2014 DOE SOLID-STATE LIGHTING MARKET DEVELOPMENT WORKSHOP

Detroit, MI

November 12, 2014

Tuning the Spectrum: Light, Health & the Pursuit of Happiness

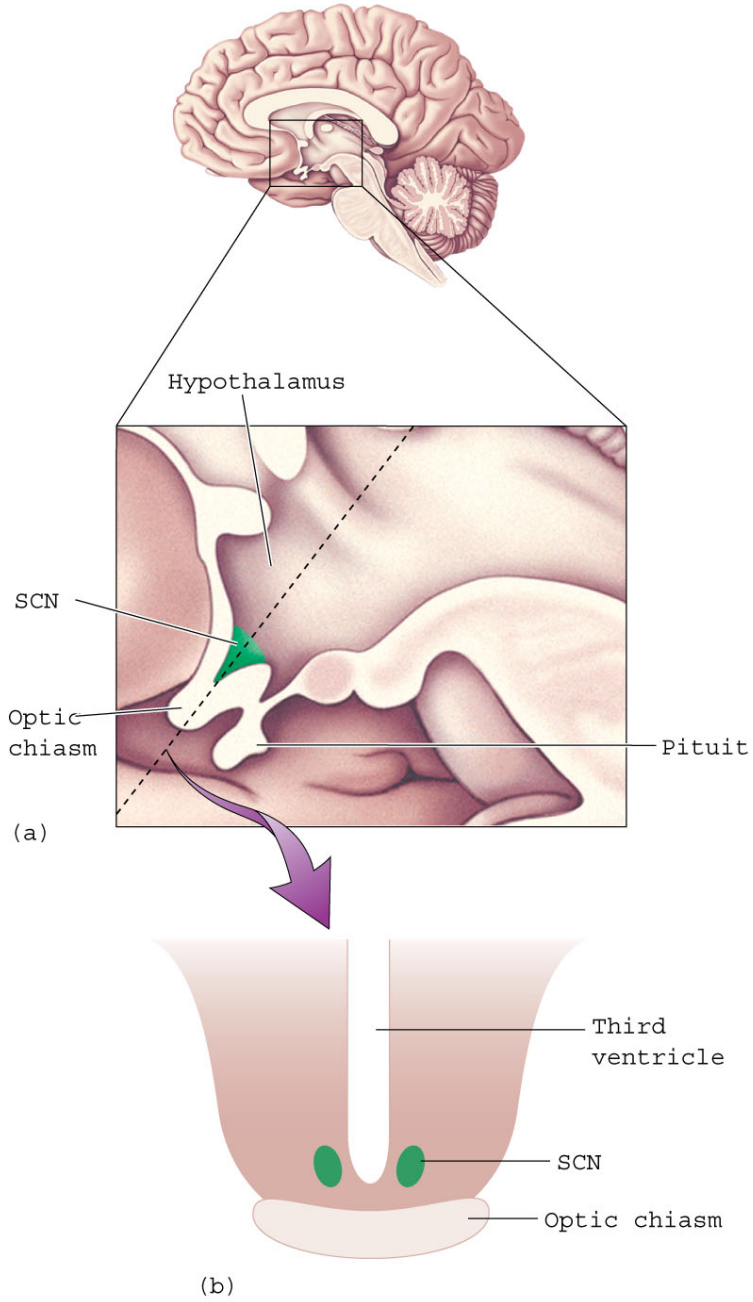
Steven W. Lockley, Ph.D.

Neuroscientist, Brigham and Women's Hospital, Boston

Associate Professor of Medicine, Harvard Medical School, Boston

Professor, Monash University, Melbourne

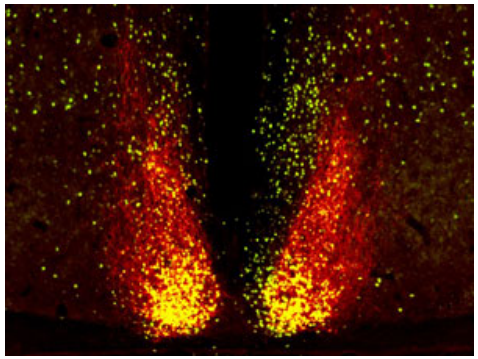
slockley@hms.harvard.edu



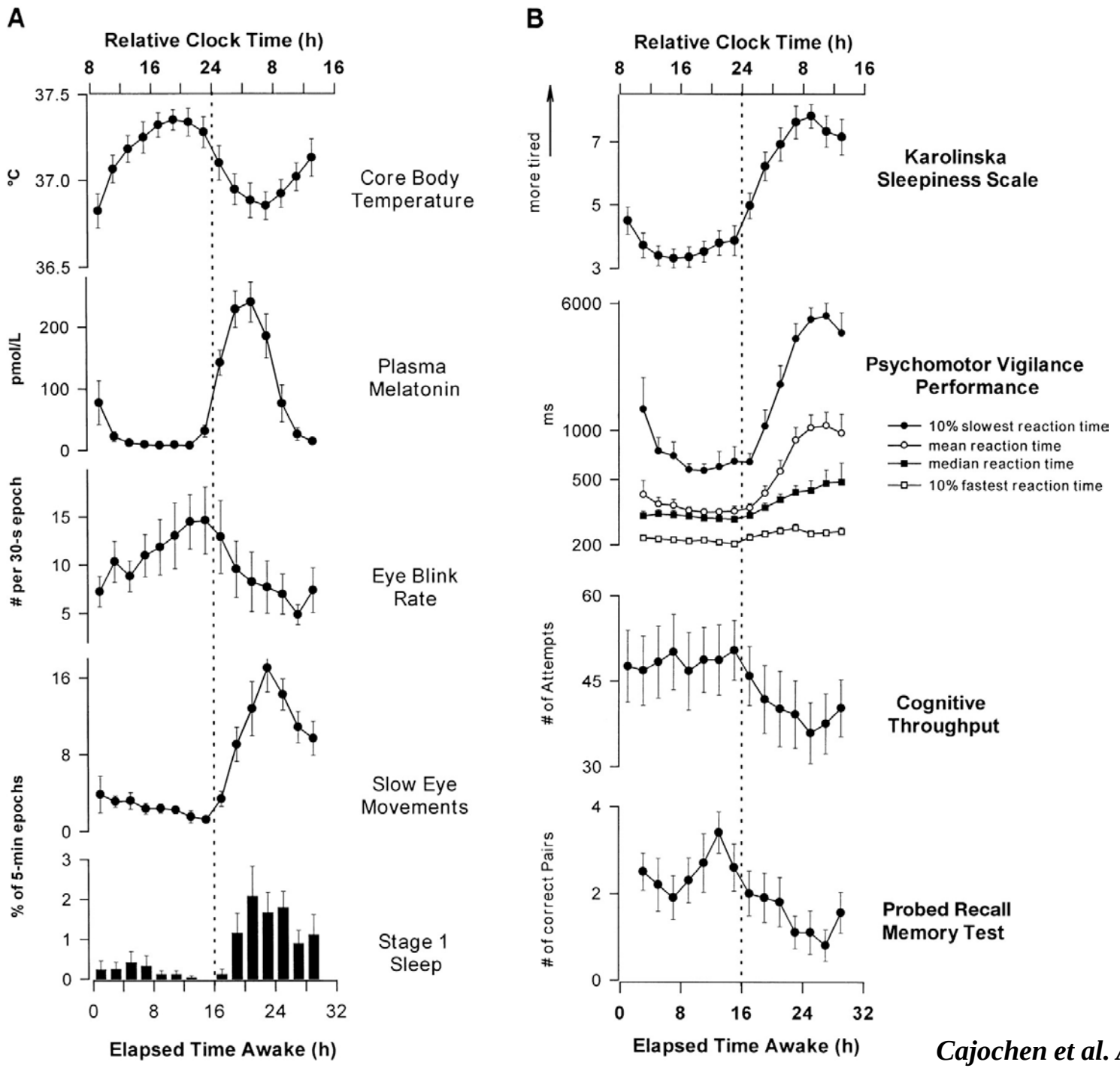
http://www.bioon.com/book/biology/whole/html/

The ‘body clock’ or circadian pacemaker is situated in suprachiasmatic nucleus (SCN) of hypothalamus

It controls the timing of most 24-hour behavioral and physiological rhythms including the sleep-wake cycle, alertness and performance rhythms, hormone production, temperature regulation, and metabolism.

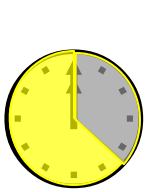


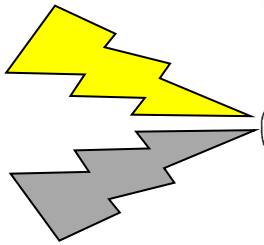
‘circadian’ - ‘about a day’

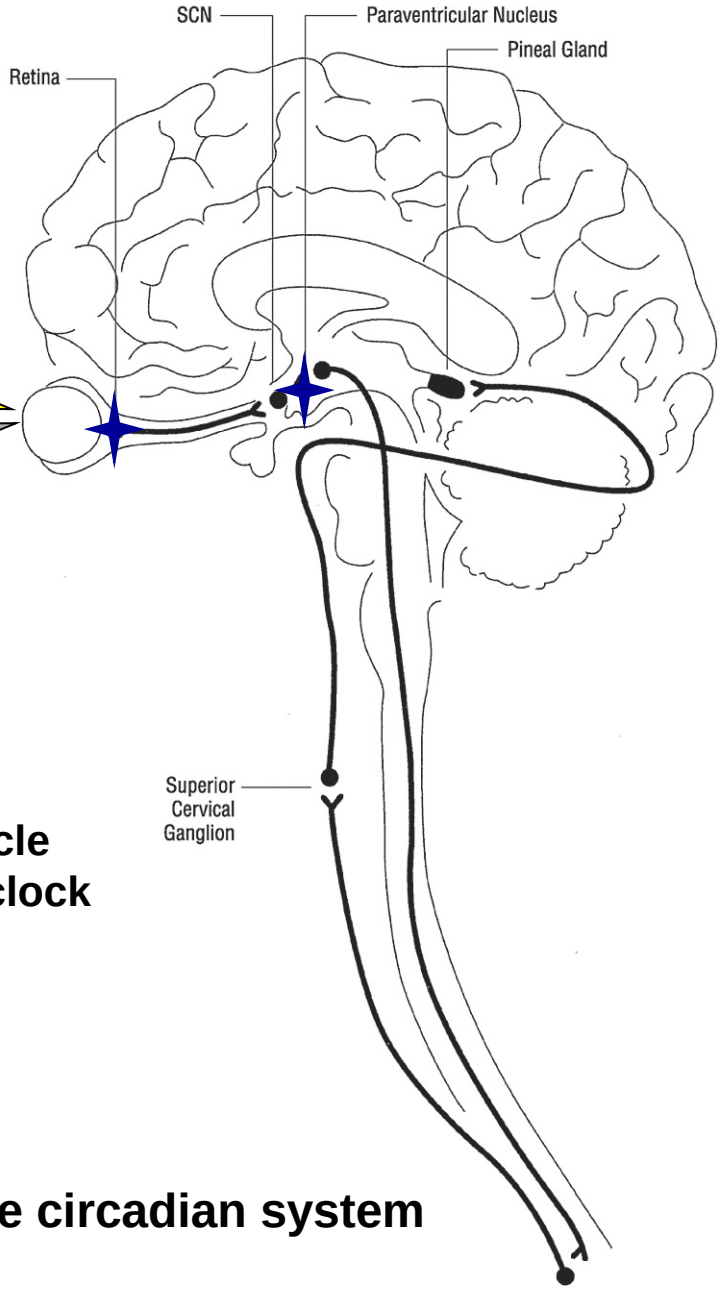


Cajochen et al. Am J Physiol 1999

Daily 24-hour Light-dark cycle





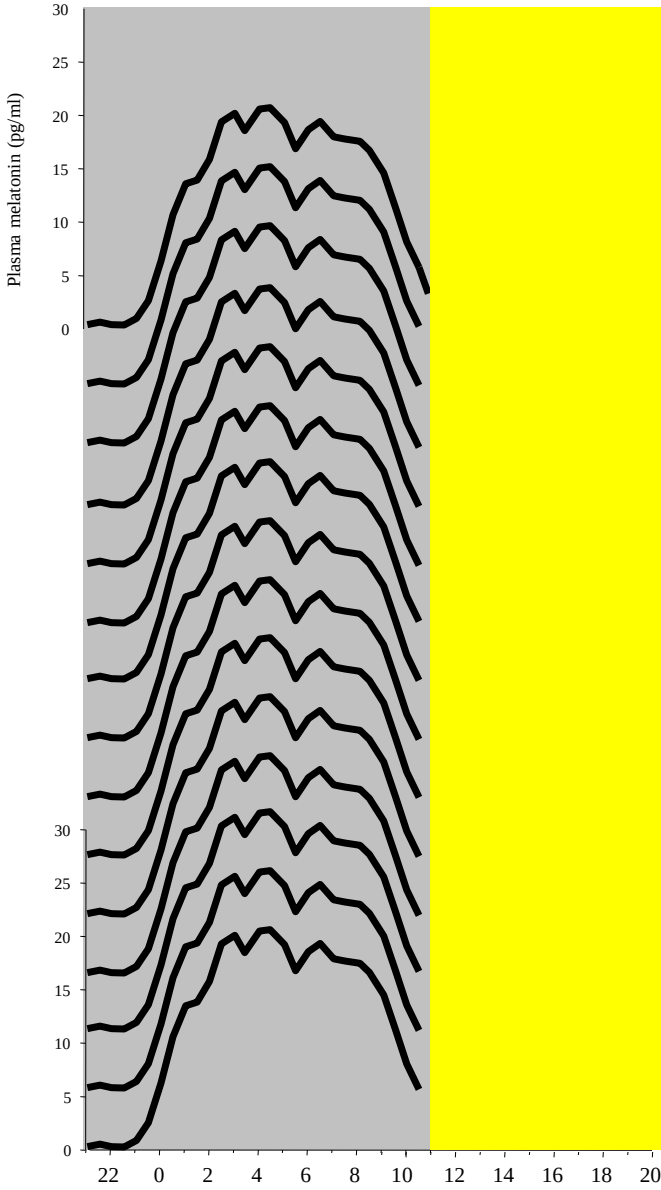


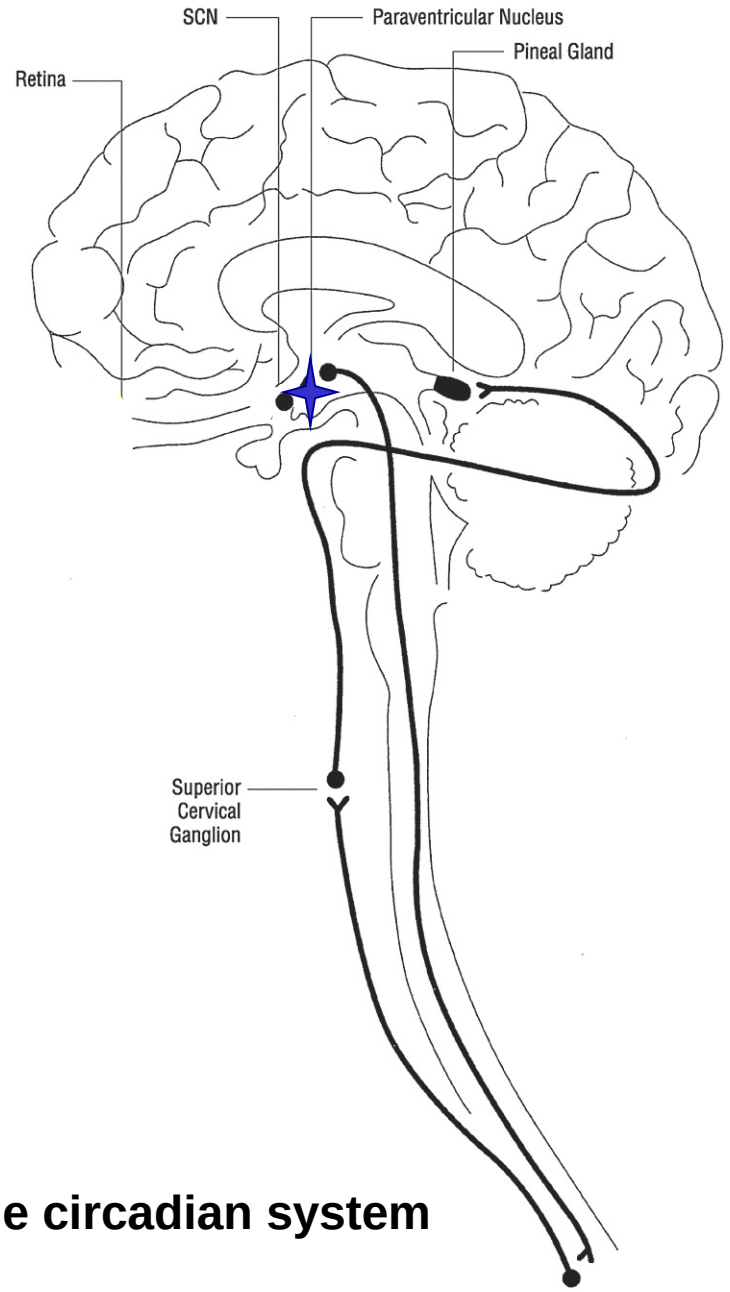
24-hour light-dark cycle resets the circadian clock on a daily basis

Neuroanatomy of the circadian system

Pineal melatonin response

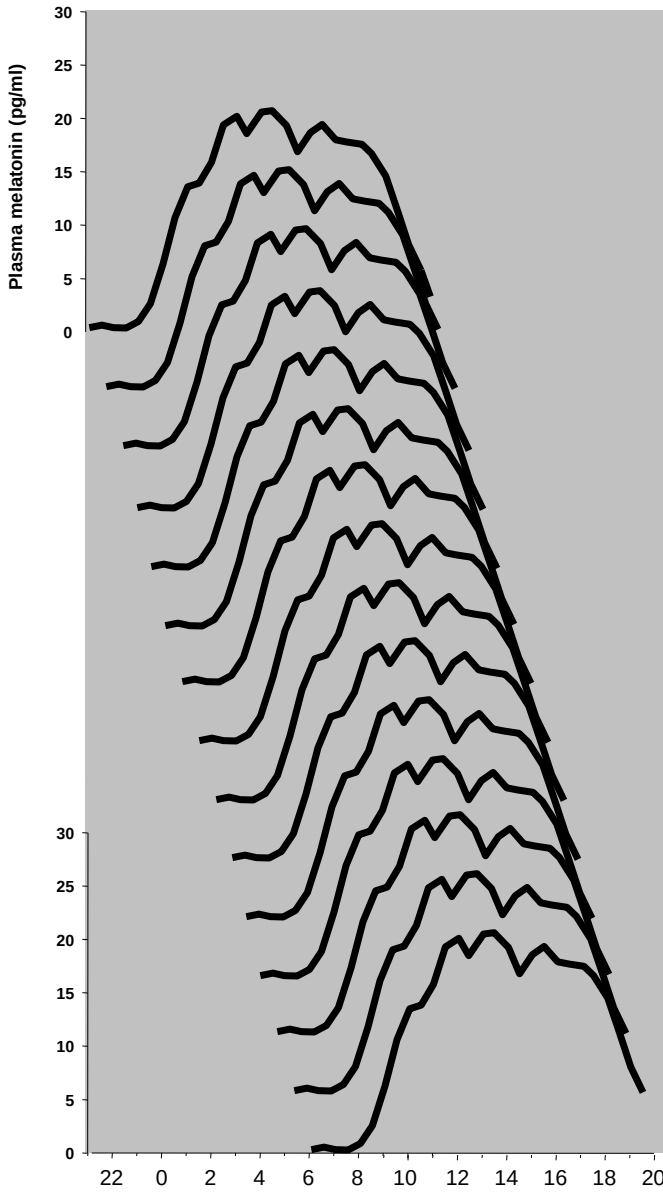
Entrainment by light





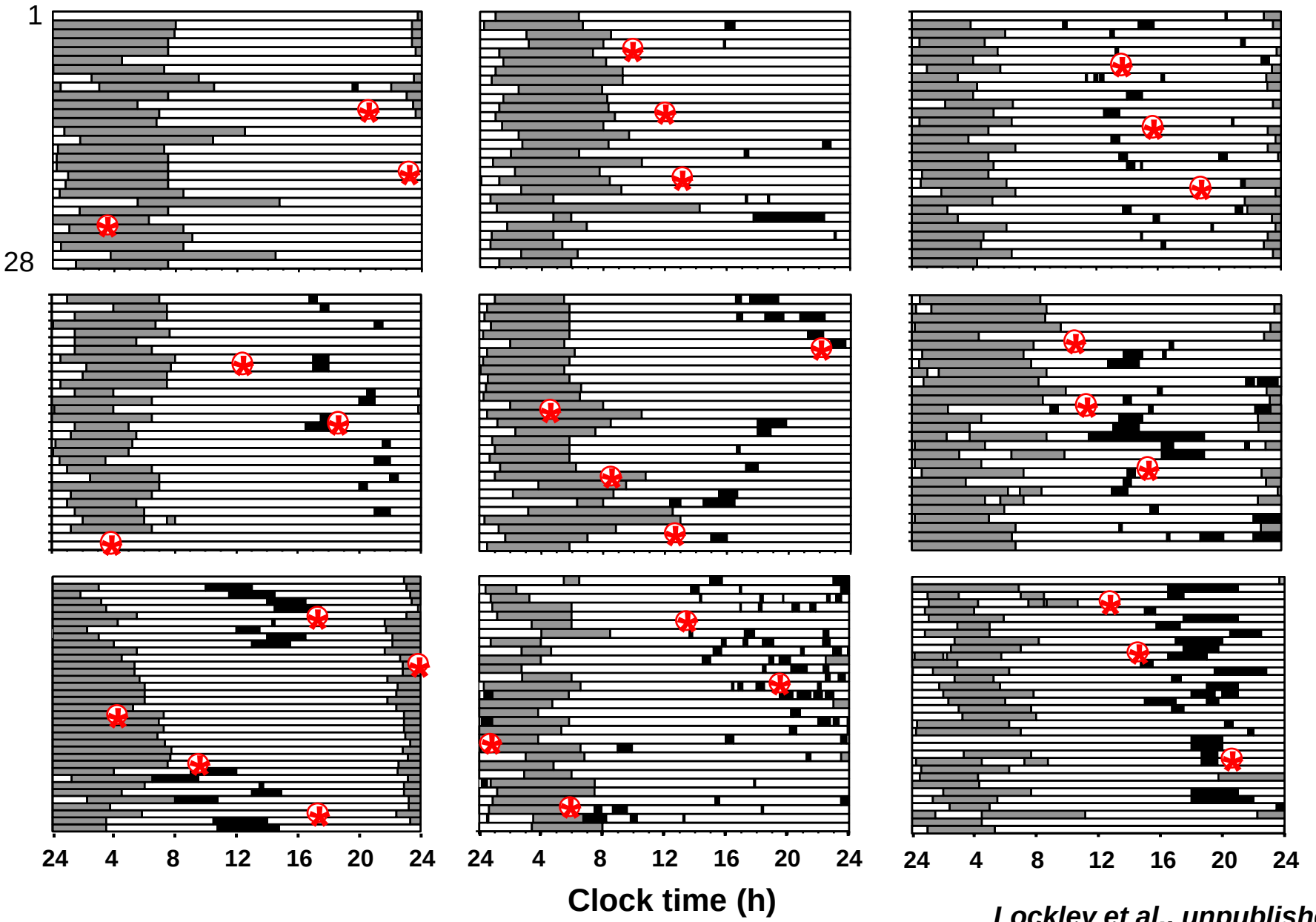
Pineal melatonin response

Total blindness



Neuroanatomy of the circadian system

Non-24-hour sleep-wake disorder in the blind (n = 9)



Lockley et al., unpublished

Non-Visual Photoreception

Multiple neuroendocrine and neurobehavioral responses

- Light is the most powerful time cue for resetting the circadian pacemaker and ensuring correct synchronization of the internal clock with the environment

- Failure to entrain the circadian pacemaker results in sleep disorders, fatigue, performance problems, hormone and metabolic disorders

- Common examples include the circadian desynchronization caused by shift-work, jet-lag and Advanced- and Delayed Sleep Phase Disorder

Non-Visual Photoreception

Multiple neuroendocrine and neurobehavioral responses

- Circadian entrainment
- Circadian phase shifting

- Melatonin suppression
- Subjective alertness / EEG
- Neurobehavioral performance
- Cortisol stimulation
- Cardio- and thermoregulation
- Pupillary reflex
- Stimulation of clock gene expression

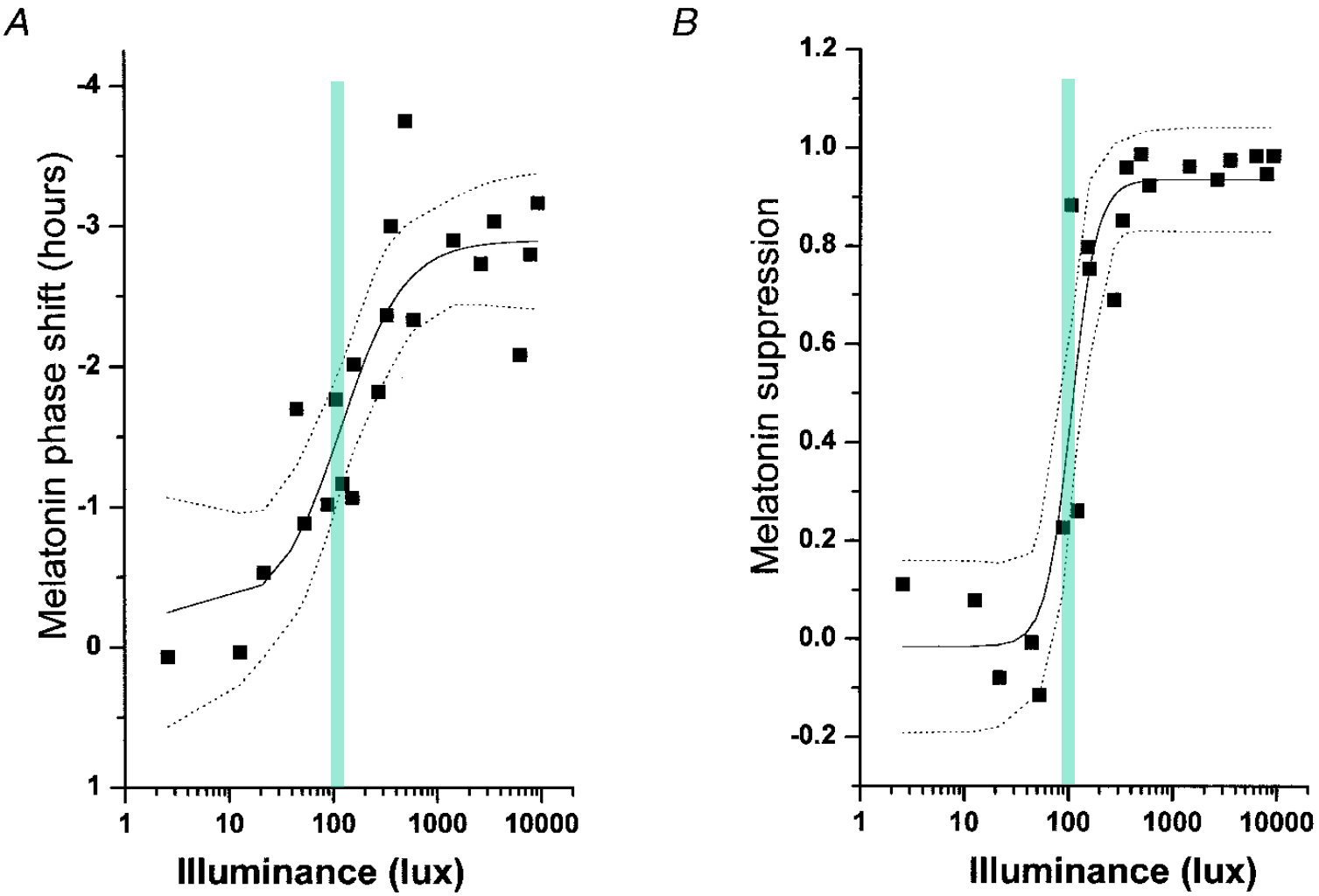
- Photoperiodism and seasonality
- Solar navigation

Non-Visual Photoreception

Properties of light affecting circadian photoreception

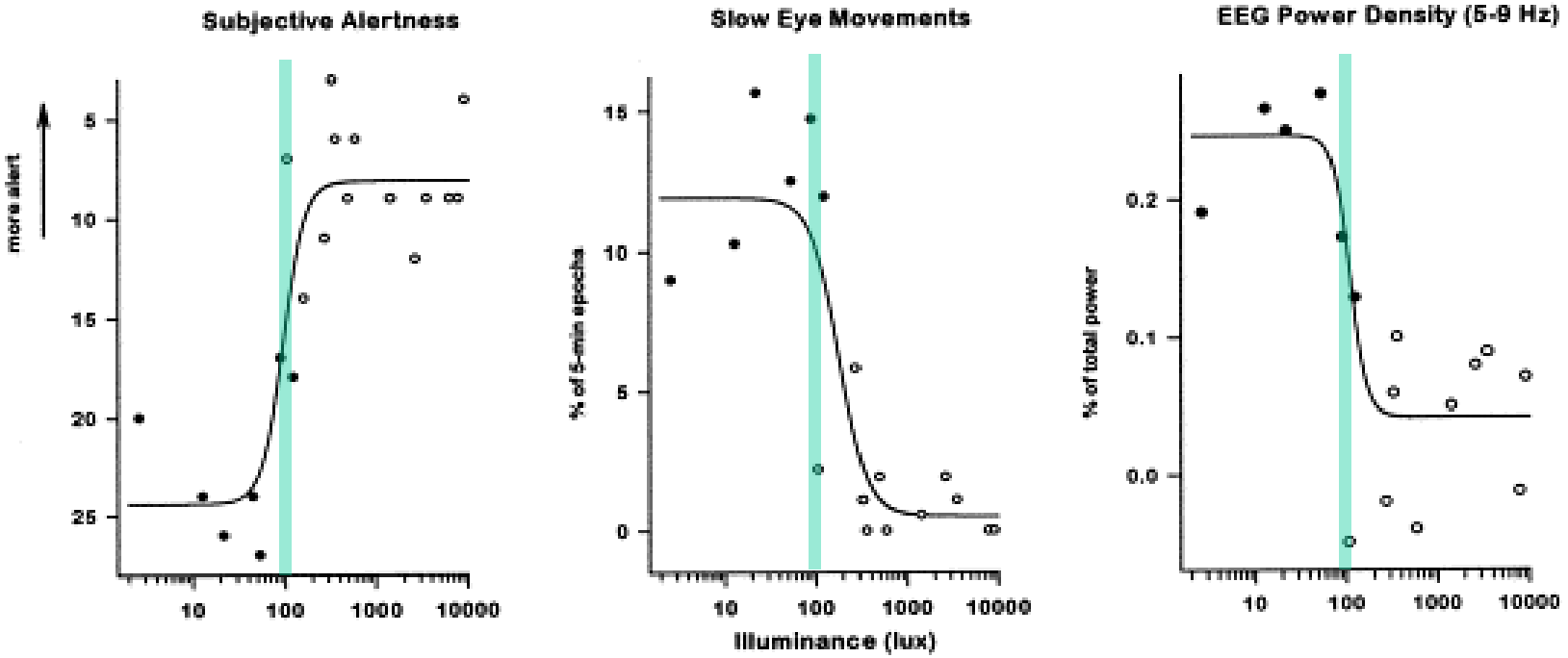
- **Intensity**
- **Timing**
- **Pattern**
- **Light history**
- **Wavelength**

Phase-shifting and melatonin suppressive effects of night-time white light exposure are dose-dependent



Zeitzer et al. J Physiol 2000

Acute enhancement of alertness by 6.5 h of night-time white light exposure is dose-dependent



Cajochen et al. Behav Brain Res 2000

Non-Visual Photoreception

Properties of light affecting circadian photoreception

- Intensity
- Timing
- Pattern
- Light history
- Wavelength

Non-Visual Photoreception

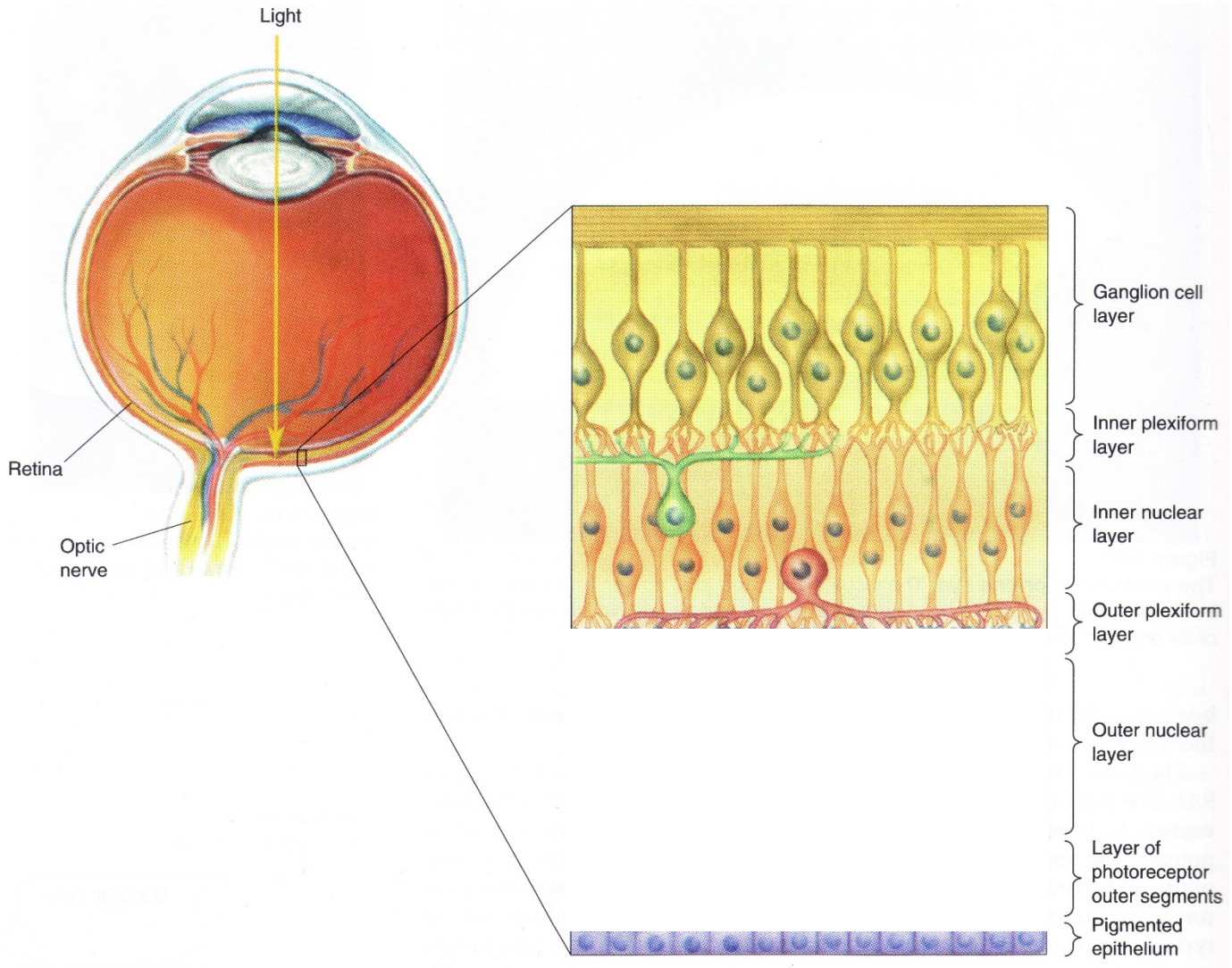
Multiple neuroendocrine and neurobehavioral responses

- Much like the ear has dual functions for audition and balance, the human eye has a dual role in detecting light for a range of behavioral and physiological responses separate and apart from sight

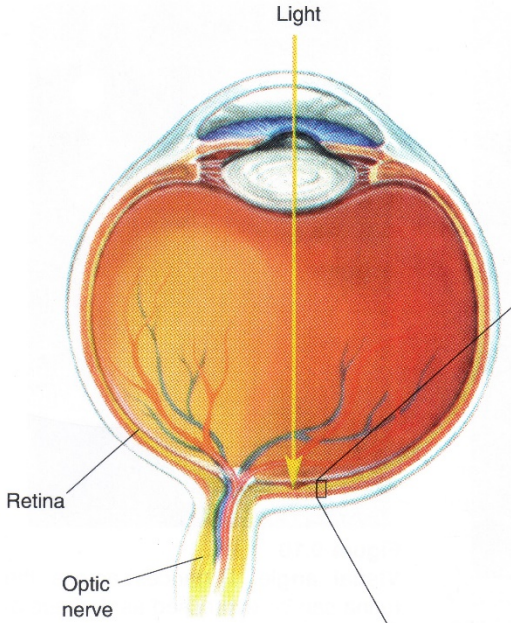
- These ‘non-visual’ effects of light are mediated by a novel non-rod, non-cone photoreceptor located in the ganglion cell layer of the eye

- These photosensitive ganglion cell contain a novel opsin, melanopsin, to detect light which is maximally sensitive to short-wavelength (blue) visible light (λ_{max} ~480 nm)

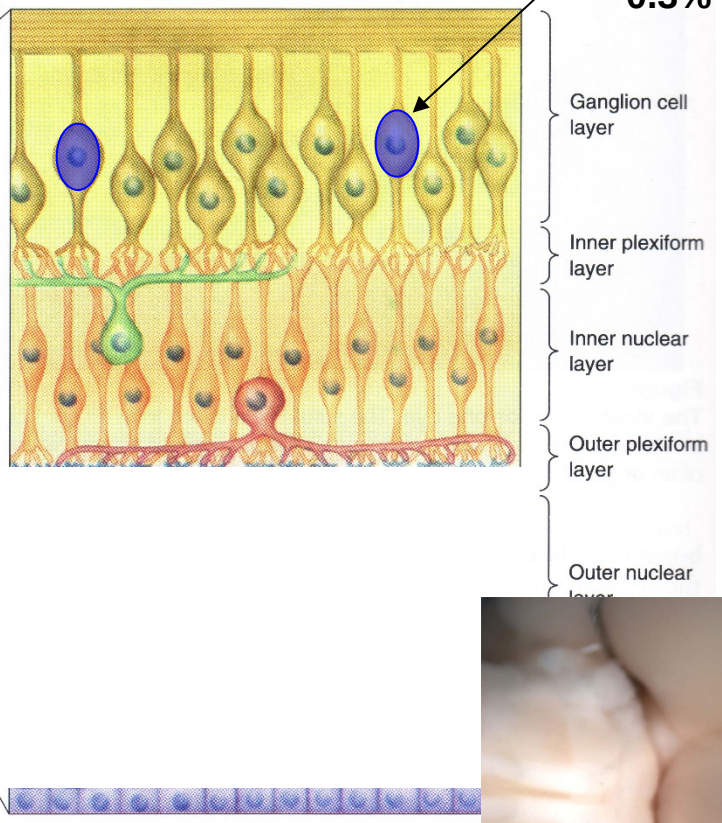
Laminar Organization of the Retina

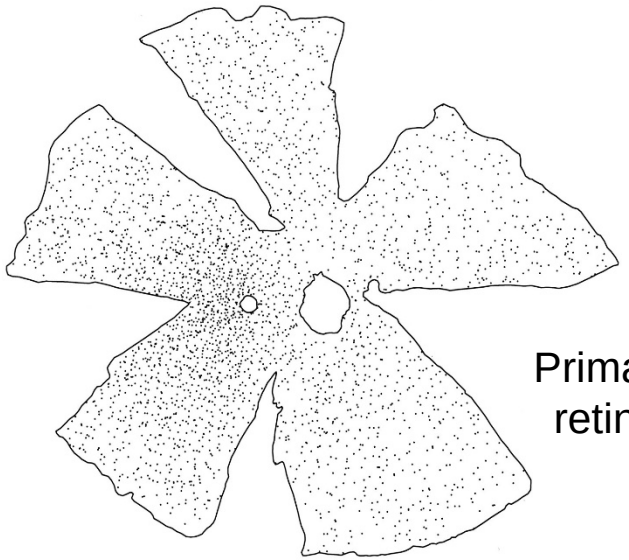


Laminar Organization of the Retina

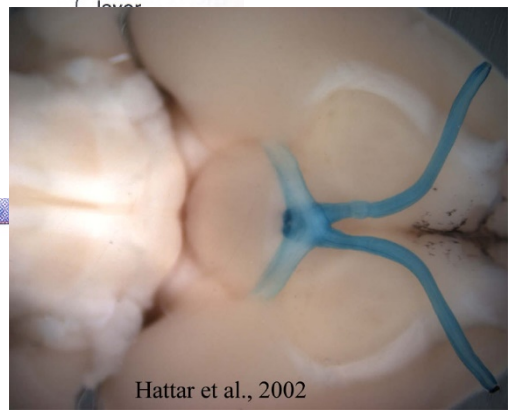


Melanopsin-containing intrinsically photosensitive retinal ganglion cells (ipRGCs) ~0.3% of all GCs





Primate retina



Dacey et al., Nature 2005

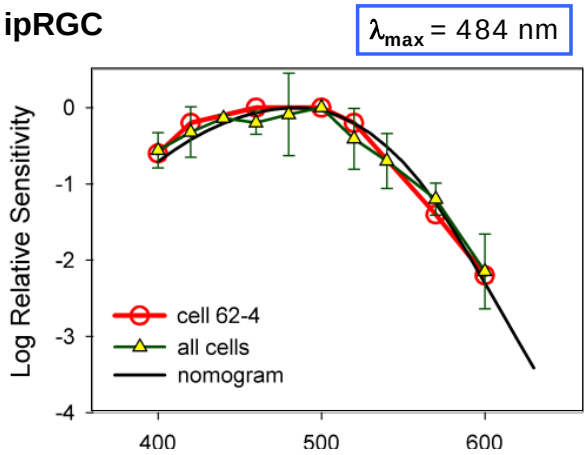
Hattar et al., Science 2002

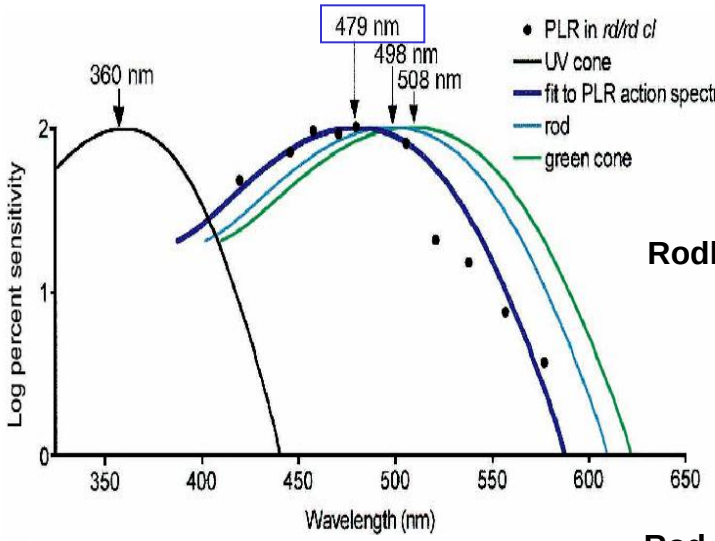
Action spectra demonstrate short-wavelength sensitivity (λ_{max} ≈480 nm) for non-rod, non-cone photoreceptor system

Melanopsin-containing intrinsically photosensitive retinal ganglion cells

Pupillary reflex to light in totally visually blind mice and human

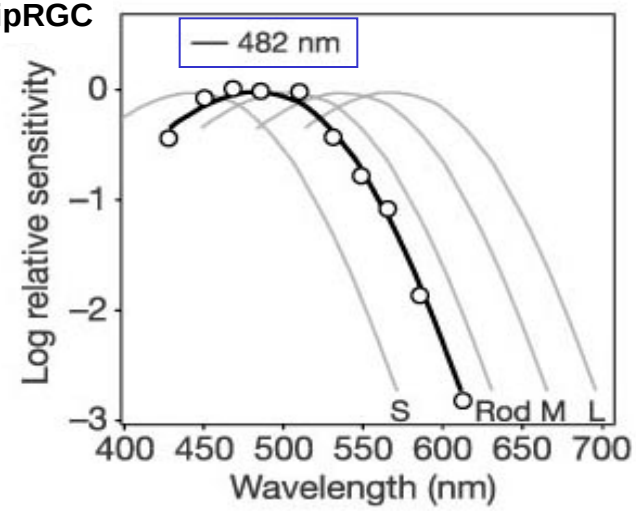
Rat ipRGC



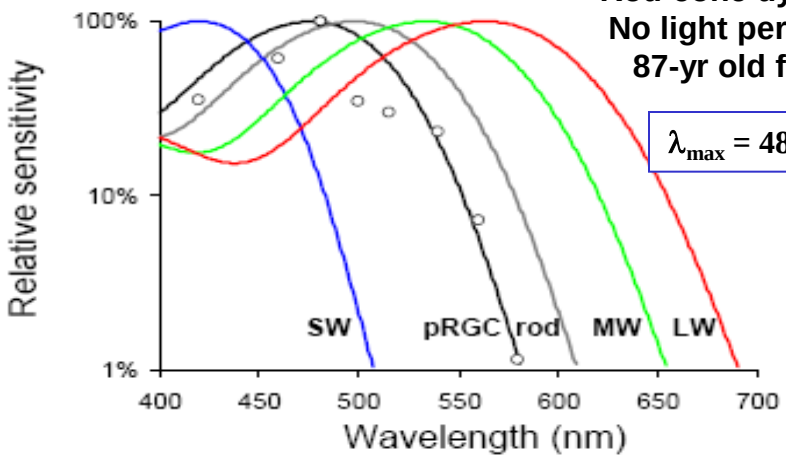


Rodless-coneless mouse

Primate ipRGC



Rod-cone dystrophy
No light perception
87-yr old female

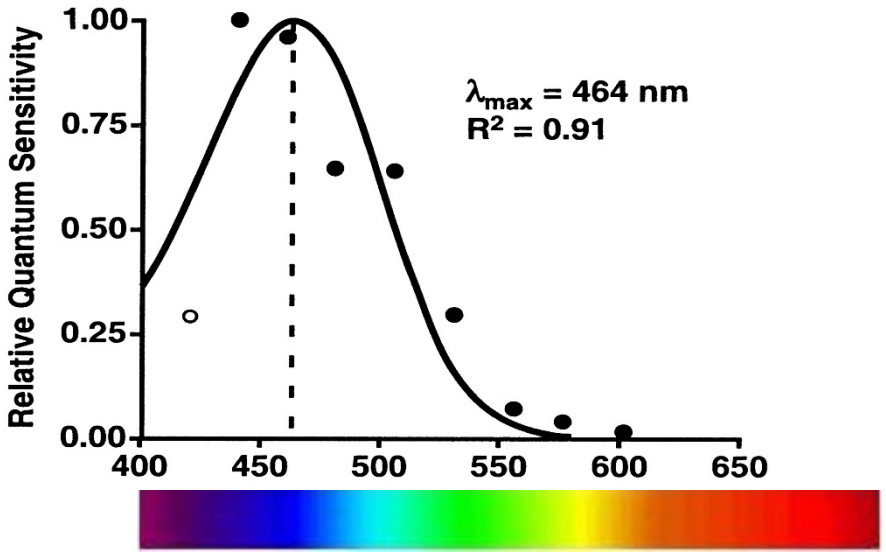


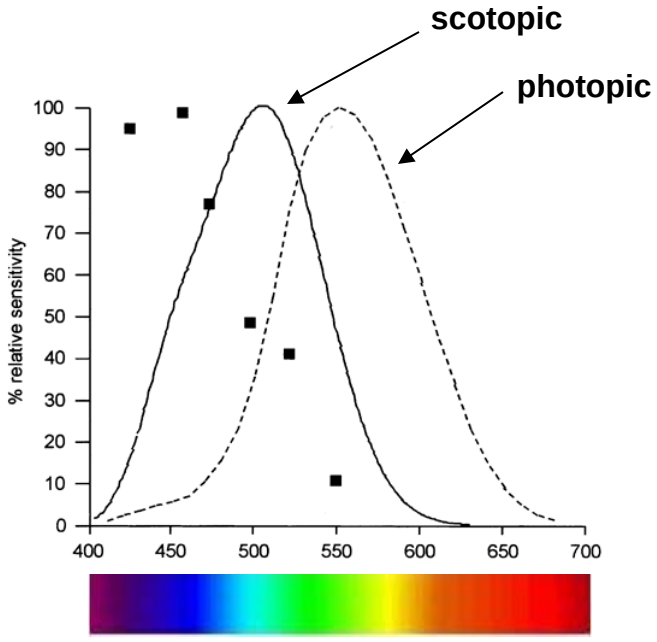
Berson et al. Science 2002; Lucas et al. Nature Neurosci 2001; Dacey et al. Nature 2005; Zaidi et al., Curr Biol 2007

Non-Visual Photoreception

What is the evidence for a novel photoreceptor system?

Action spectra for melatonin suppression peak at ~460 nm and do not match known rod and cone photoreceptors





λ_{max} = 446-477 nm
90 mins exposure

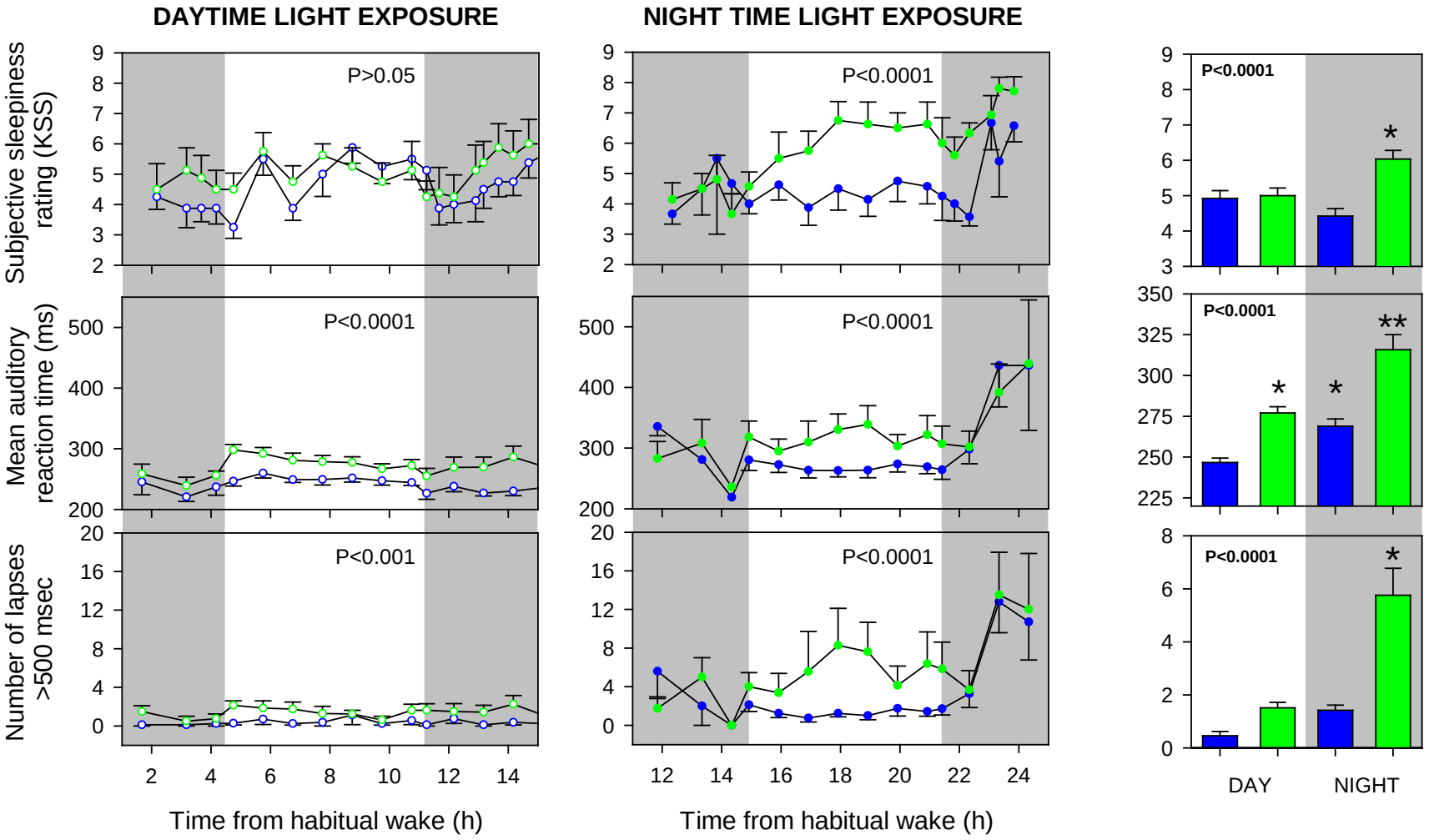
Brainard et al. J Neurosci 2001

λ_{max} = 459 nm
30 mins exposure

Thapan et al. J Physiol 2001

Short-wavelength sensitivity for the acute alerting effects of light

460 nm light is more effective at enhancing alertness and performance than 555 nm light during both night and day



Lockley et al., Sleep 2006; Rahman et al., Sleep 2014

Short-duration (<1') blue light preferentially activates the brain

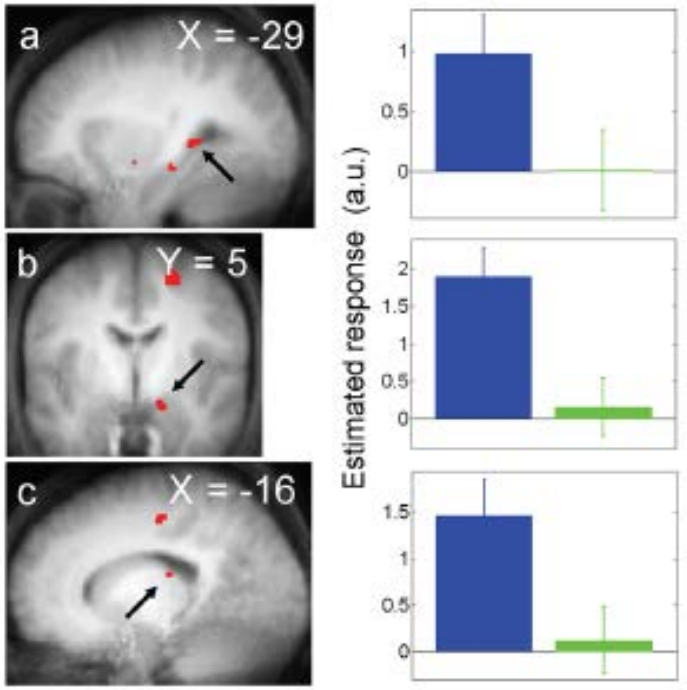
473 nm light increases activity in brain areas associated with alertness, performance and mood during the day compared to 430 nm or 527 nm light

Transient effects at light onset

Left Hippocampus
Memory

Right Amygdala
Emotion
Mood

Left thalamus



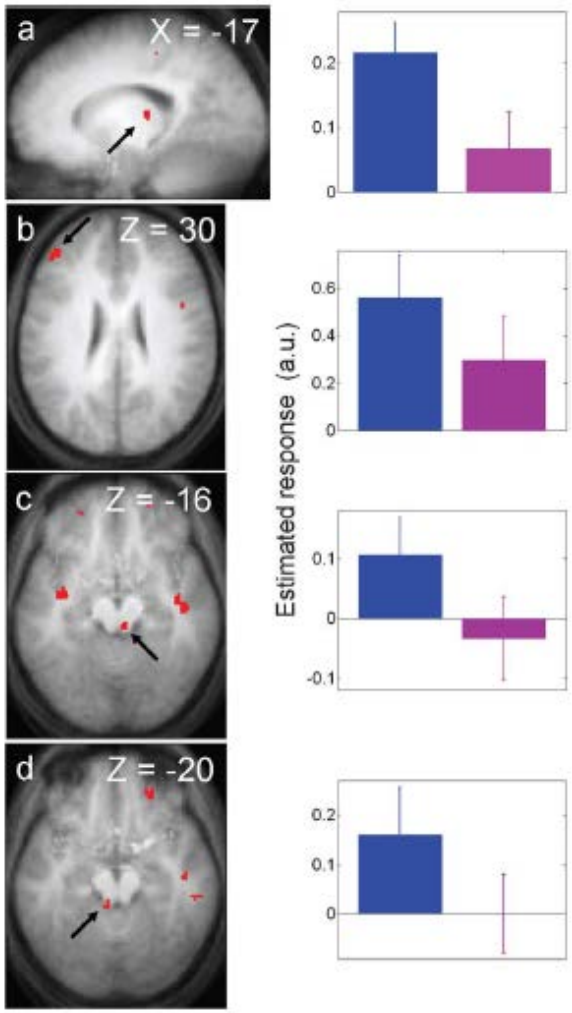
Sustained effects during 35s 2-back task

Left Thalamus
Alertness
Cognition
Memory

Left middle frontal gyrus
Working memory

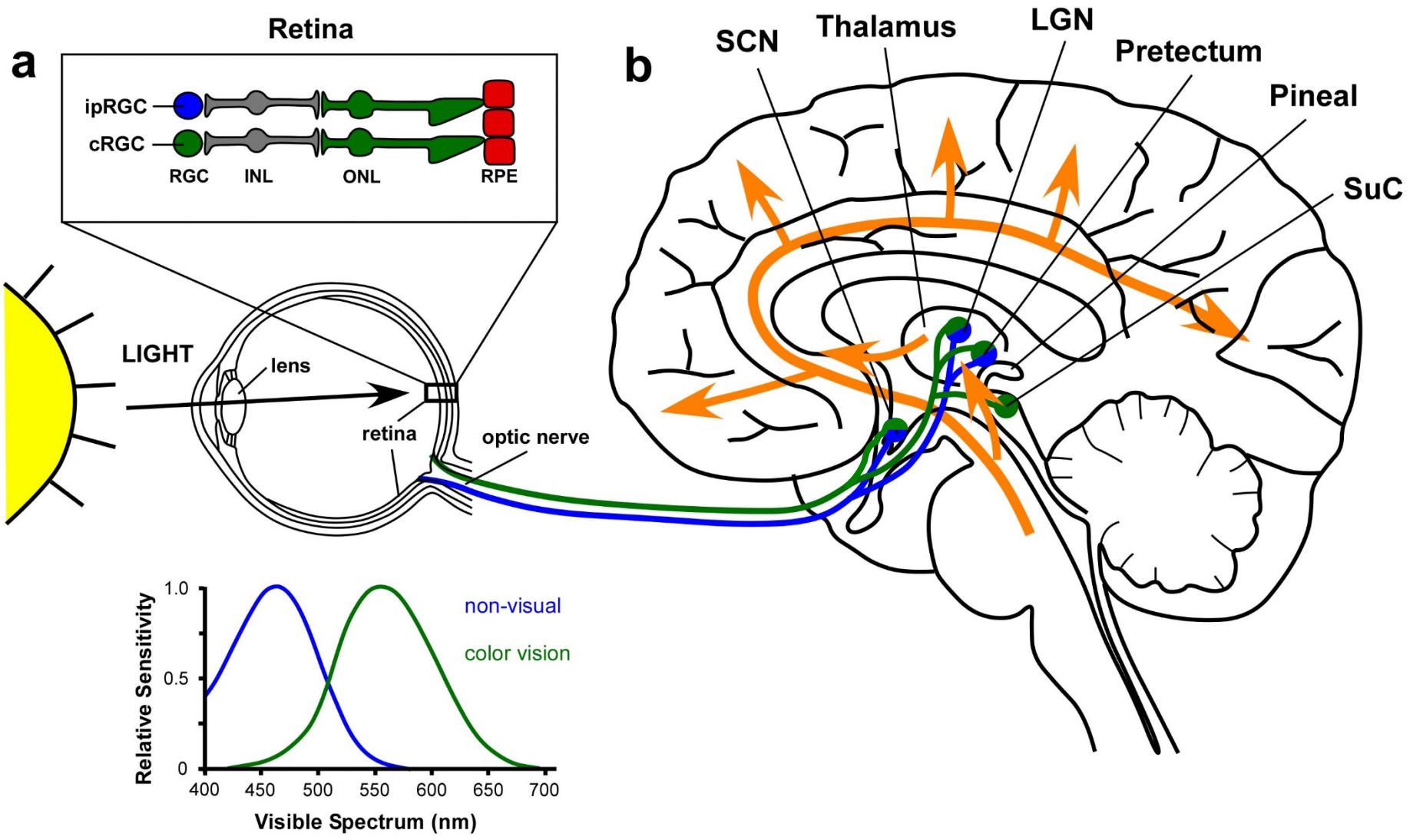
Right and Left brainstem
Arousal
Cognition
Executive function

Locus Coeruleus?
NE; arousal



fMRI– Functional Magnetic Resonance Imaging

Vandewalle et al., PLoS One 2007



ipRGCs → Non-visual brain areas

cRGCs → Visual brain areas

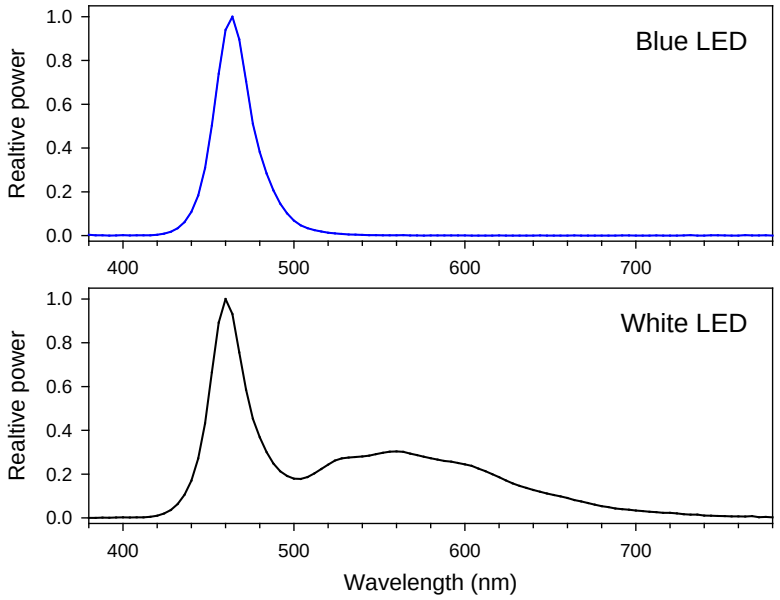
? → Ascending Arousal System, Cortical Activation, Increased Alertness

Adapted from Lockley & Gooley, Curr Biol 2006

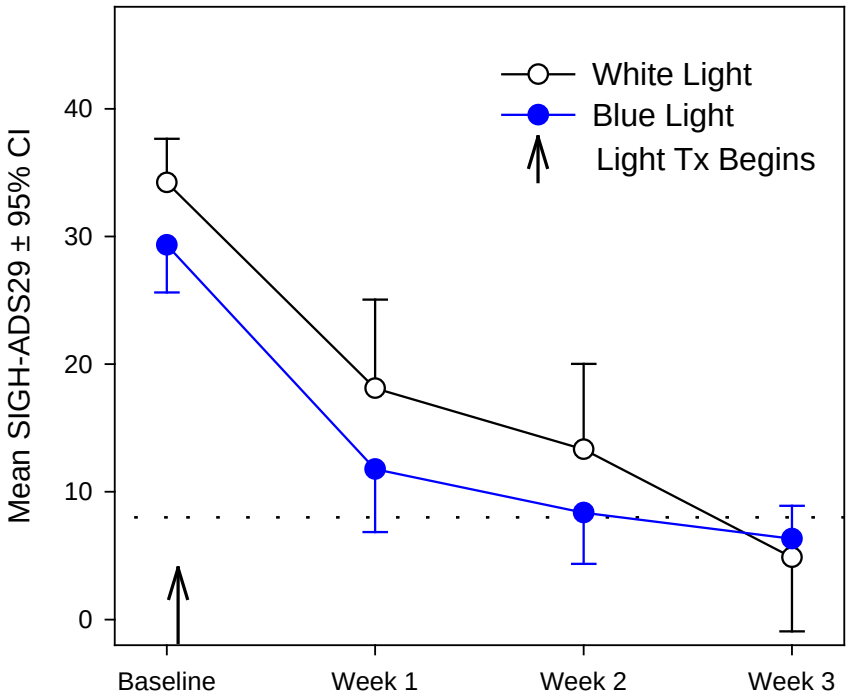
Light Applications - Clinical

- **Treatment of circadian rhythm sleep disorders**
  - Advanced-, Delayed-, Non-24-hour Sleep Disorders
  - Shift-work Disorder, Jet-lag
  - Sleep timing changes due to adolescence and aging
- **Entrainment to non-24-hour ‘days’**
  - Space flight and bases, Submariners, Antarctica
- **Treatment of affective disorders**
  - Seasonal Affective Disorder
  - Dementia
  - General mood, non-seasonal depression
- **Improving sleep patterns and stability**
  - Hospital patients
  - Care home patients
  - Psychiatric inpatients
  - Child and adolescent sleep

Treatment of SAD



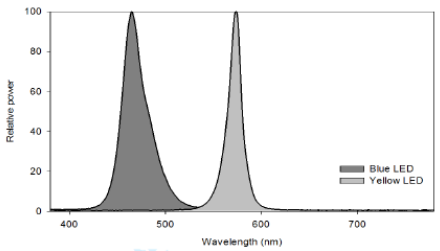
Device	Spectral characteristics	Irradiance ($\mu W/cm^2$)	Illuminance (Lux)	Photon density (photons/cm^2/s) 380-780 nm	Photon density (photons/cm^2/s) 424-532 nm
Blue goLITE	Narrow bandwidth λ_{max} = 464 nm	144	98	3.38×10^{14}	3.35×10^{14}
White goLITE	Broad bandwidth λ_{max} = 460 nm	262	711	7.00×10^{14}	3.46×10^{14}



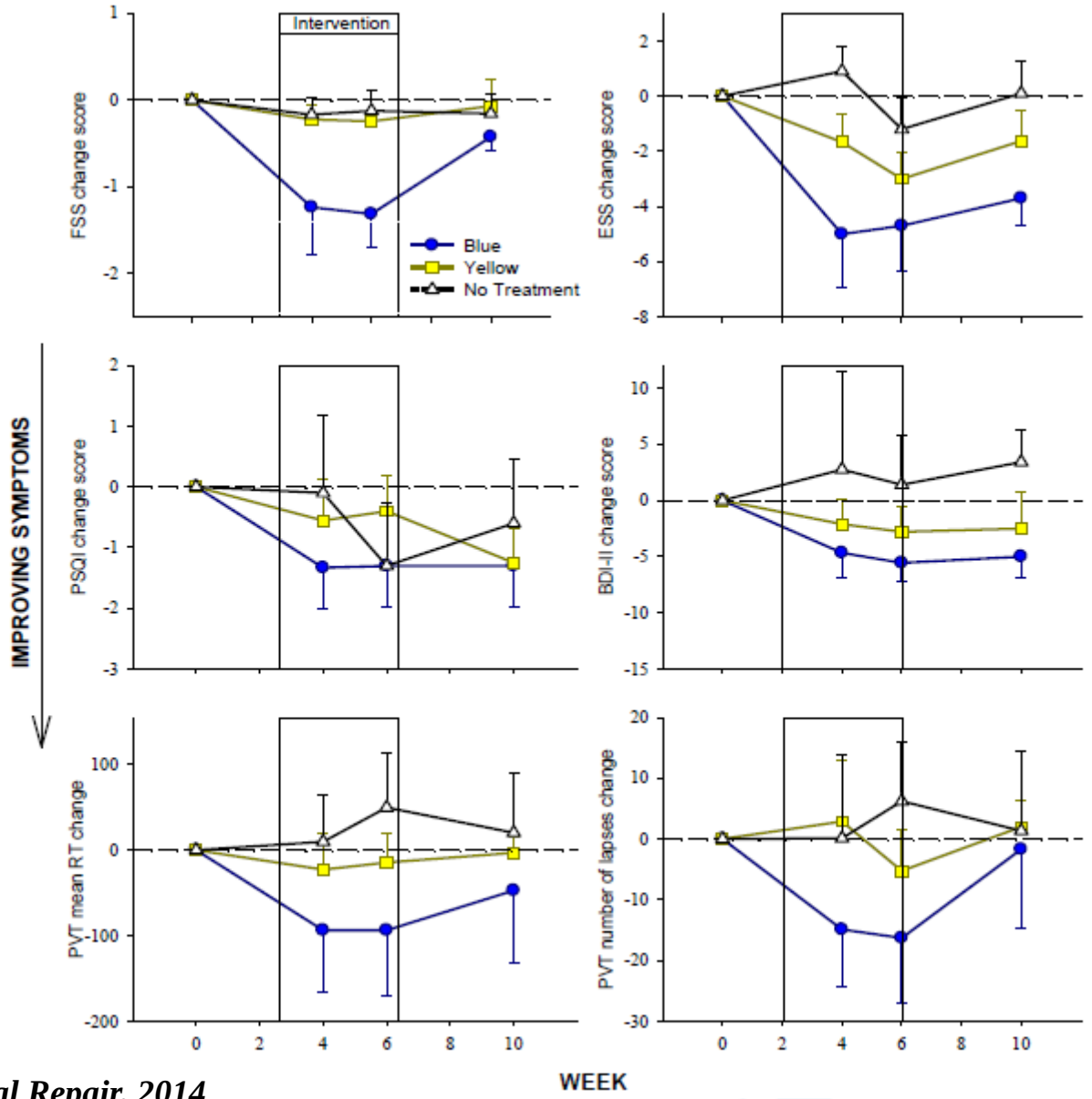
Blue light = 86% remission
White light = 78% remission

Anderson et al., Acta Psychiatr Scand, 2009

Treatment of fatigue in Traumatic Brain Injury

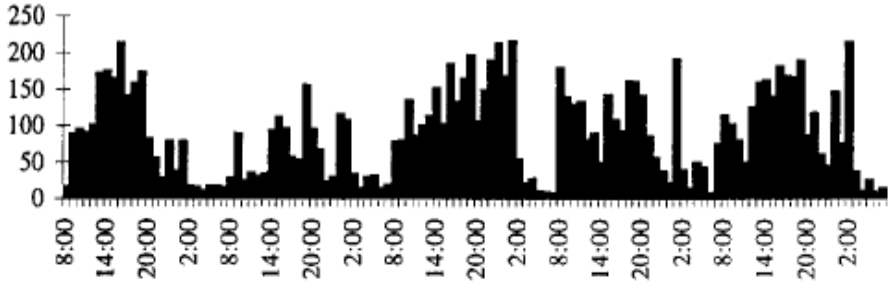


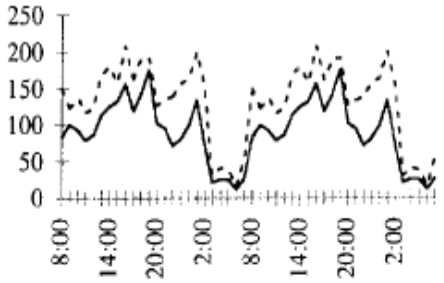
n = 10 blue
n = 10 yellow
n = 10 none



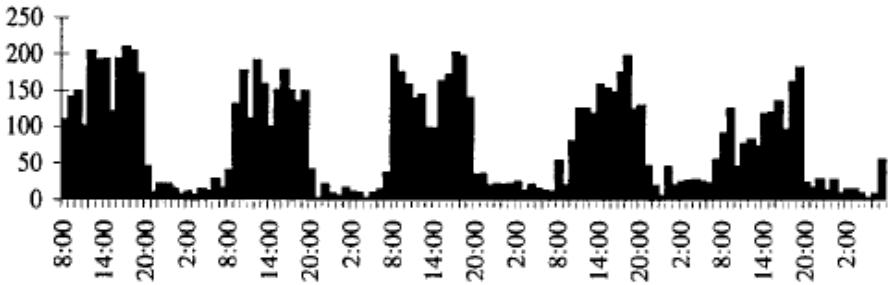
Sinclair et al., Neurorehabil Neural Repair, 2014

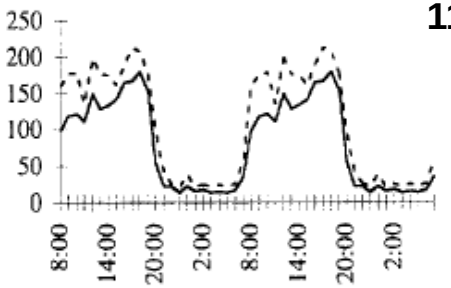
Light treatment for dementia





436 ± 90 lux





1136 ± 89 lux

JAMA®

Online article and related content current as of July 22, 2008.

Effect of Bright Light and Melatonin on Cognitive and Noncognitive Function in Elderly Residents of Group Care Facilities: A Randomized Controlled Trial

Rixt F. Riemersma-van der Lek; Dick F. Swaab; Jos Twisk; et al.

JAMA. 2008;299(22):2642-2655 (doi:10.1001/jama.299.22.2642)

Van Someren et al Biol Psychiat 1997

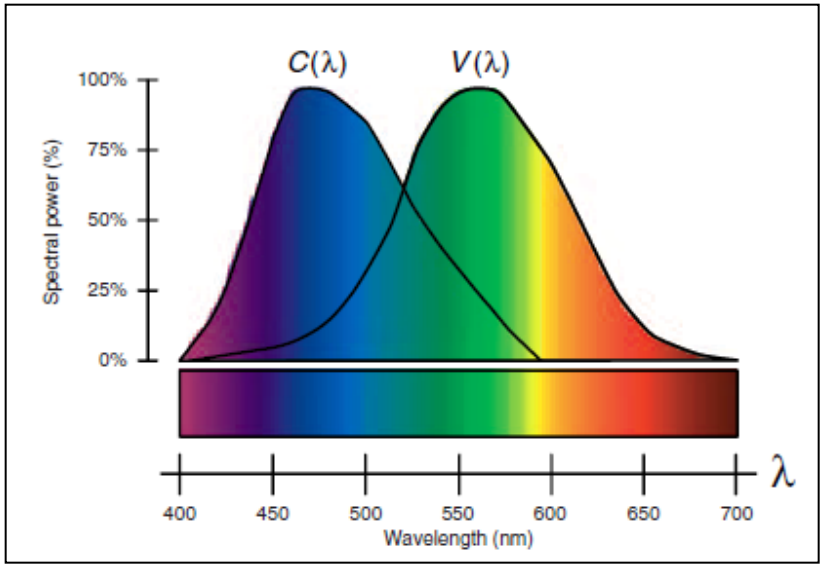
Light Applications - General

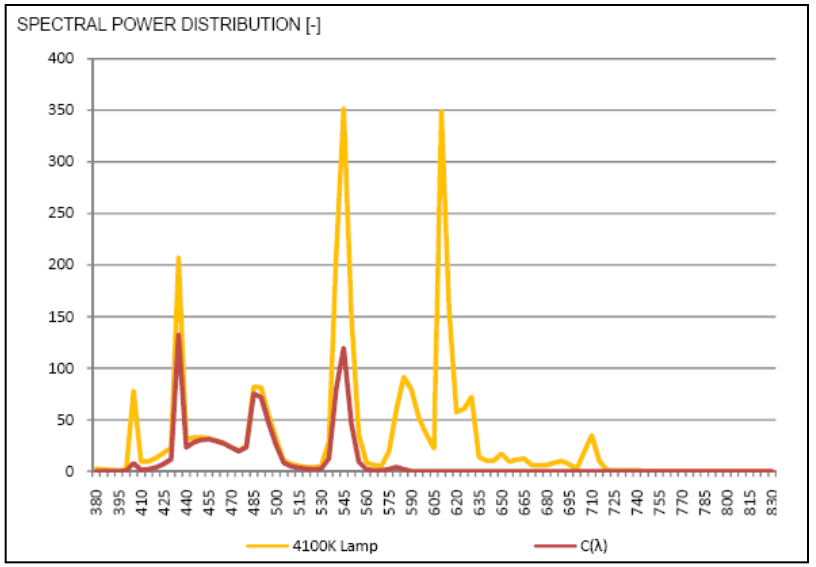
- **Non-pharmacological sleepiness countermeasure**
- **Safe, reversible, short-acting, inexpensive**
- **High levels of caffeine use illustrate need**

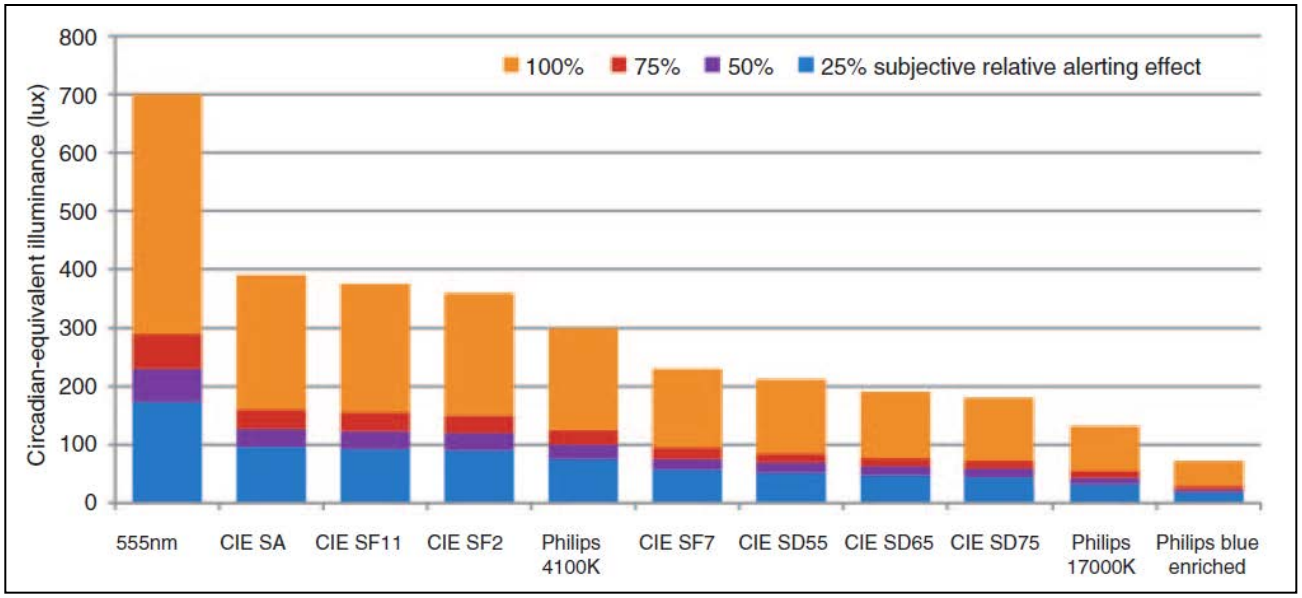
  - Offices, schools, colleges, factories, control rooms…
  - Military, security, transport (pilots, captains, truck/car/train drivers)
  - Safety-sensitive occupations (physicians, nurses, nuclear…)
  - Anywhere where enhanced alertness and safety is important

- **Challenge is to incorporate these benefits into design**
- **Lighting design to optimize visual and non-visual effects**
- **Flexible, ‘smart’ lighting systems with user interaction**

Modeling ‘circadian efficacy’ and architectural design for lighting



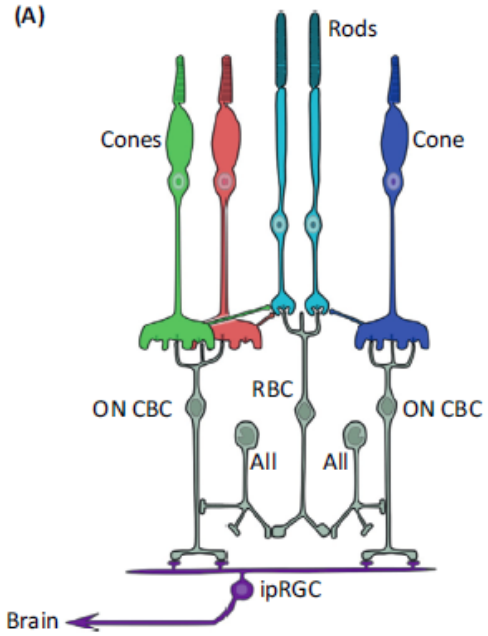


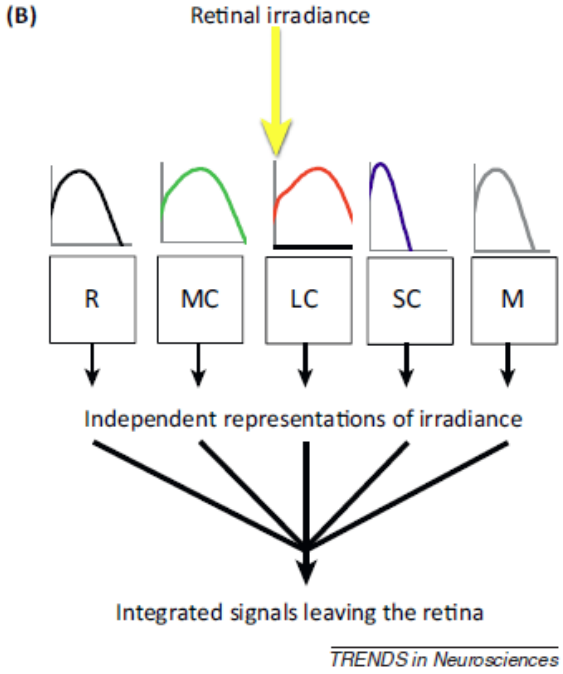


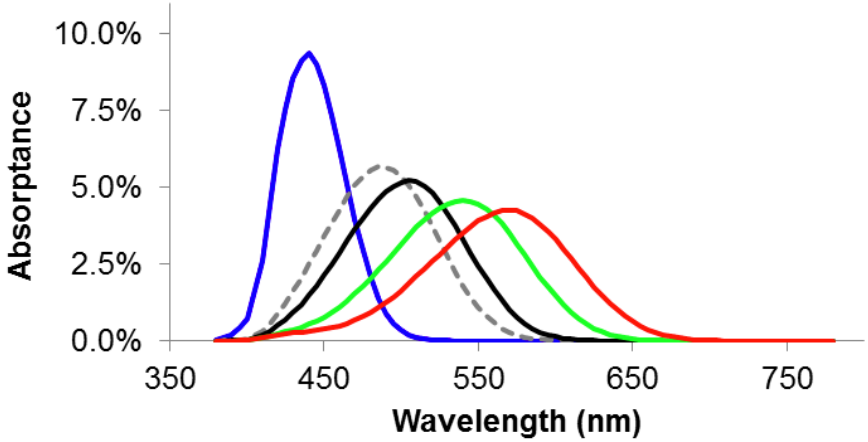
Pechacek et al LEUKOS 2008; Andersen et al., Lighting Res Technol 2012

Measuring and using light in the melanopsin age

RJ Lucas, S Peirson, D Berson, T Brown, H Cooper, CA Czeisler, MG Figueiro,
PD Gamlin, SW Lockley, JB O'Hagan, LLA Price, I Provencio, DJ Skene, GC Brainard







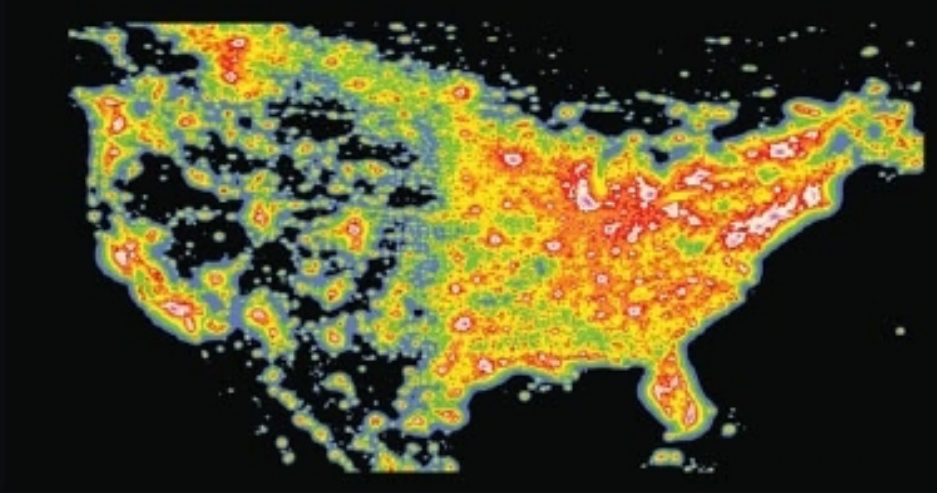
Free on-line tool (Excel) to permit quantification of irradiance by each of these 5 photoreceptors to try and standardize light measurement and description in human and animal studies

Lucas et al., Trends in Neurosci 2014

Late 1950s

Mid 1970s

1997



2025

Source: http://www.lightpollution.it/ © 2001 P. Cinzano, F. Falchi, C.D. Elvidge

SHORT SLEEP

=

LONG LIGHT

Light exposure AT NIGHT stimulates multiple circadian, hormonal and behavioral responses in humans

- **Phase-shifting the timing of the circadian pacemaker**
  - ↳ **DESYNCHRONIZES INTERNAL CIRCADIAN RHYTHMS AND DISRUPTS SLEEP AND HORMONE SIGNALS**
- **Suppression of pineal hormone melatonin at night**
  - ↳ **ABOLISHES BIOCHEMICAL SIGNAL OF DARKNESS**
- **Enhancement of alertness and neurobehavioral performance**
  - ↳ **ALERTS THE BRAIN AND DISRUPTS SLEEP**
- **Increase in heart rate and temperature at night**
  - ↳ **WIDESPREAD IMPACT ON PHYSIOLOGY, METABOLISM, AND GENE EXPRESSION BRAIN- AND BODY-WIDE**

Circadian Disruption and Cancer-Making the Connection

New York Academy of Sciences and
The Mushett Family Foundation
June 9, 2009

http://www.nyas.org/

Summary

- Blue light is an effective countermeasure for night-time performance decrements associated with circadian desynchrony and can restore performance to near-daytime levels in the laboratory
- Blue light is an effective countermeasure for day-time performance decrements in the laboratory
- Multiple healthcare applications show benefits of acute light therapy (SAD, fatigue) and stronger light-dark cycles (dementia, sleep-wake) with higher intensity or CCT light
- Office and shiftwork studies during the day and night show improvements in alertness and performance with higher CCT light
- Pilot school studies show benefits of higher CCT fluorescent and LED lighting on concentration and performance although mechanism (circadian and/or acute effects) unknown
- Ground studies underway testing the effects of a prototype LED polychromatic lighting system on pre-sleep sleepiness, post-wake alertness and circadian phase resetting for the Space Station

Key Questions

- **How do we incorporate these findings in real-world applications?**
- **How do lighting designers model the dual effects of light?**
- **What more information do designers need?**
- **How to approach ‘smart lighting’?**
- **Energy considerations?**
- **Safety considerations?**
- **Light pollution, role of darkness?**

www.understandingsleep.org

DIVISION OF
SLEEP MEDICINE
HARVARD MEDICAL SCHOOL

www.sleep.med.harvard.edu