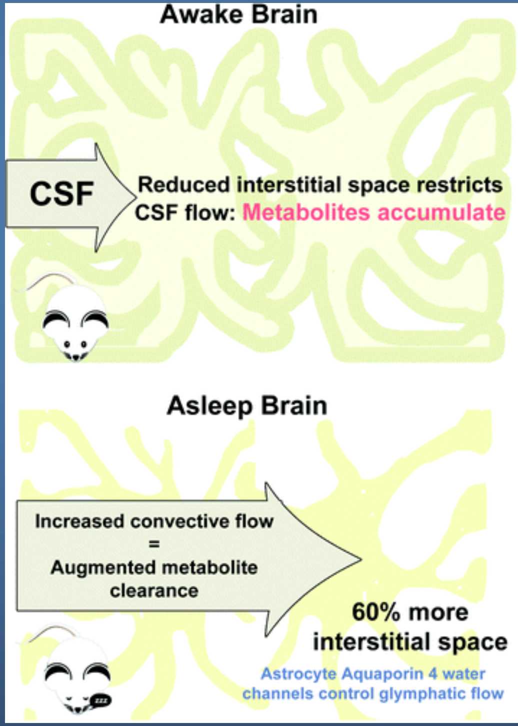




Why do we sleep?

- Sleep cleans up the debris in the brain that we accumulate during wakefulness





Jessen NA, Munk AS, Lundgaard I, Nedergaard M. The Glymphatic System: A Beginner's Guide. *Neurochemical Research*. 2015;40(12):2583–2599. doi:10.1007/s11064-015-1581-6

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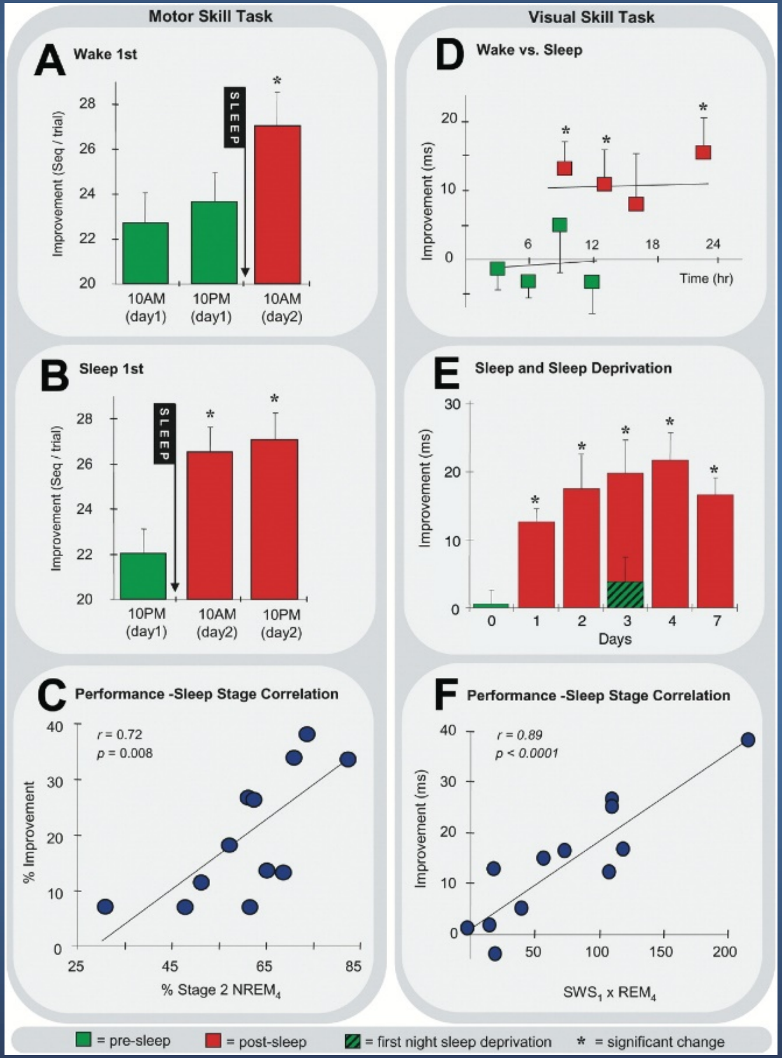
Why do we sleep?

- Sleep promotes learning and consolidates memory
  - Different types of tasks are correlated with different sleep stages



Walker MP, Stickgold R. Sleep-dependent learning and memory consolidation. *Neuron*. 2007;44(1):121–133.

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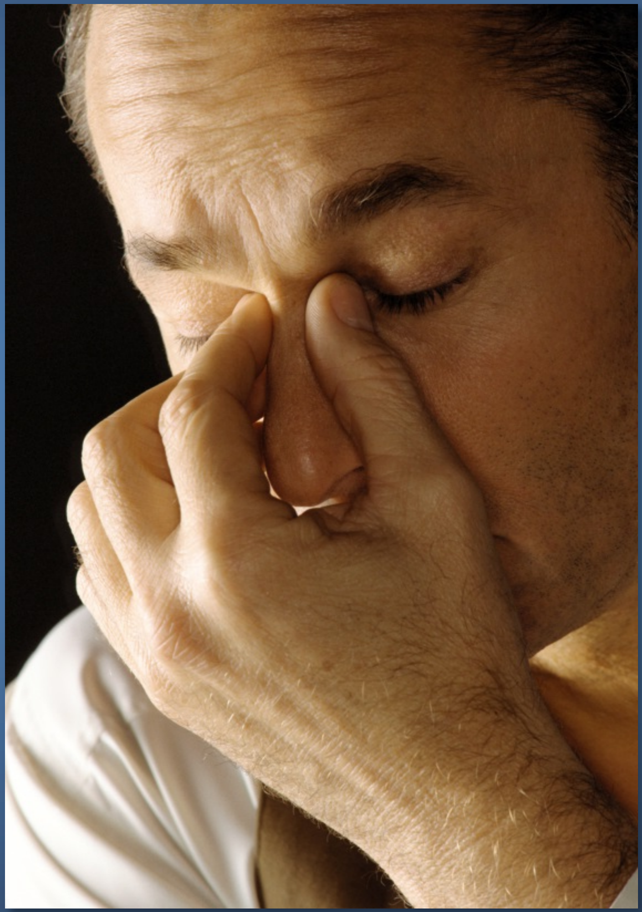
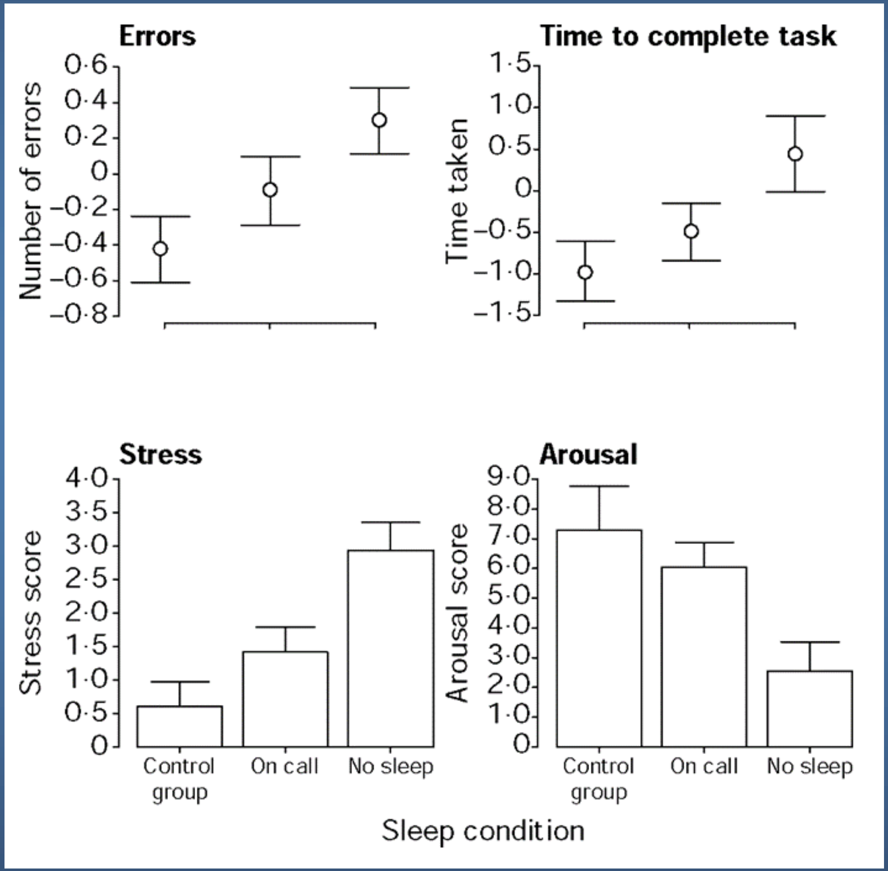
Consequences of sleep deprivation

- Sleep deprivation has been linked to:
  - Reduced performance
  - Increased risk for diabetes, obesity, and cardiovascular disease
  - Increased risk for depression
  - Increased risk for Alzheimer's disease
  - Increased risk for falls



Sleep and surgeon's dexterity performance

- Surgeons who were awake all night:
  - Made 20% more errors and took 14% longer to complete the same tasks than those who had had a full night's sleep
  - Showed increased stress and decreased arousal
  - Showed a decrease in operative dexterity



Taffinder NJ, McManus IC, Gul Y, Russell RCG, Darzi A. Effect of sleep deprivation on surgeons' dexterity on laparoscopy simulator. *The Lancet*;352(9135):1191.

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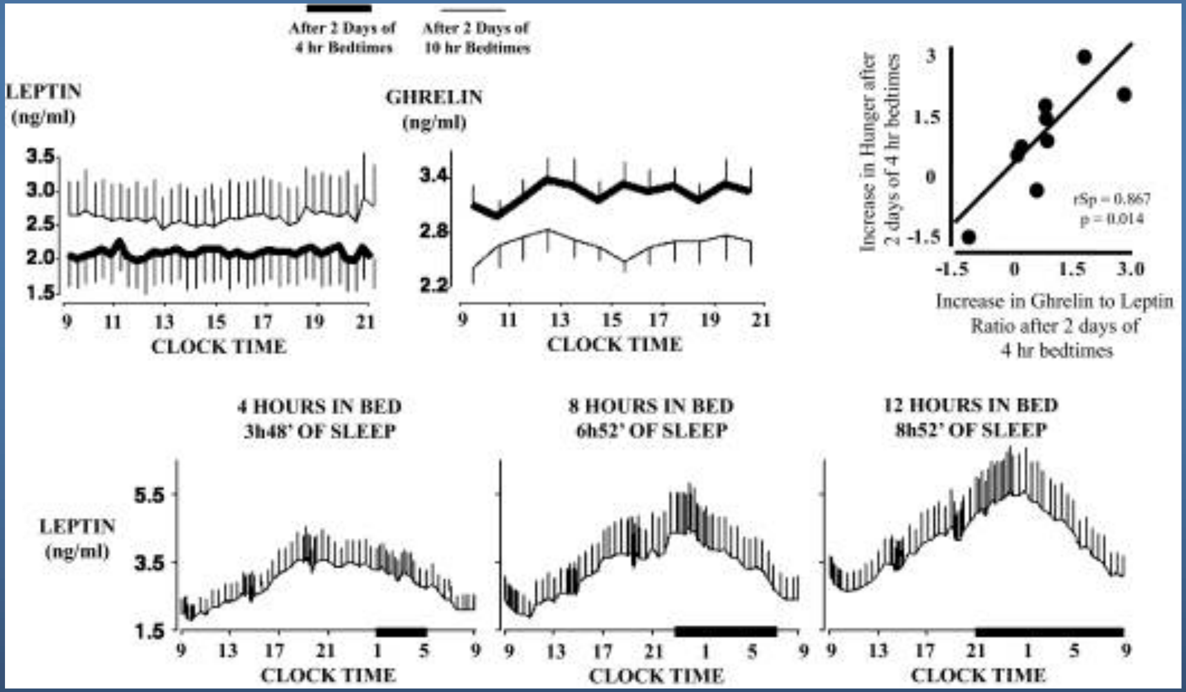
Sleep and cardio-metabolic functions

- 2 days of 4-hour bedtimes decreased leptin (satiety hormone), increased ghrelin (hunger hormone), and increased self-reported hunger



Hanlon EC, Van Cauter E. Quantification of sleep behavior and of its impact on the cross-talk between the brain and peripheral metabolism. *Proceedings of the National Academy of Sciences*. 2011;108 Suppl 3(Suppl 3):15609–15616. doi:10.1073/pnas.1101338108

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Sleep and Alzheimer's disease (AD)

- Sleep – wake disturbances are a common and often debilitating feature of Alzheimer's disease (AD)
- Sleep – wake disturbances may be one of the earliest symptoms in preclinical AD
- Evidence from animal and human studies suggests that AD pathology disrupts the sleep – wake cycle, including increased sleep fragmentation and wakefulness, and decreased slow-wave sleep
- Evidence from animal and human studies also suggests that prolonged wakefulness may increase levels of soluble Aβ in the brain, and may both exacerbate and accelerate the onset of AD pathology

Lim MM, Gerstner JR, Holtzman DM. The sleep-wake cycle and Alzheimer's disease: what do we know? *Neurodegenerative Disease Management.* 2014;4(5):351-362.

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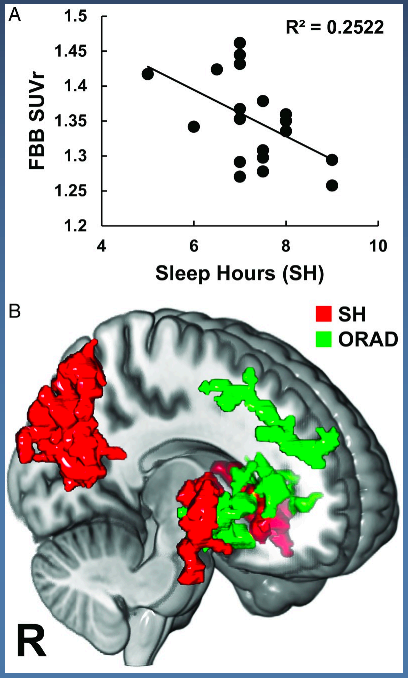
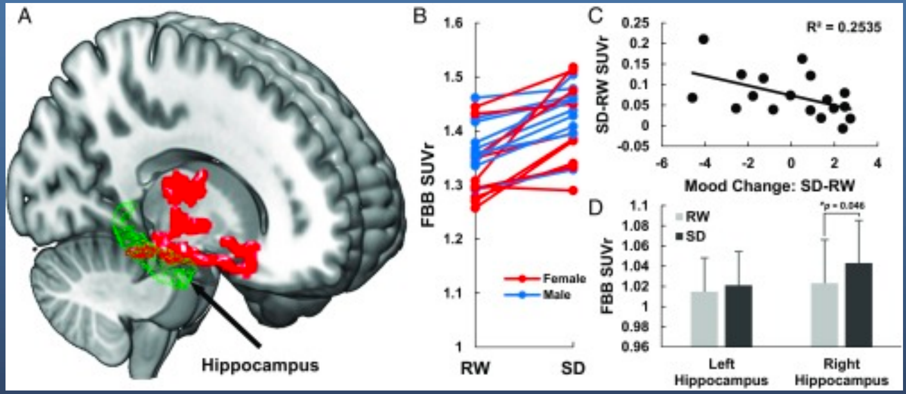
Sleep and AD

- One night of sleep deprivation, relative to baseline, resulted in significant increases in Aβ burden in the right hippocampus and thalamus
- These increases were associated with mood worsening following sleep deprivation, but were not related to the genetic risk (APOE genotype) for AD



Shokri-Kojori E, Wang G-J, Wiers CE, Demiral SB, Guo M, Kim SW, et al. β-Amyloid accumulation in the human brain after one night of sleep deprivation. *Proceedings of the National Academy of Sciences*. 2018;115(17):4483-4488.

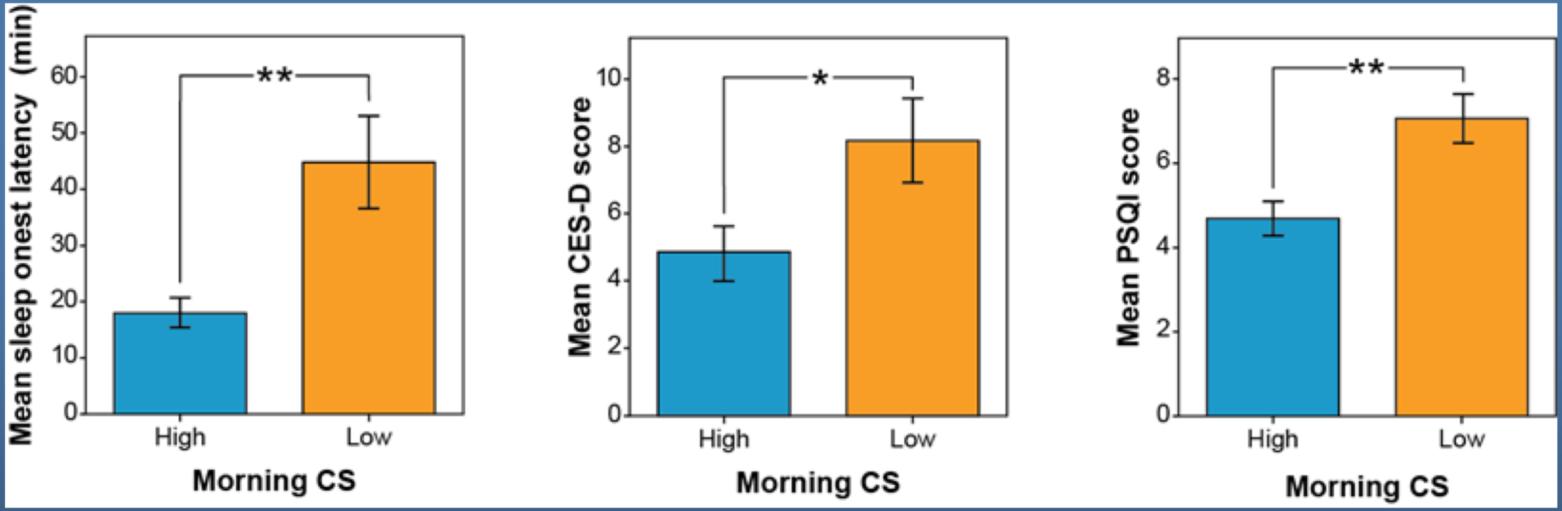


How does light affect sleep and circadian rhythms?

- Light entrains the biological clock to the local time on Earth
  - Short-wavelength, blue light (peak close to 460 nm) is maximally effective
- Light has an acute, direct effect on humans
  - Increases measures of alertness
  - Impacts production of hormones
  - Decreases reaction times
  - Reduces feelings of sleepiness
- Light provides perceptual cues of the environment
  - Increases postural control and stability

Light and sleep in office workers

- Those exposed to higher morning (08:00 a.m. to noon) circadian stimulus (CS) (CS > 0.3) fell asleep faster (less sleep onset latency) and reported better sleep and feeling less depressed than those exposed to low morning CS (CS < 0.15)



Figueiro M.G., Steverson B., Heerwagen J., Kampschroer K., Hunter C.M., Gonzales K., Rea, M.S. (2017). The impact of daytime light exposures on sleep and mood in office workers. Sleep Health; 3(3):204-215.

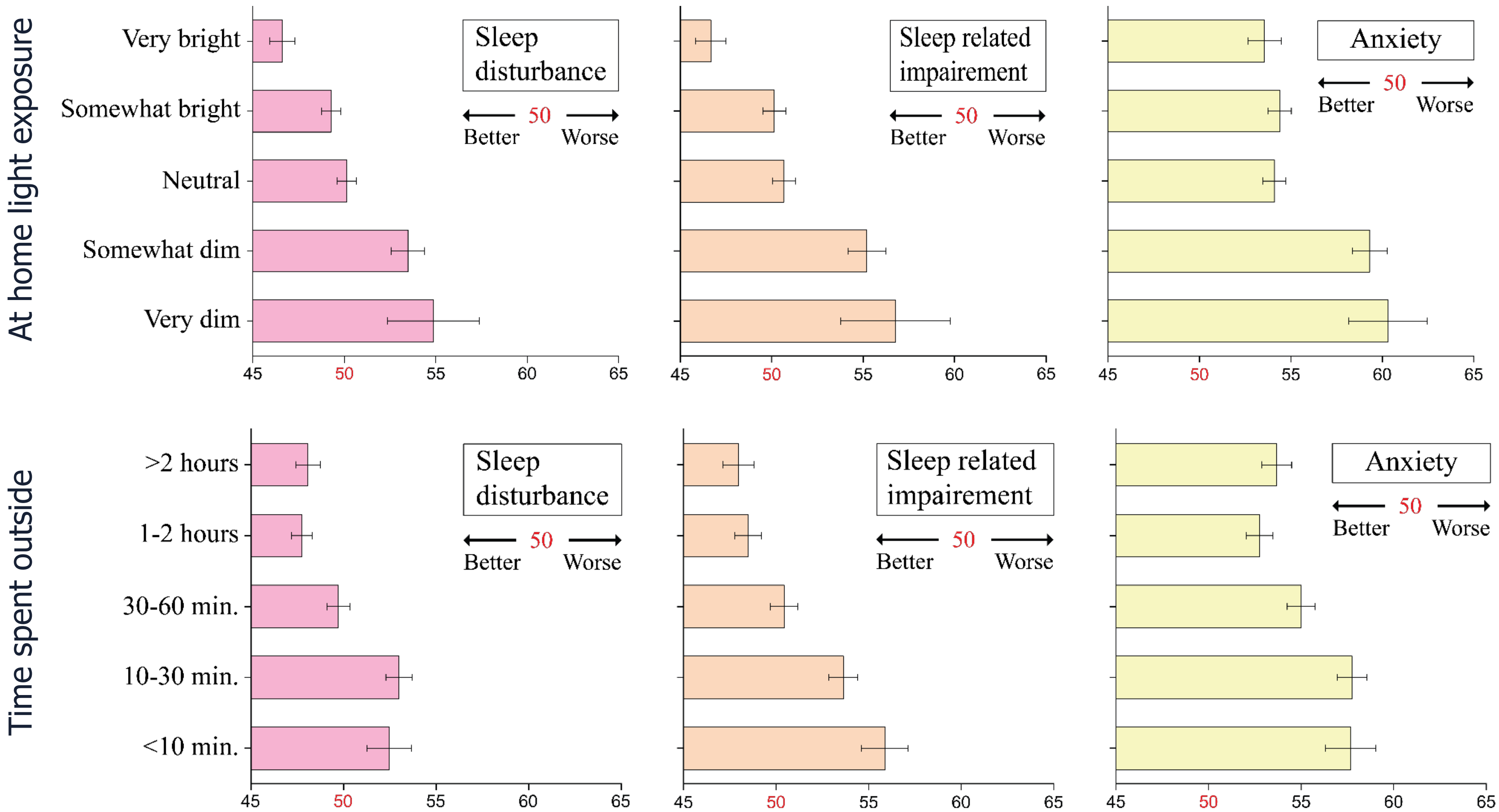
(** = $p < .01$; * = $p < 0.05$)

Source: U.S. General Services Administration

Light and sleep survey

- During COVID-19 pandemic we sent out a survey probing people's light exposures (indoors and outdoors) and how that impacted measures of sleep, mood and anxiety
- Hypothesis: more light during the day = better sleep and mood
  - Over 700 responses
  - Included in the analyses are those who are employed but working at home or unemployed and staying home

Light and sleep survey



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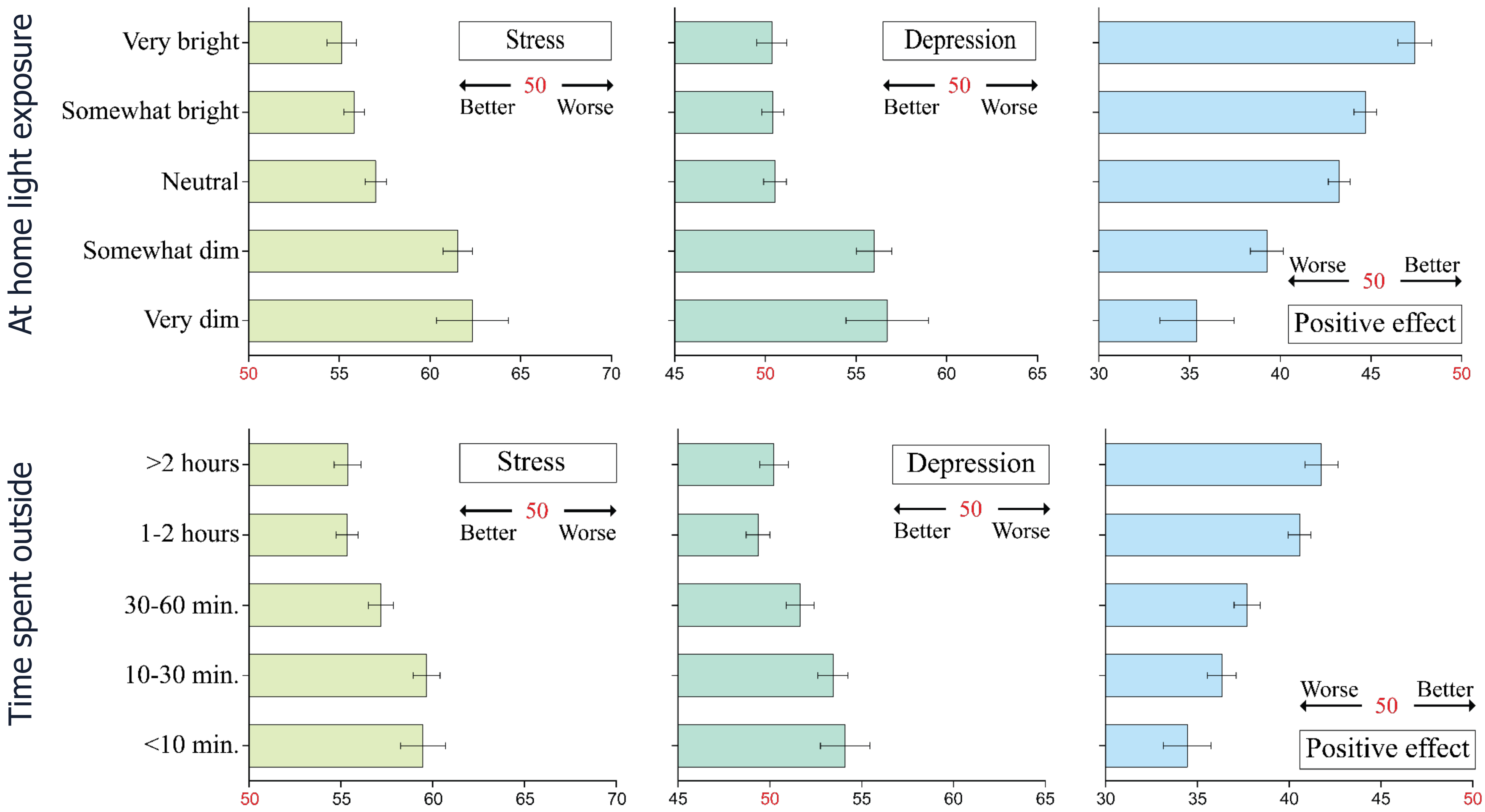
Light and sleep survey



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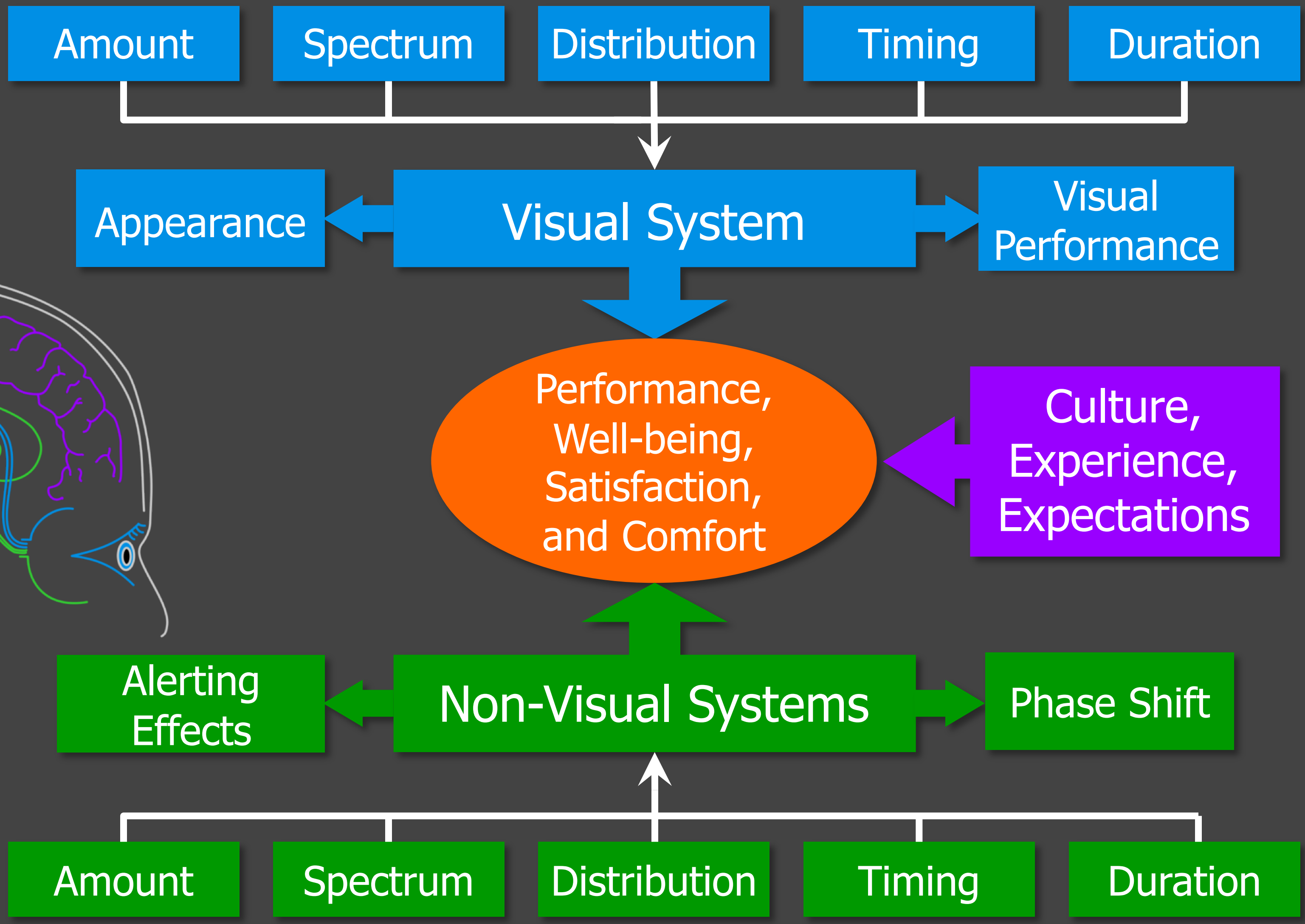
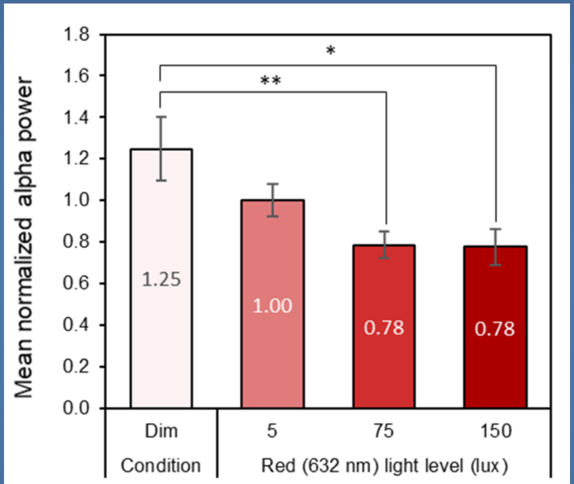
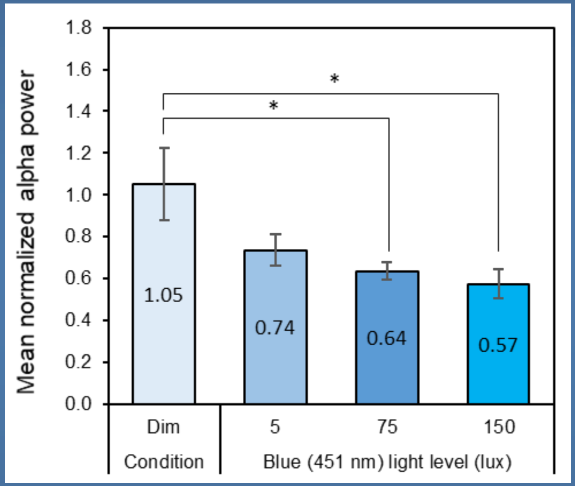
Lighting affects three systems: Visual + Non-visual + Message/Perceptual



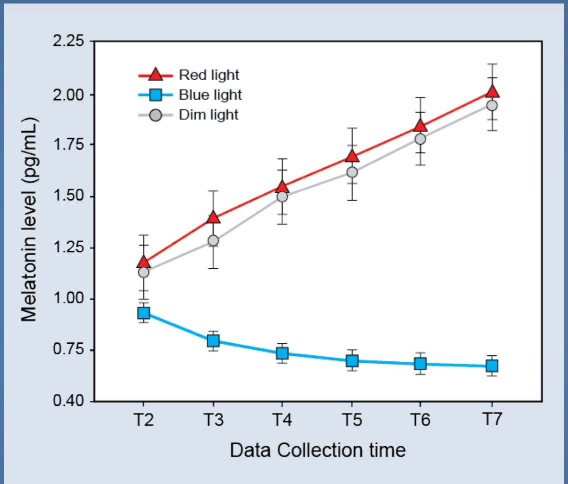
Light's alerting effects
It does not have to be blue light!

Alertness (brain activity)





Melatonin levels



4 light levels: dim (D), low (5 lux), medium (75 lux), and high (150 lux)

Error bars represent standard error of the mean
* $P < 0.05$, ** $P < 0.01$

Source: Office of Naval Research

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Summarizing what we know so far…….
Science

- Light sets the timing of the biological clock (promotes entrainment)
  - For entrainment
    - Morning light is needed to advance the timing of the clock (timing is important)
    - Short-wavelength and high light levels at the eye are most effective
    - Any white light can be used, however, if you increase light levels, change fixture distribution, or increase duration
    - Melatonin is used as a marker, but melatonin suppression and phase shifting of the clock, but may use different pathways in the brain to accomplish that
- Light has a direct (acute) effect on people (cup of coffee)
  - Does not have to be blue light, but it must be at the eye!
  - Any time of day is effective
  - Effect is generally observed within 15-30 min

What Does the Research Tell Us?

1. Ambient light therapy to promote entrainment in cancer patients

Sources: National Cancer Institute and Acuity Brands

Study 1: Light therapy and melatonin in myeloma transplant patients — Protocol

- In collaboration with Dr. William Redd (Icahn School of Medicine at Mt. Sinai, NYC), we investigated the impact of a CS = 0.3 (1000 lux at pillow, 3000 K light source) between 07:00 and 10:00 on entrainment, sleep, fatigue, and depression

  - 30 patients undergoing bone marrow transplant received the circadian active light (CS = 0.3) and 30 patients received a circadian-inactive light (CS < 0.1)
  - Urine melatonin, actigraphy, questionnaires were collected at baseline and at the end of hospitalization

Sources: National Cancer Institute and Acuity Brands

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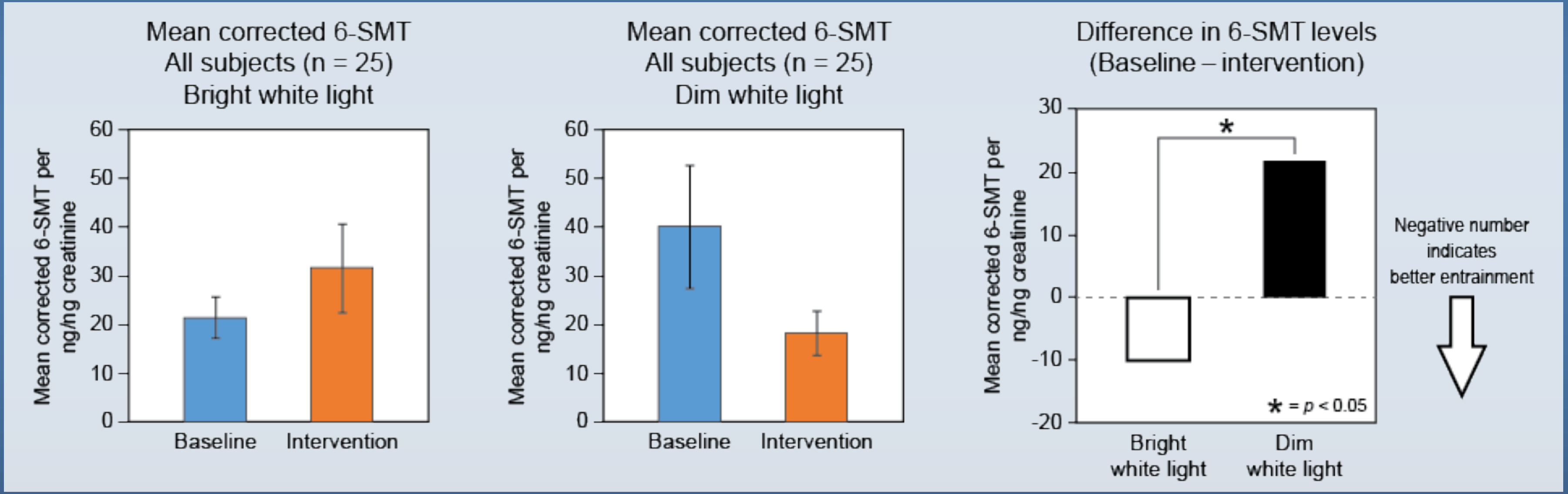
Study 1: Light therapy and melatonin in myeloma transplant patients — Results

- Urinary melatonin increased in those receiving the active intervention and decreased in those receiving the inactive intervention, suggesting better entrainment in those receiving the active intervention



Concentrations of creatinine-adjusted urinary melatonin (6-sulfatoxymelatonin [6SMT]), a major melatonin metabolite, for participants exposed to the bright white (left) and dim white (right) lighting interventions compared to baseline

A positive number means that melatonin levels were lower after intervention compared to baseline. (* $P < 0.05$)

Sources: National Cancer Institute and Acuity Brands

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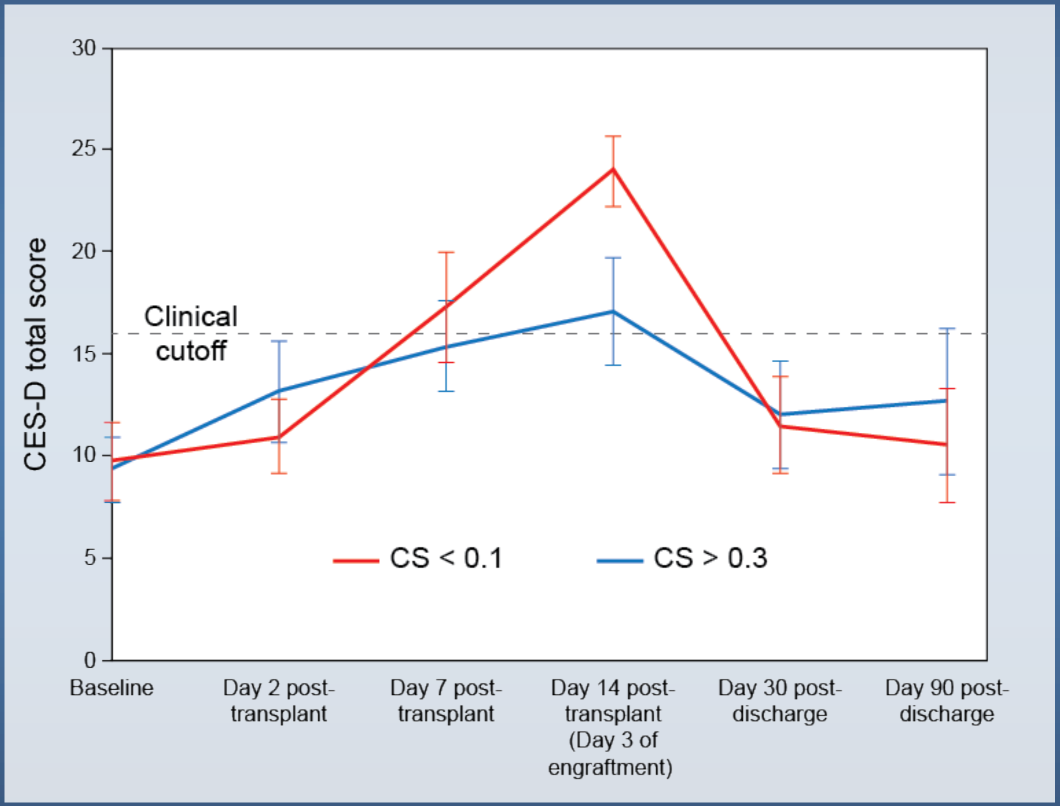
Study 1: Light therapy and melatonin in myeloma transplant patients — Results



High CS exposure led to significantly lower CES-D total scores (depression) than low CS exposures ($P = 0.0051$)

Source: National Cancer Institute and Acuity Brands

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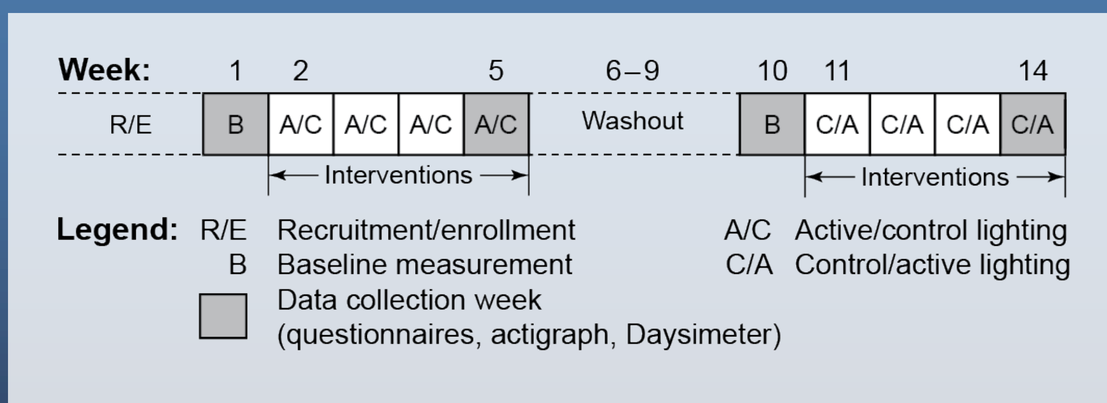
2. Tailored lighting intervention (TLI) for patients with Alzheimer's disease and related dementias (ADRD) in long-term care facilities

Source: National Institute on Aging

Study 2a: Short-term TLI for patients with ADRD Protocol

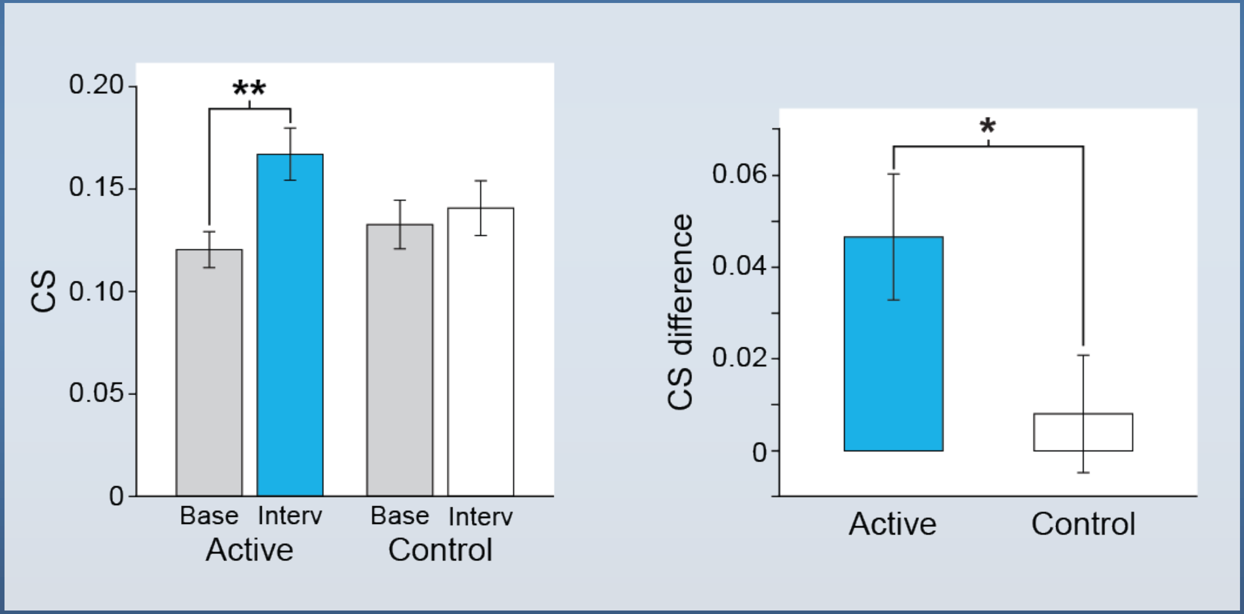
- 14-week randomized, placebo-controlled, crossover design clinical trial
- Administered all-day (≈ 06:00 – 08:00 to 18:00) active (high circadian stimulus [CS] = 0.4) or control (low CS < 0.1) TLI
- 46 patients with ADRD in 8 long-term care facilities for two 4-week periods (separated by a 4-week washout)



Source: National Institute on Aging

Study 2a: Short-term TLI for patients with ADRD Results

- Participants' CS exposures were significantly greater during the active TLI compared to baseline



* *P* < 0.05, ** *P* < 0.01

Source: National Institute on Aging

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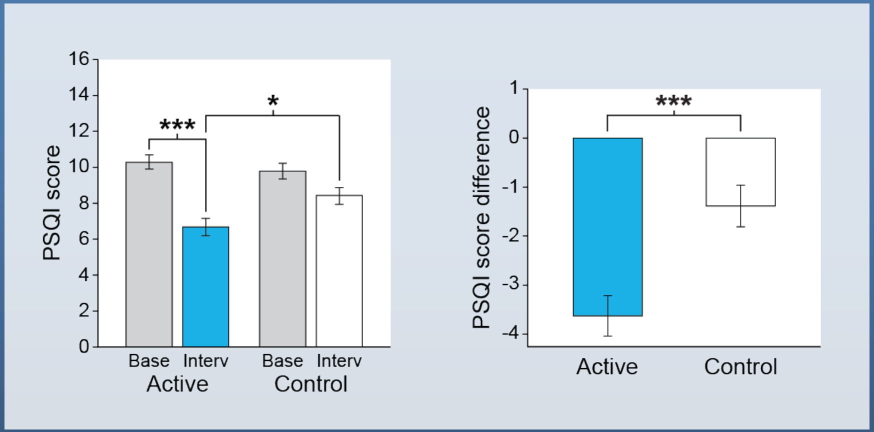
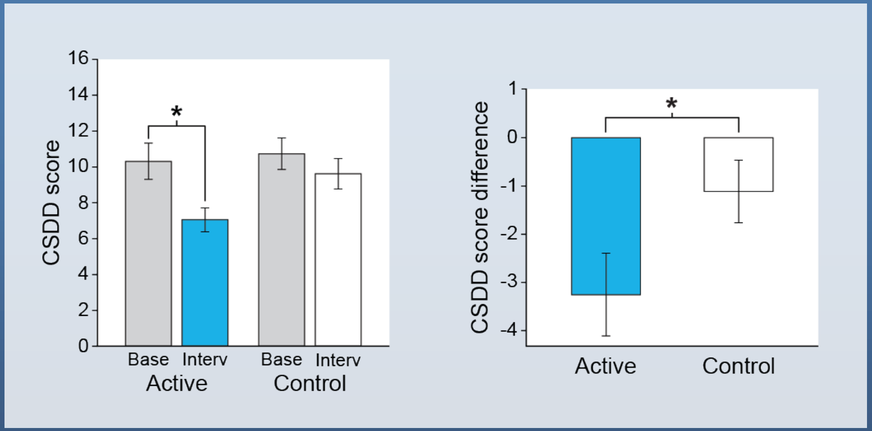
Study 2a: Short-term TLI for patients with ADRD Results

- Participants experienced fewer sleep disturbances (PSQI scores) and depressive symptoms (CSDD scores) during the active TLI compared to baseline and the control

Sleep disturbances



Depression scores



* $P < 0.05$, *** $P < 0.001$

Source: National Institute on Aging

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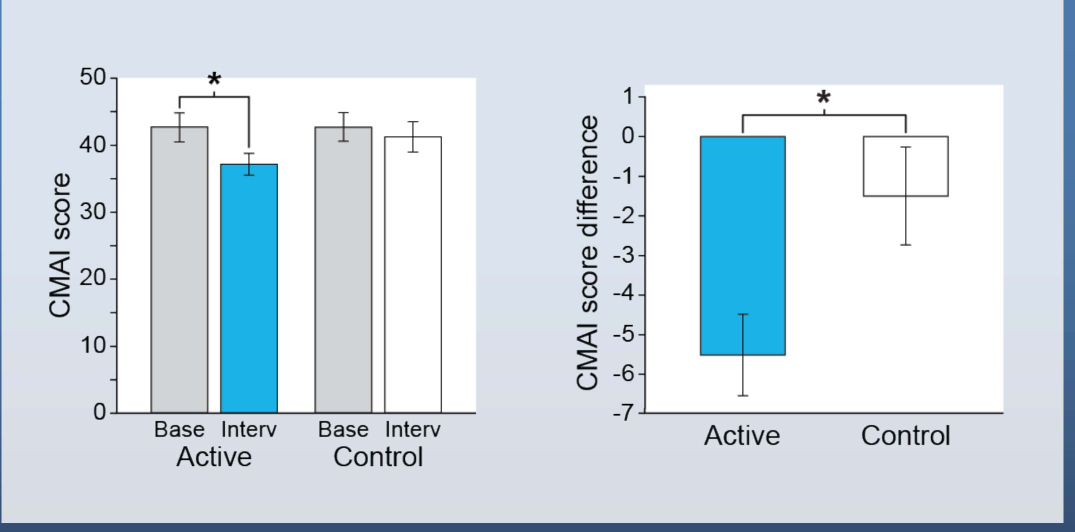
Study 2a: Short-term TLI for patients with ADRD Results

- Participants experienced fewer agitated behavior symptoms (CMAI scores) during the TLI compared to baseline and greater reductions in symptoms compared to the control

Agitation scores



* $P < 0.05$

Source: National Institute on Aging

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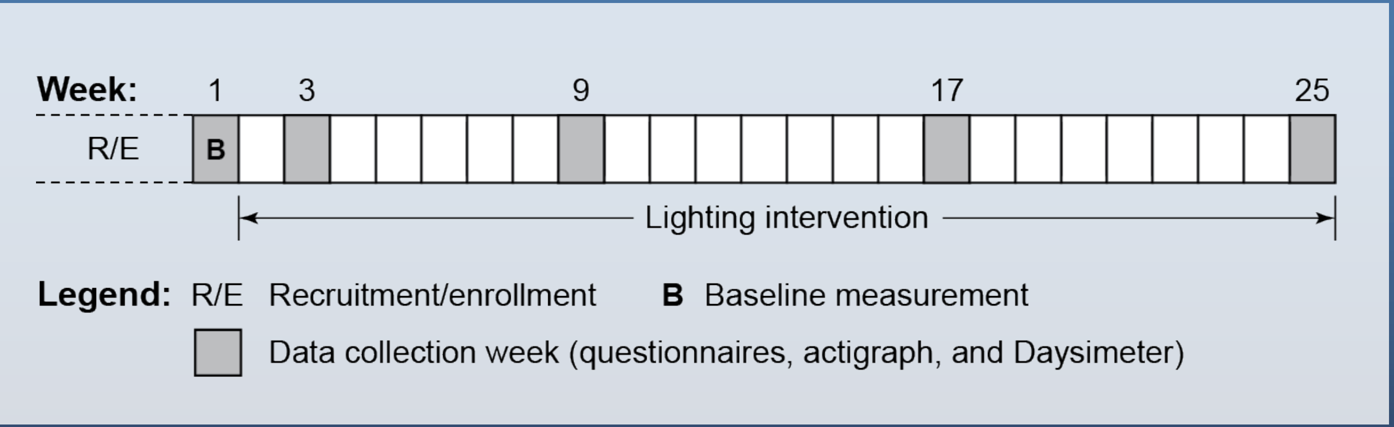
Study 2b: Long-term TLI for patients with ADRD Protocol

- 6-month randomized single-arm, within-subjects design clinical trial
- Administered all-day (≈06:00 – 08:00 to 18:00) active TLI (high CS = 0.4)
- 47 patients with ADRD in 9 long-term care facilities

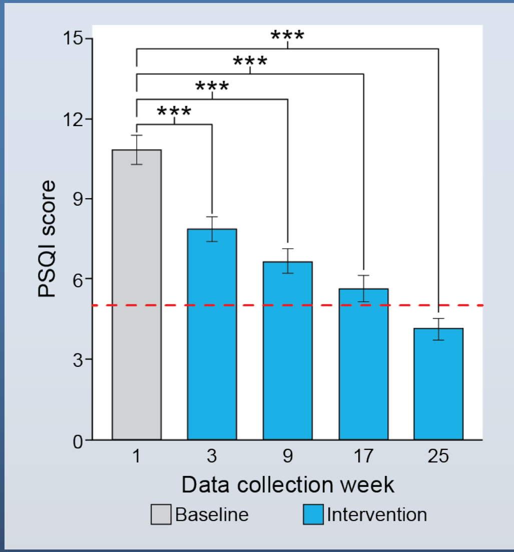


Source: National Institute on Aging

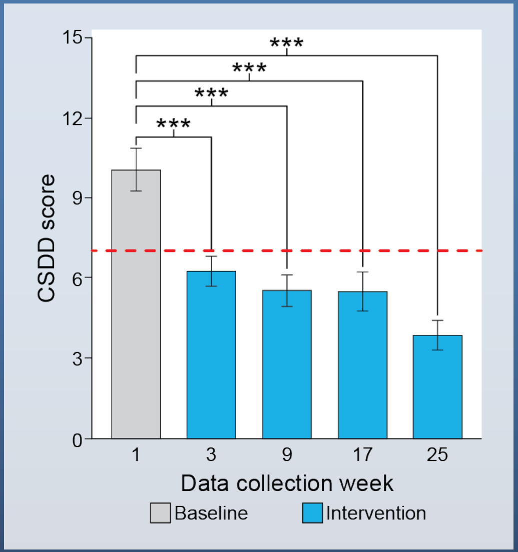
Study 2b: Long-term TLI for patients with ADRD Results

- Participants experienced fewer sleep disturbances (PSQI scores) and depressive symptoms (CSDD scores), along with fewer agitated behavior symptoms (CMAI scores), during the TLI compared to baseline

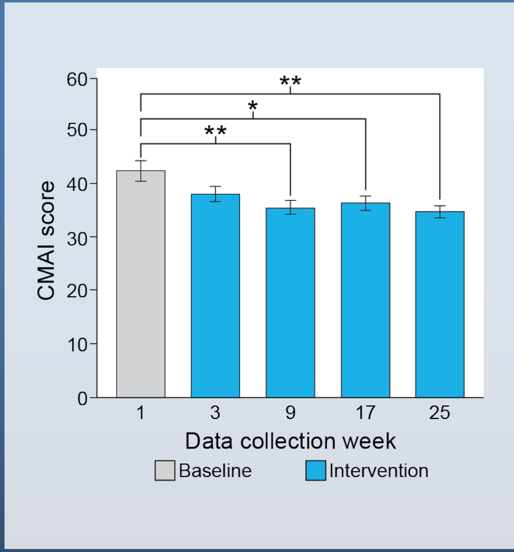
Sleep disturbances



Depression scores



Agitation scores



* P < 0.05, ** P < 0.01, *** P < 0.001

Source: National Institute on Aging

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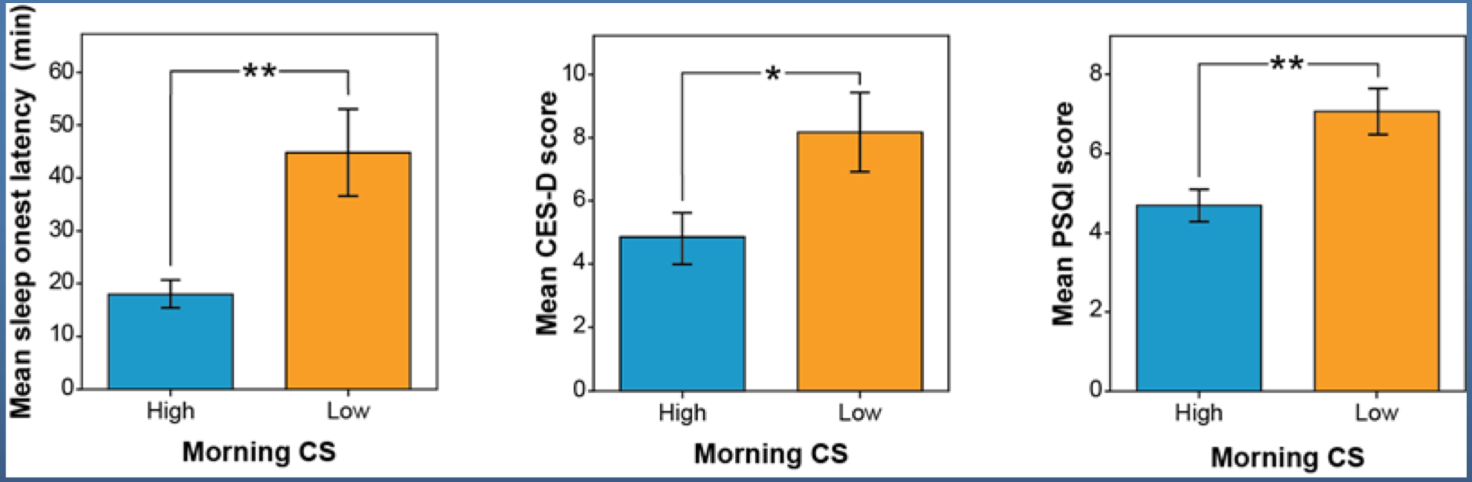
3. Lighting to promote entrainment and increase alertness in office workers

Source: General Services Administration and US Department of State

Study 3a: Circadian entrainment in office workers

- Those exposed to higher morning (08:00 – 12:00) CS (CS > 0.3) fell asleep faster (less sleep onset latency) and reported better sleep and feeling less depressed than those exposed to low morning CS (CS < 0.15)



Figueiro MG, Steverson B, Heerwagen J, Kampschroer K, Hunter CM, Gonzales K, Rea MS. The impact of daytime light exposures on sleep and mood in office workers. Sleep Health. 2017;3(3):204-215.

(* $P < 0.05$, ** $P < .01$)

Source: U.S. General Services Administration

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Study 3b: Daytime office workers Protocol

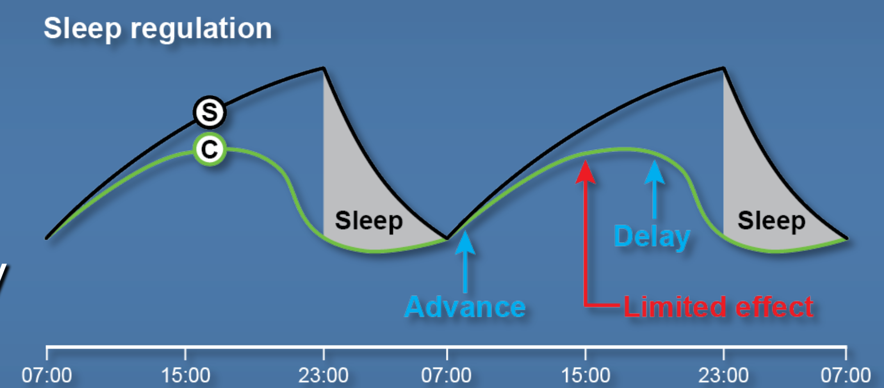
- Test, in a 3-week field study, the impact of morning blue light and afternoon red light on:
  - Sleep quality at home
  - Subjective sleepiness and vitality scores during work

	Week 1 (Days 1–5)	Week 2 (Days 1–5)	Week 3 (Days 1–5)
Time of day	Arrive, 12:00, 15:00, Depart	Arrive, 12:00, 15:00, Depart	Arrive, 12:00, 15:00, Depart
Wear Daysimeter	Waking to bedtime	No	Waking to bedtime
Wear actigraph	24 h	No	24 h
Lighting intervention	Off	On	On
Questionnaires	KSS SVS (Arrive), KSS SVS (12:00), KSS SVS (15:00), KSS SVS (Depart); PSQI, PSS-10, CES-D: First day of week 1 only		KSS SVS (Arrive), KSS SVS (12:00), KSS SVS (15:00), KSS SVS (Depart); PSQI, PSS-10, CES-D: Last day of week 3 only

Source: U.S. General Services Administration

Study 3b: Daytime office workers Hypotheses

- Morning blue light (CS ≥ 0.3):
  - Promote circadian entrainment, advance circadian phase
  - Advance sleep onset at night, sleep offset in the morning
  - Advance activity acrophase
- Morning blue light (CS ≥ 0.3):
  - Elicit acute alerting response
  - Reduce subjective sleepiness
  - Increase subjective vitality/energy
- Afternoon red light (CS = 0):
  - Elicit acute alerting response
  - Reduce subjective sleepiness
  - Increase subjective vitality/energy, especially around 15:00 (the post-lunch dip)
  - Avoid excessive CS exposure in late afternoon, thereby limiting any possible light-induced delay of circadian phase



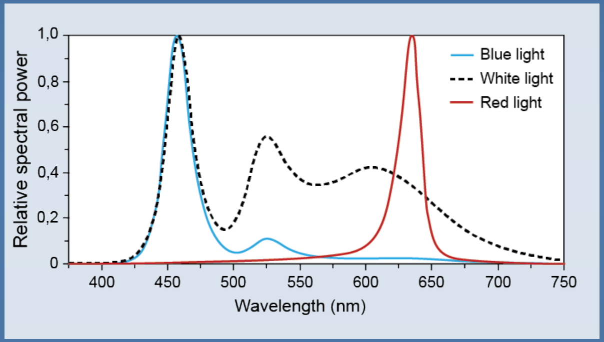
Homeostatic sleep Process S vs. circadian Process C and the effects of blue vs. red light on circadian phase

Graphic adapted from: Borbély, A. A. A two process model of sleep regulation. *Human Neurobiology*. 2017;1(3):195-204.

Source: U.S. General Services Administration

Study 3b: Daytime office workers
Lighting interventions

- LRC developed and built 20 plug-in LED luminaires, mounted on participants' desktops



Time of Day	Lighting Intervention	λ_{max} (nm)	E_V (lux)	CS
06:00 to 12:00	blue	455	50	0.30
12:00 to 13:30	white (6500 K)	n/a	200	0.30
13:30 to 17:00	red	634	50	0

Source: U.S. General Services Administration

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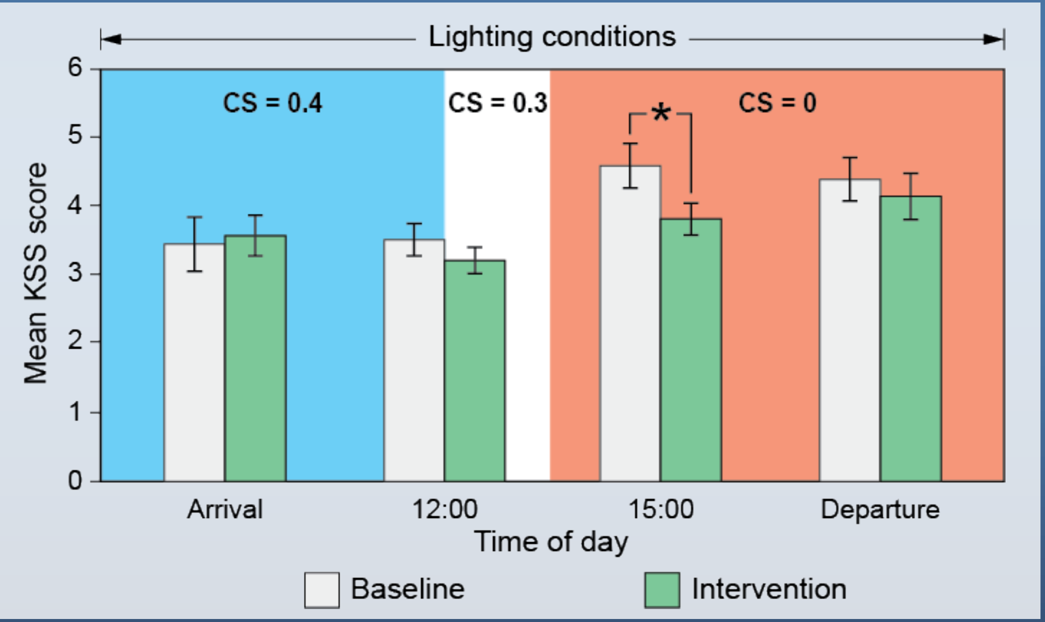
Study 3b
Results — Questionnaires

- Sleepiness (KSS) scores were reduced significantly during the intervention (week 3) at 15:00 (with red light)



Error bars represent standard error of the mean (* $P < 0.05$)

Source: U.S. General Services Administration

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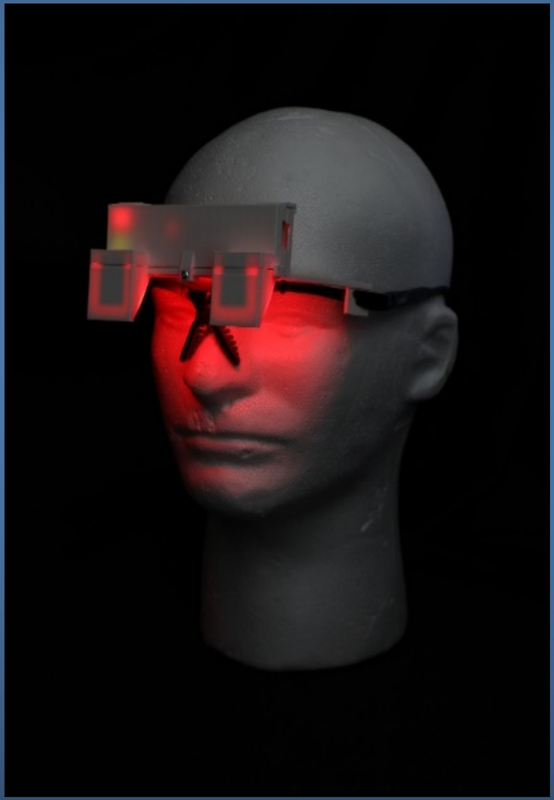
4. Light for day- and night-shift nurses

Source: National Institute for Occupational Safety and Health (NIOSH)

Study 4: Red light for shift-working nurses

- Translate lab findings into the field
  - 20-week protocol
  - 45 day-shift nurses (07:00 – 19:00)
    45 night-shift nurses (19:00 – 07:00)
  - Outcome measures:
    - Reaction time performance testing
    - Saliva samples for melatonin and cortisol levels
    - Subjective sleep and global health questionnaires
    - Actigraphy



Source: National Institute for Occupational Safety and Health (NIOSH)

Study 4: Red light for shift-working nurses Lighting interventions

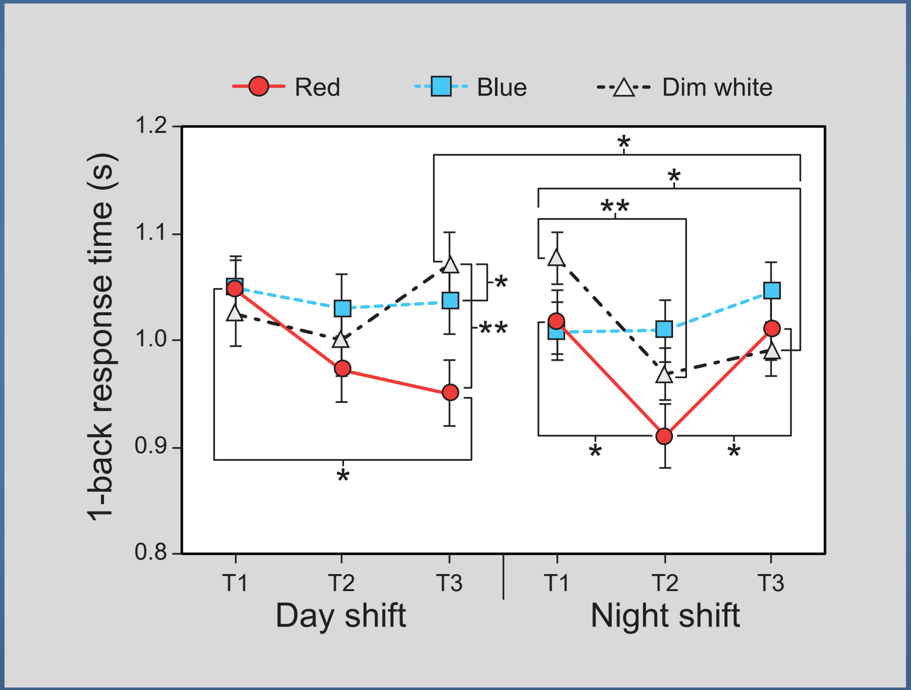
- Intervention sessions:
  - Every workday for 2 weeks
- Experimental conditions:
  - 50 lux blue light (476 nm)
  - 50 lux red light (630 nm)
  - 30 lux white light (2700 K)
- Light goggles worn for 30 min, 3 times per shift
  - Beginning, middle, and end of shift
- Performance tests and saliva samples collected before and after wearing light goggles

Source: National Institute for Occupational Safety and Health (NIOSH)

Study 4: Red light for shift-working nurses Preliminary results

Source: CDC/NIOSH

- Workers responded faster after red light at the end of the dayshift and at the middle of the nightshift, when they were likely to be more tired



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5. Using light to increase alertness in train operators

Source: Metro Istanbul

Study 5: Using light to increase alertness in a train dispatch center

- Investigate whether exposure to high CS in the morning and low CS (red combined with white light) in the afternoon and at night would promote circadian entrainment (phasor magnitude) and increase objective (actigraphy) and subjective sleep quality (PSQI) as well as alertness (KSS) in the operational context

Source: Metro Istanbul

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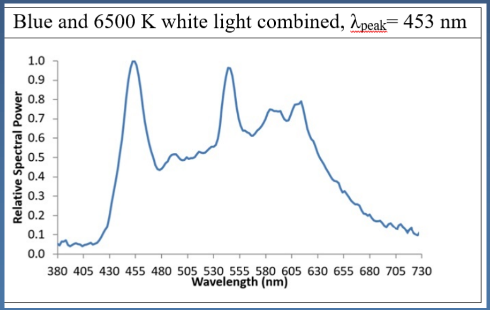
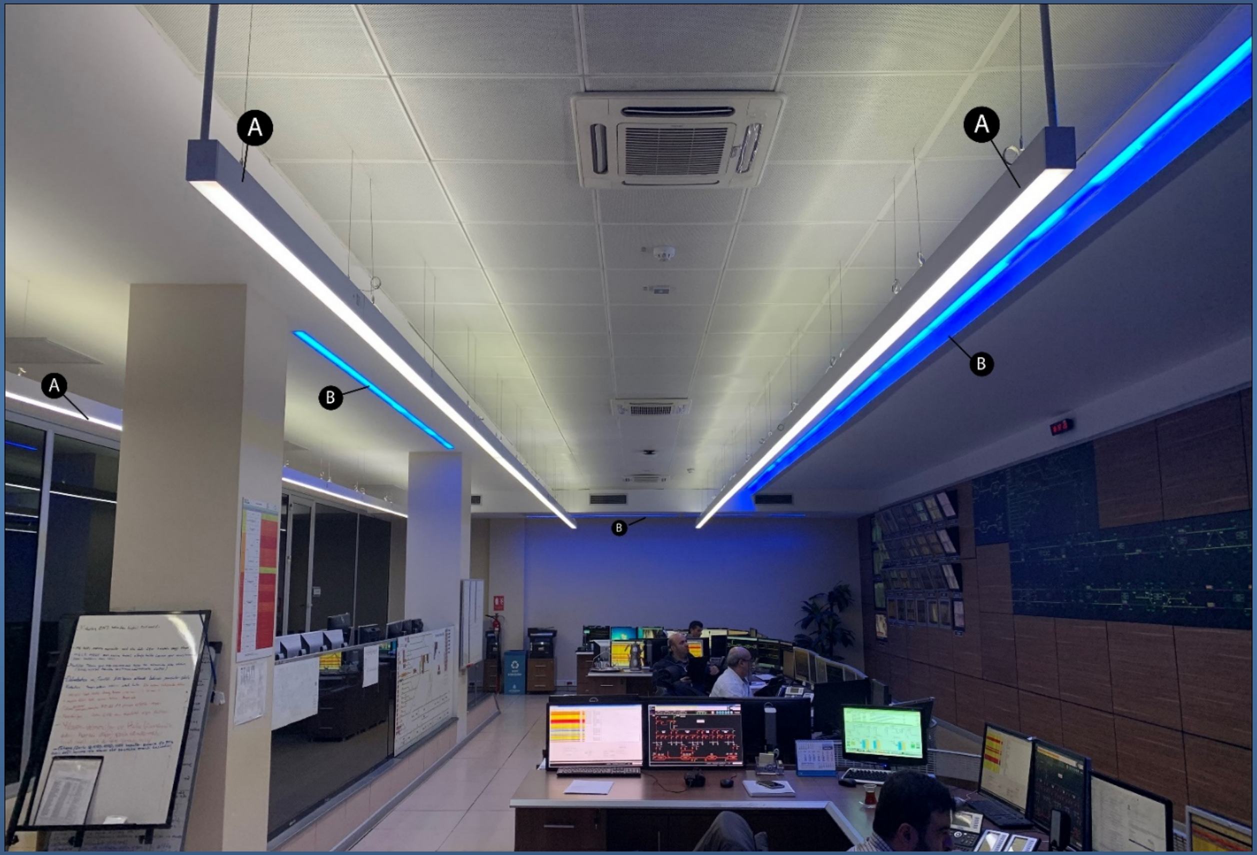
Study 5: Using light to increase alertness in a train dispatch center — Lighting interventions

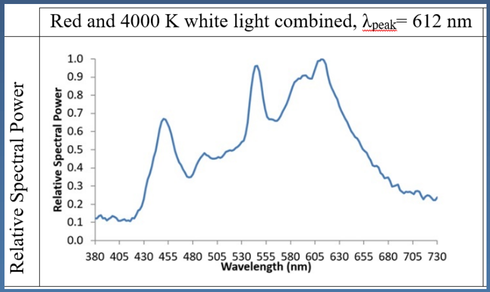




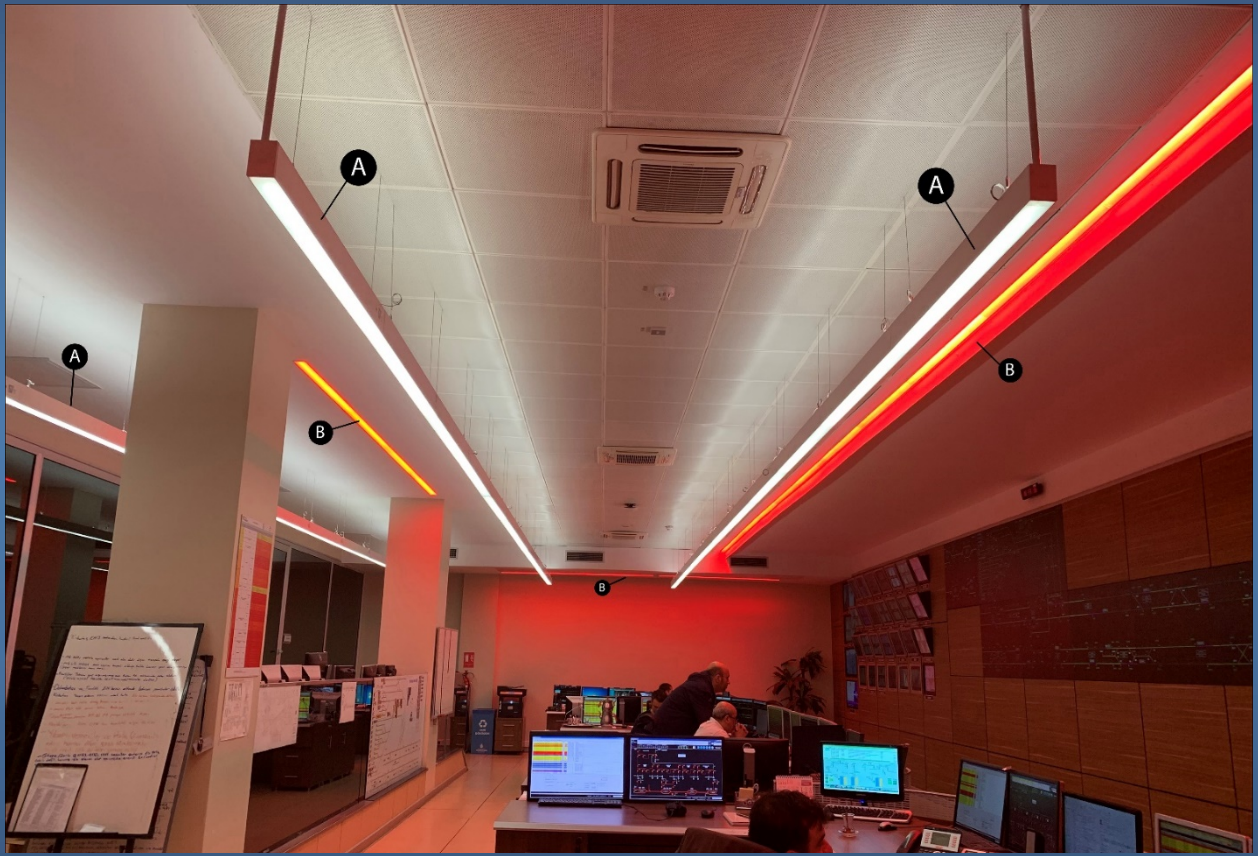
- Morning schedule
  - 07:00 – 12:00
  - CS > 0.3
  - (A) 6500K white light
  - (B) 470 nm blue light

Source: Metro Istanbul

Study 5: Using light to increase alertness in a train dispatch center — Lighting interventions



- Afternoon & night schedule
  - 12:00 – 07:00
  - CS < 0.1
  - (A) 4000K white light
  - (B) 630 nm red light



Source: Metro Istanbul

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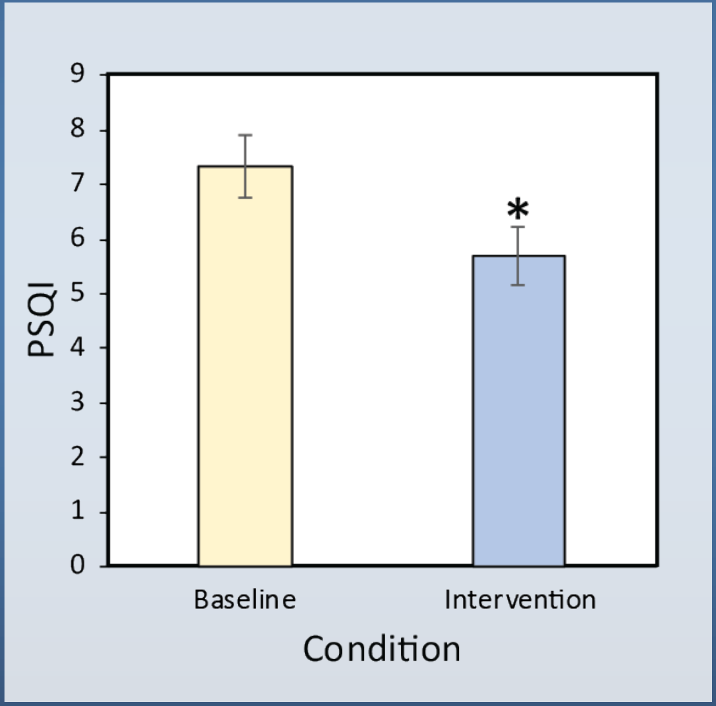
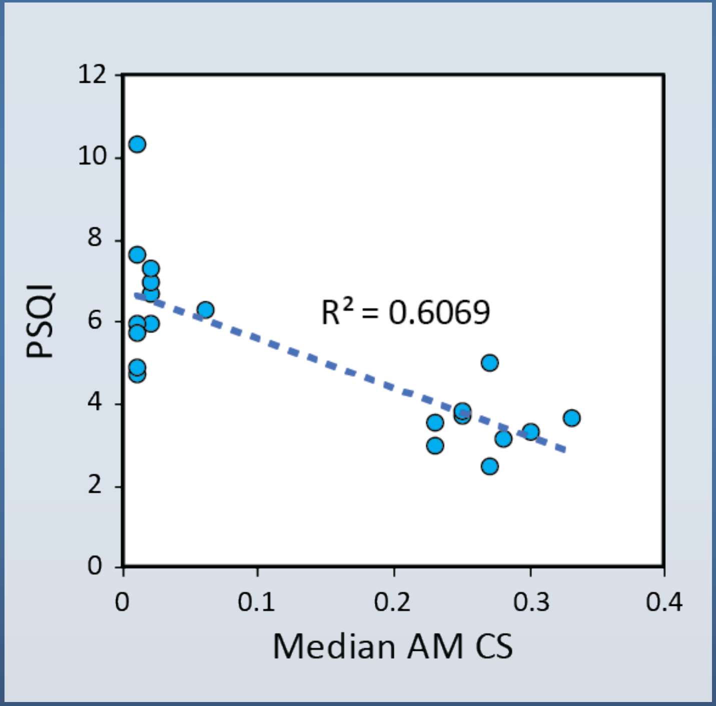
Study 5: Using light to increase alertness in a train dispatch center — Results

- Sleep Quality (PSQI)





(* *P* < 0.05)

Source: Metro Istanbul

Summary: What does the research tell us?

- Light and health is about more than just “circadian,” “tunable,” or “blue-enriched” light
- The amount, timing, duration, and distribution must be included in any design
  - Spectrum is important, but amount and duration are key for applications
- We don’t know it all, but if we “overdesign” the dose, we see positive results in the field
  - Field studies are showing promising results when using CS = 0.3 during the day (300 – 500 lux at the eye of a 3000 K source) and CS = 0.1 (< 30 lux at the eye) in the evening

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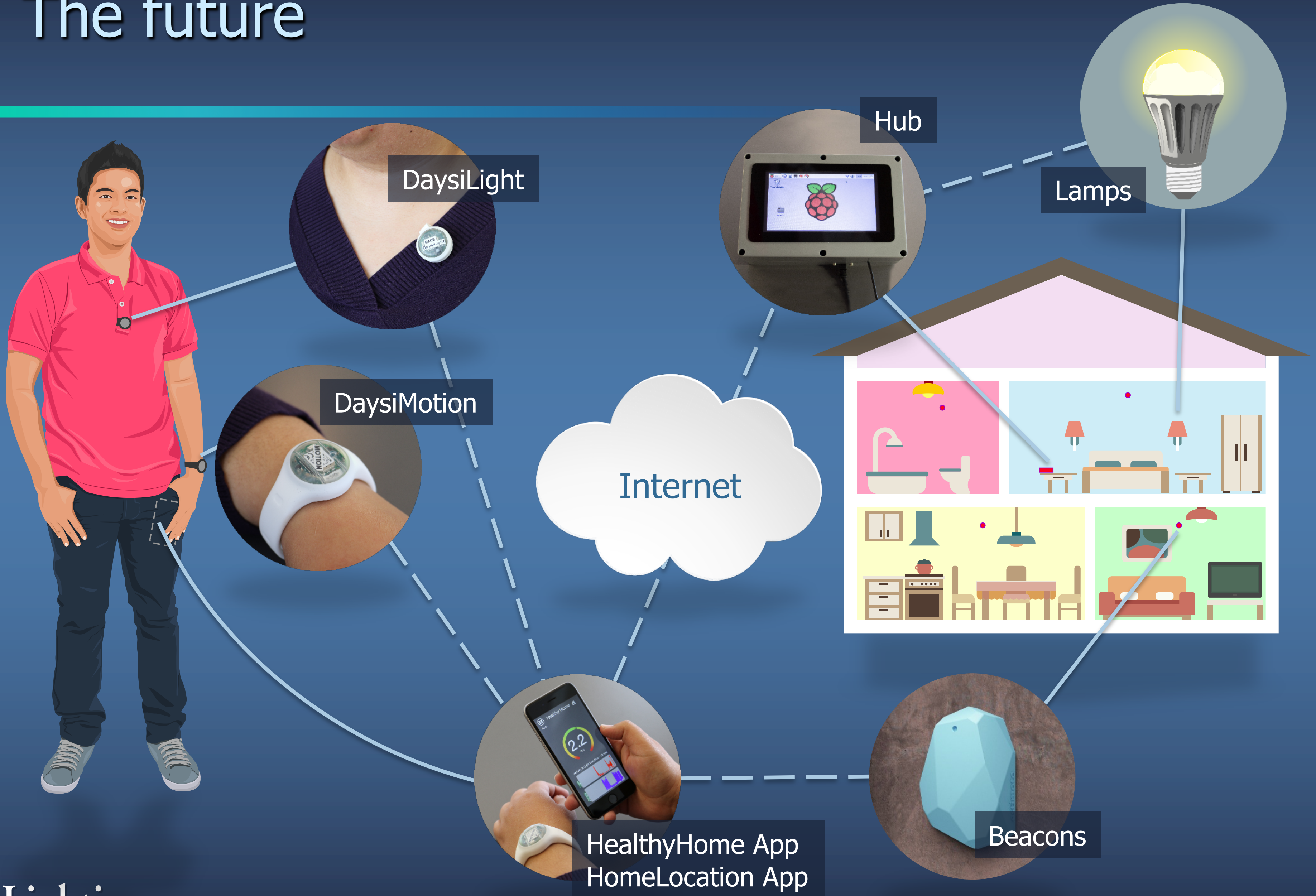
The future

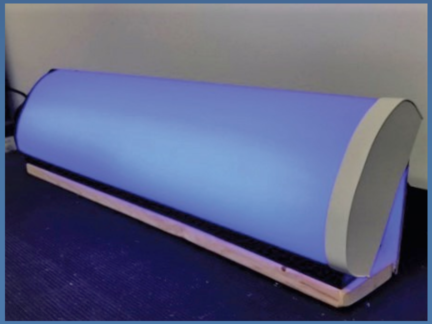

DaysiLight
DaysiMotion
Hub
Lamps
Internet
HealthyHome App
HomeLocation App
Beacons

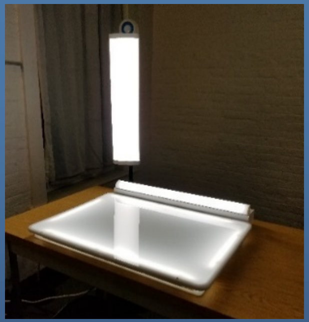
Tips for Designing for Circadian Entrainment and Alertness

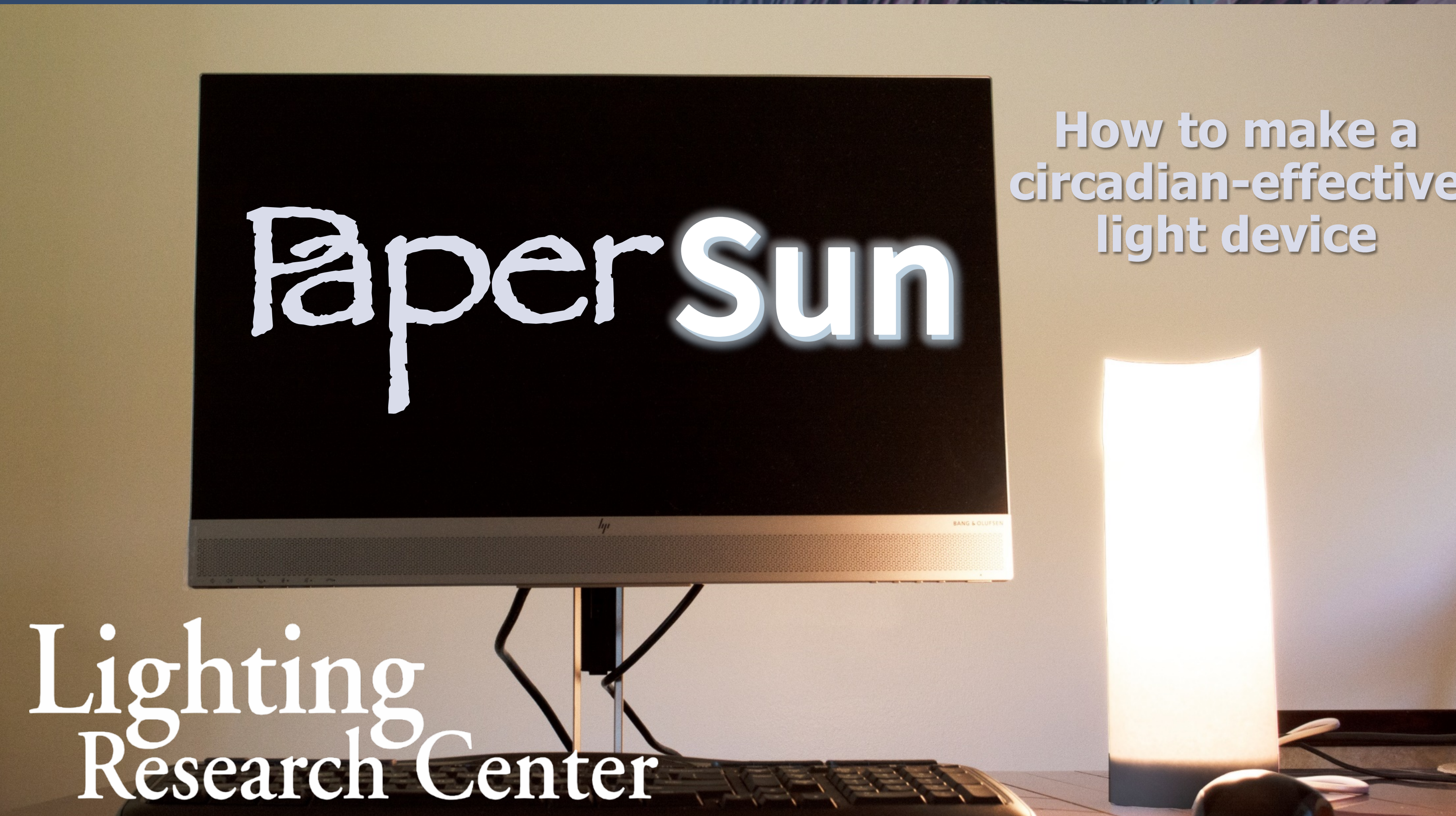
- Think about *layers* of light!
  - Some designers or specifiers may have strict energy constraints that prevent CS targets from being met
    - Consider using saturated blue (e.g., peak wavelength = 470 nm) LEDs as a way to boost CS in creative ways
  - Studies have shown that red light can have an acute alerting effect without suppressing melatonin
    - Consider using red light as a way to boost alertness for occupants

Think Beyond the Ceiling
Portable/Personal Light Devices

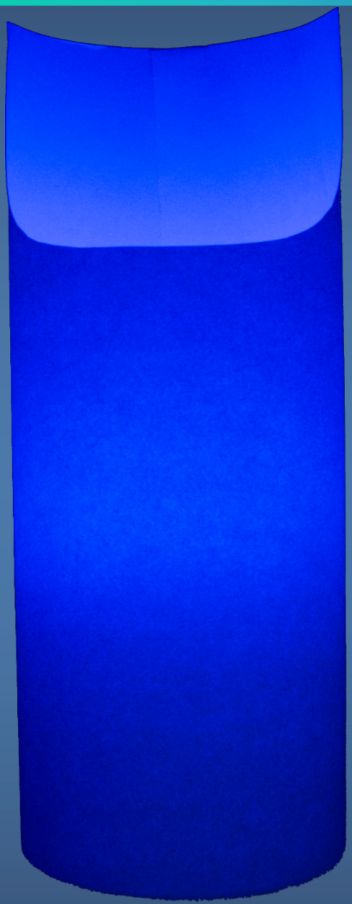
- Custom built luminaires with static/tunable spectrum light engines and manual or digitally programmable controls
- Used for field studies as well as lab experiments investigating circadian effective light as well as light for acute alerting effect
- Very few if any equivalent products commercially available
- Go outdoors for 1-2 h in the morning!







https://www.youtube.com/watch?v=__QsTrrIC2s



Saturated, narrow-band blue Peaking between 460 – 480 nm

Light at the eye: 30 lux

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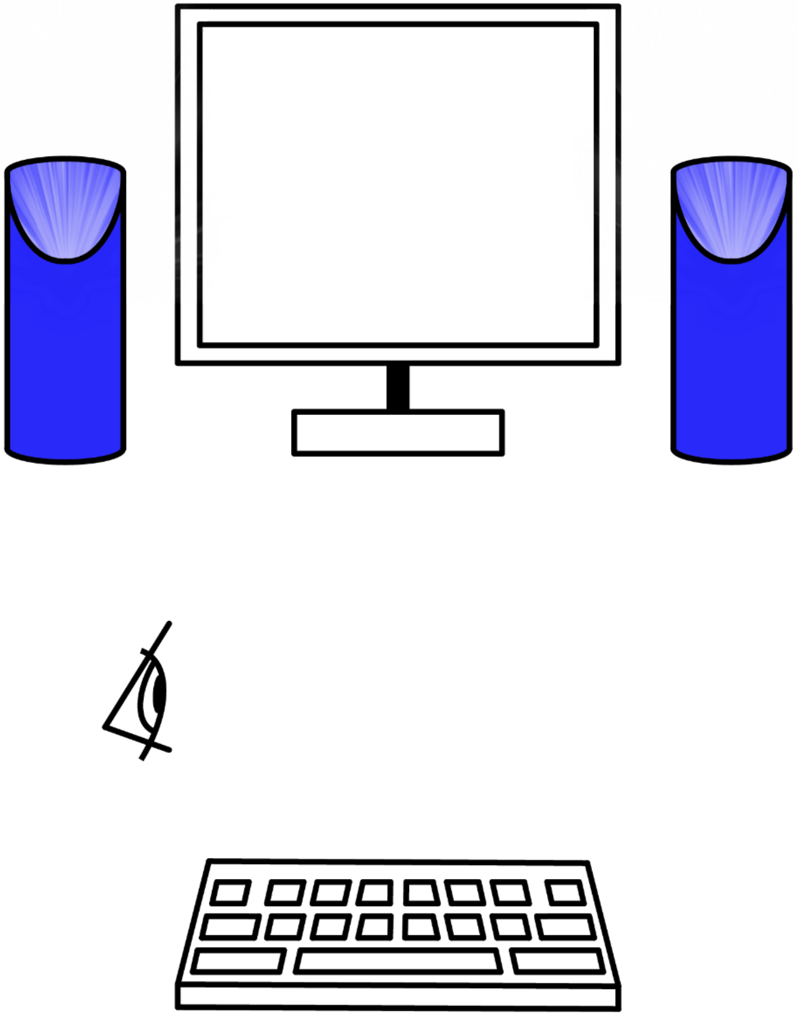
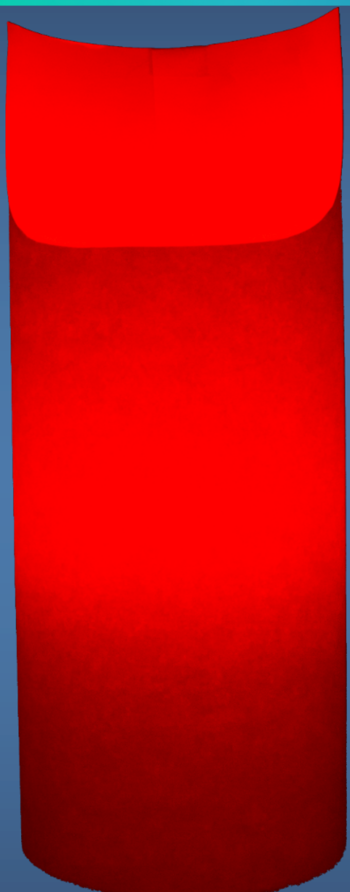
White light range

6500 K 5000 K 4000 K 3000 K 2700 K

Cool **Warm**





Saturated, narrow-band red Peaking between 625 – 635 nm

Light at the eye: 100 lux

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Key Takeaways

- Light incident on the retinae is the primary synchronizer of circadian rhythms to our local position on Earth
- Exposure to high levels of light at night can disrupt the circadian system and is associated with several major diseases, depression, and sleep problems, among other ailments
- Light can provide an alerting effect, similar to a cup of coffee, at any time of day or night
- The human circadian system is maximally sensitive to short-wavelength ("blue") light, which makes it ideal for stimulating the circadian system early in the day
- Long-wavelength ("red") light can promote alertness without disrupting the sleep and the circadian system generally

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  - LEDVANCE
  - OSRAM
  - USAI Lighting

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