Sleep, Circadian Rhythms & Environmental Light Pollution: Public Health Issues

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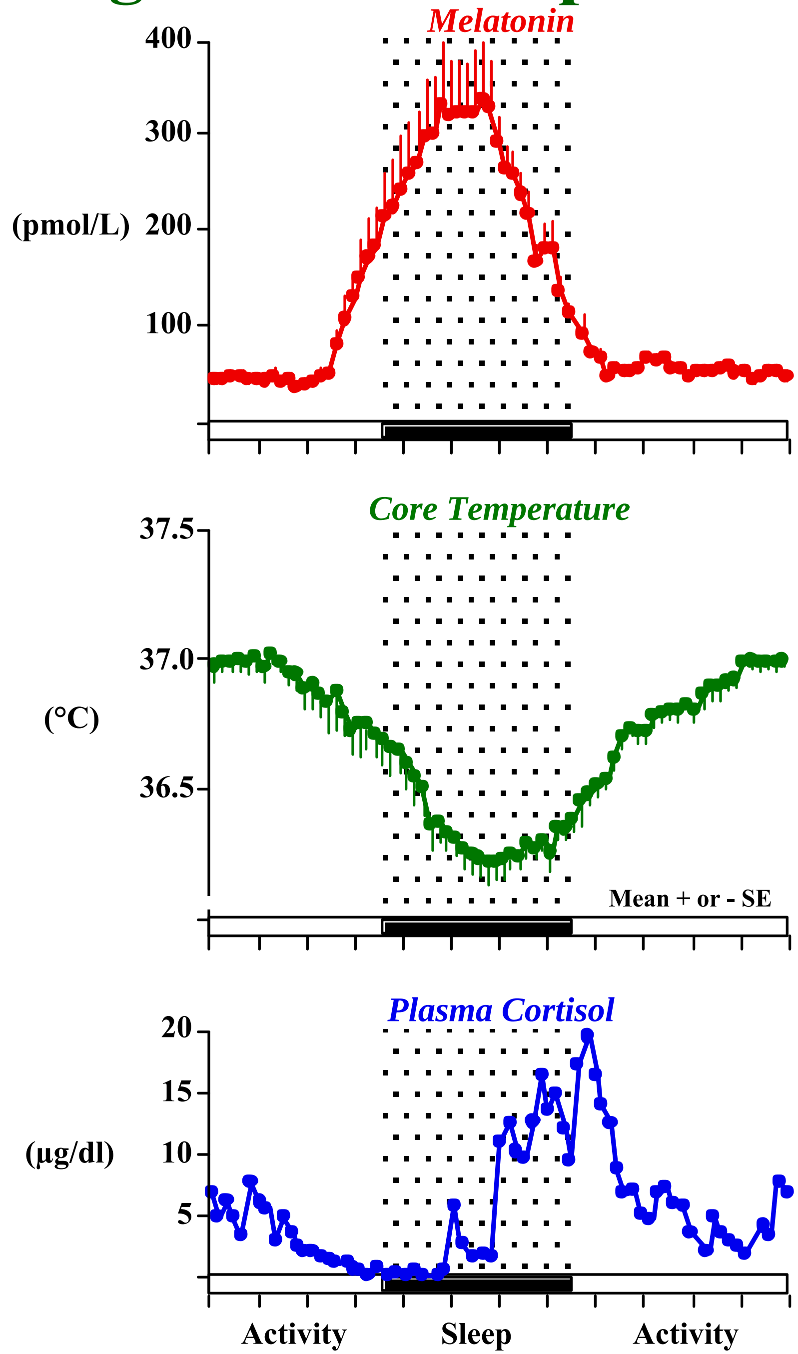
Homo sapiens: a diurnal species
We prefer a routine of activity during the light of day & sleep during the dark of night

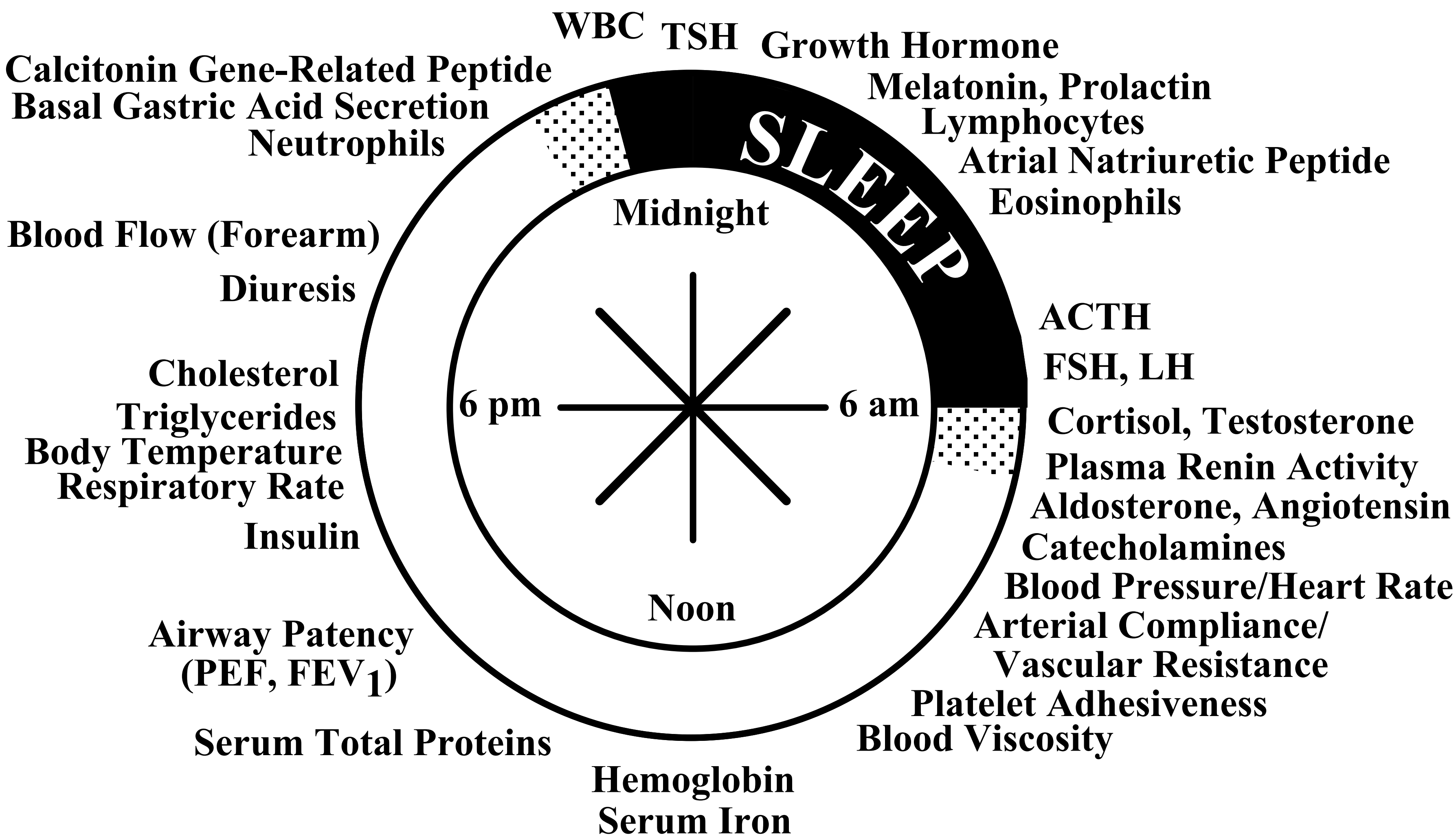
Human biology organized in time as circadian rhythms for optimal physical & mental performance during daytime activity & for rest, repair & rejuvenation during nighttime sleep

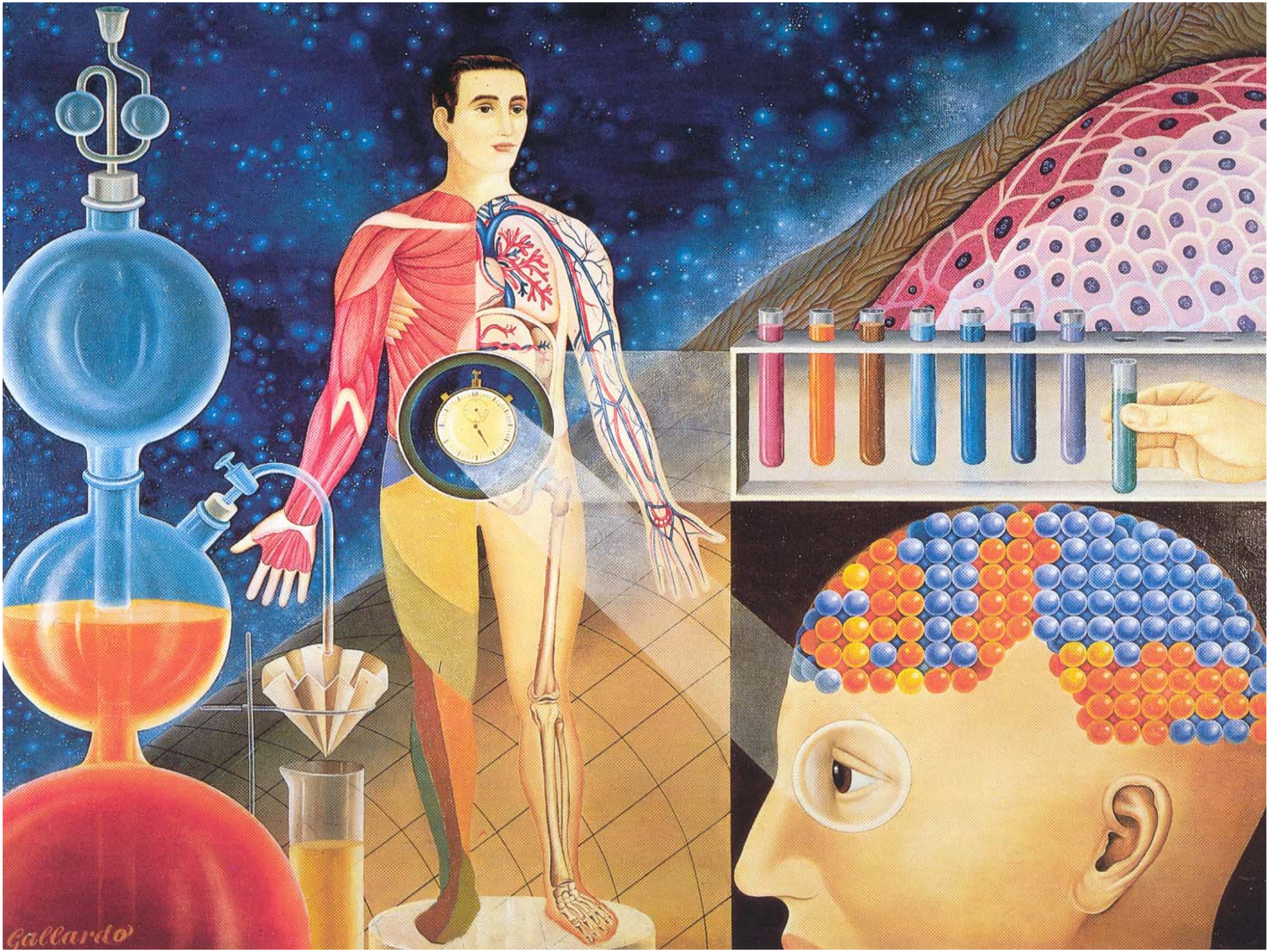
Circadian Stage Relationship of Human Rhythms

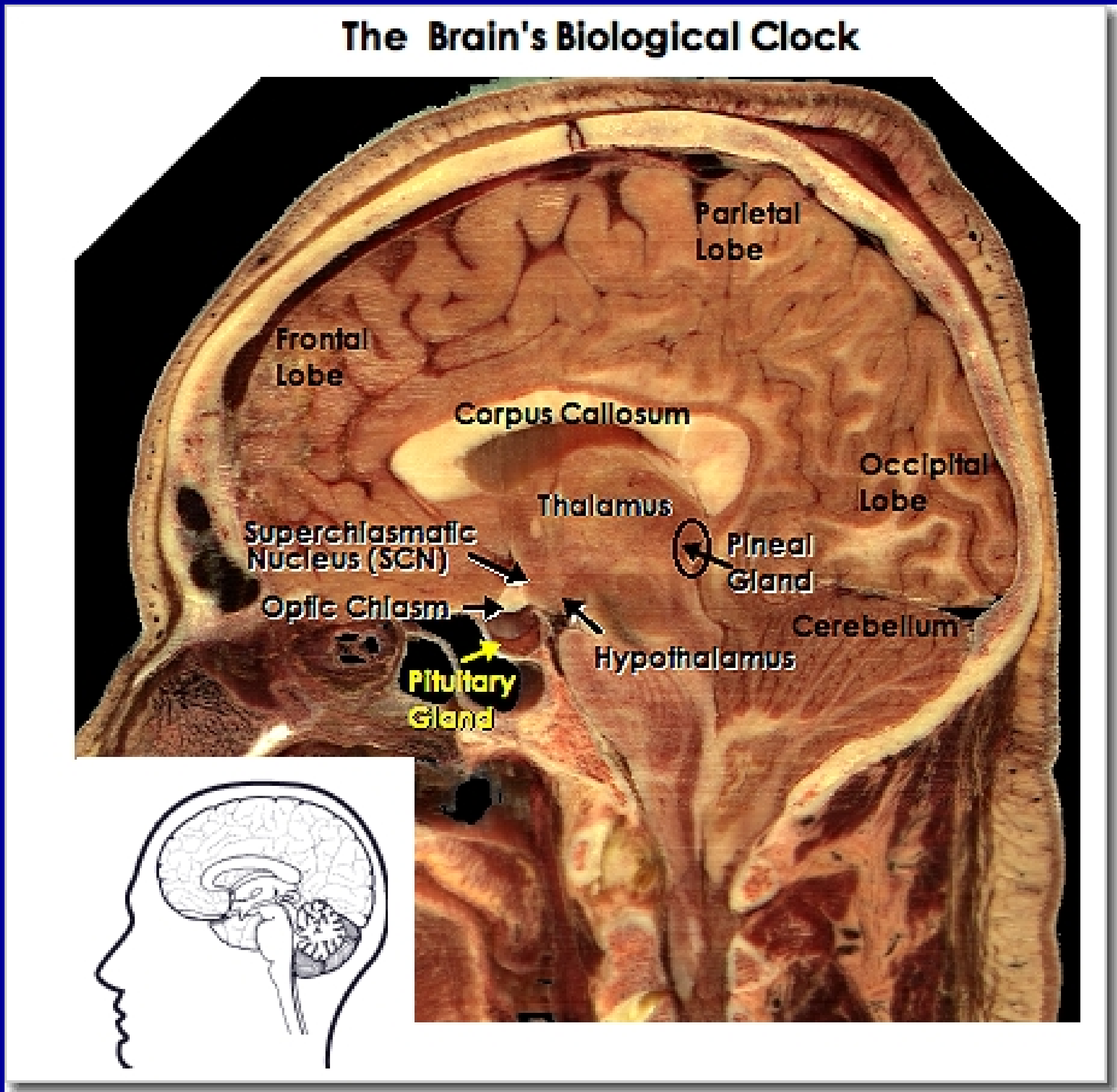


Human Circadian Time Structure

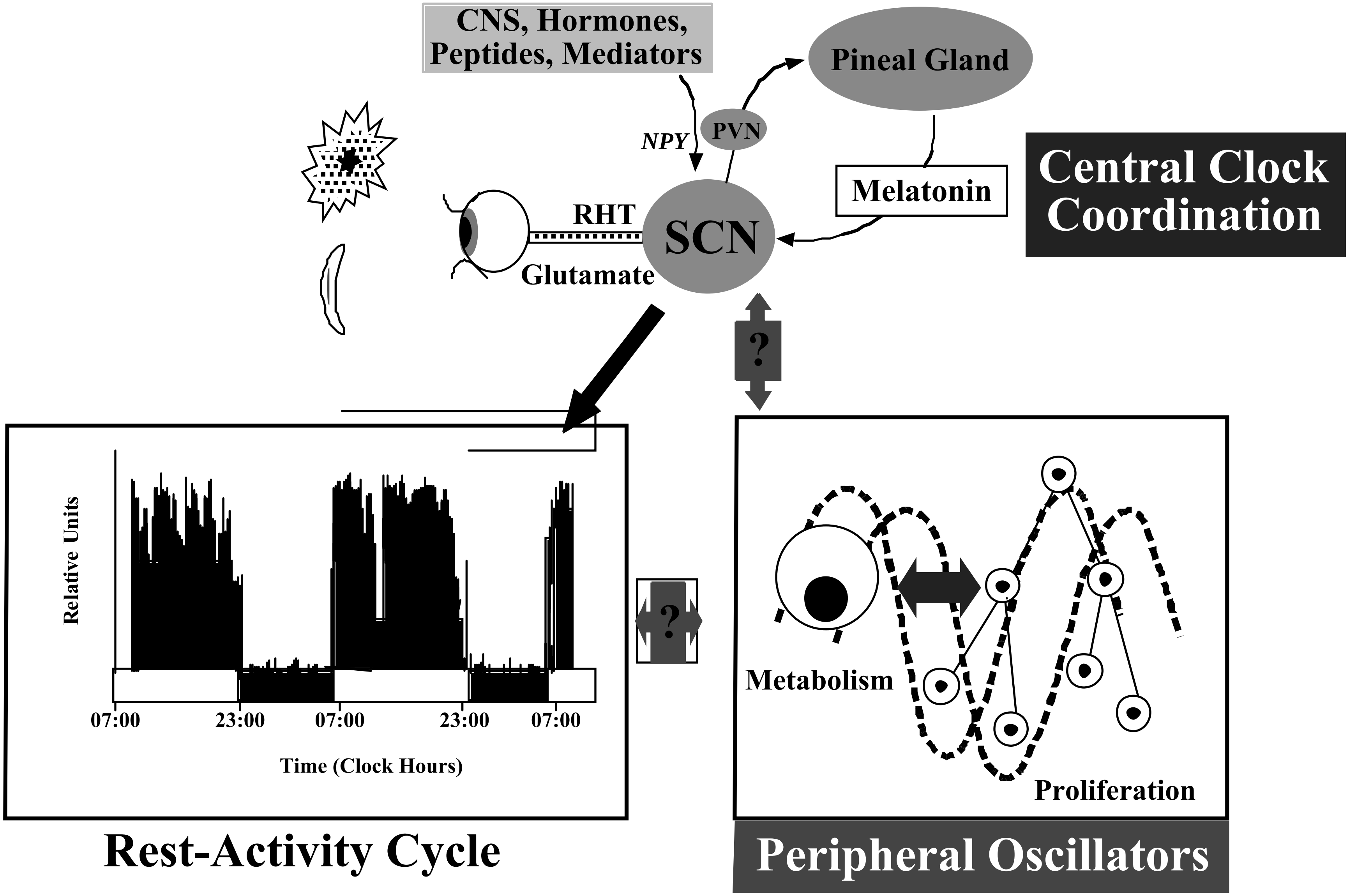
Peak Time of Functions




Gallardo


The Brain's Biological Clock
Parietal Lobe
Frontal Lobe
Corpus Callosum
Occipital Lobe
Thalamus
Superchiasmatic Nucleus (SCN)
Pineal Gland
Optic Chiasm
Cerebellum
Hypothalamus
Pituitary Gland

Schematic View of the Human Circadian Time Organization



after Levi *et al*, 2002

Circadian Rhythm Synchronization

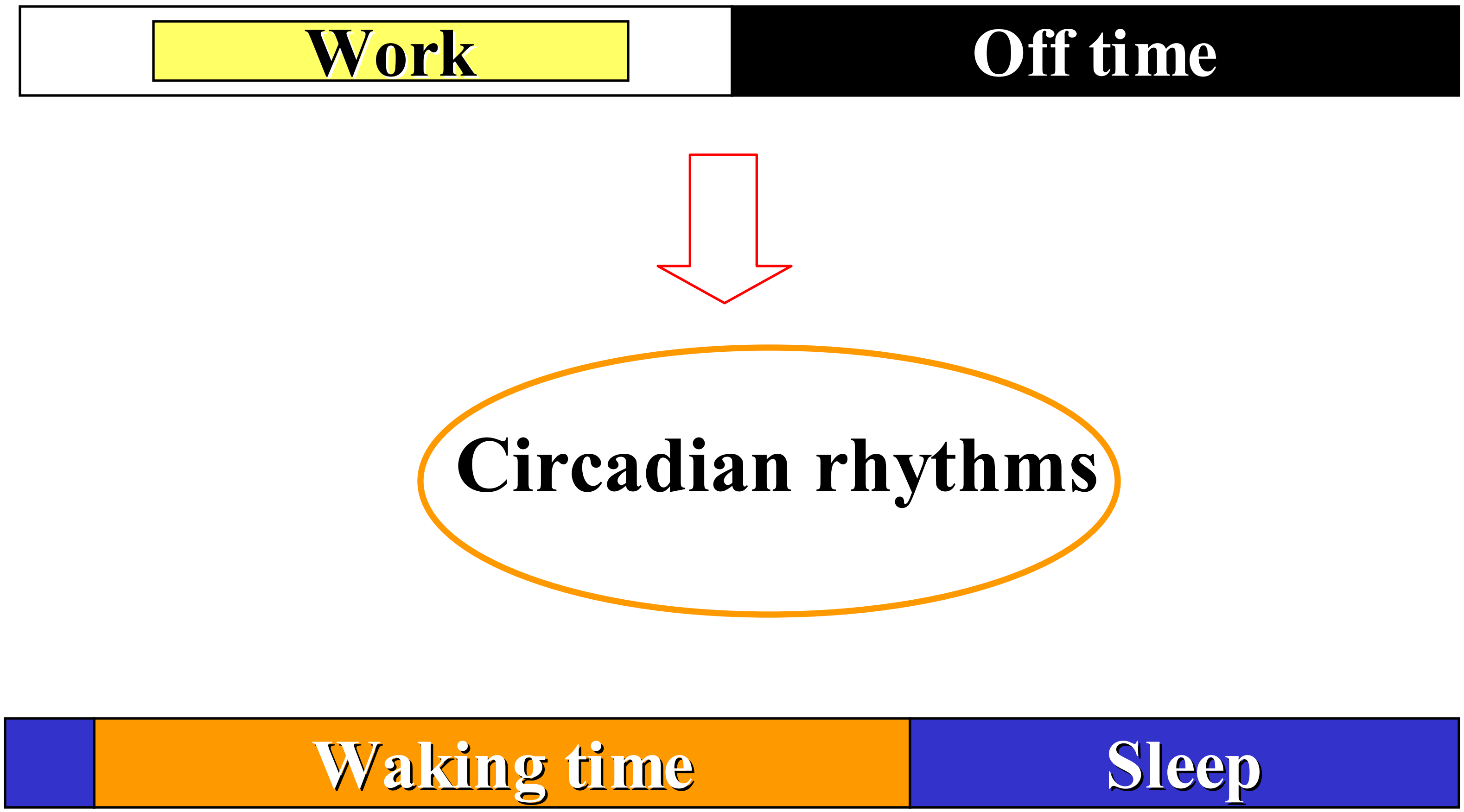
External Synchronization:

Staging of circadian rhythms during the 24 hr timed to meet the predictable-in-time demands of the cyclic natural or man-made external environment

Internal Synchronization:

Staging of the multitude of endogenous circadian rhythms precisely organized between one another for internal biological efficiency in relation to the sleep in darkness/ activity in daylight 24 hr cycle

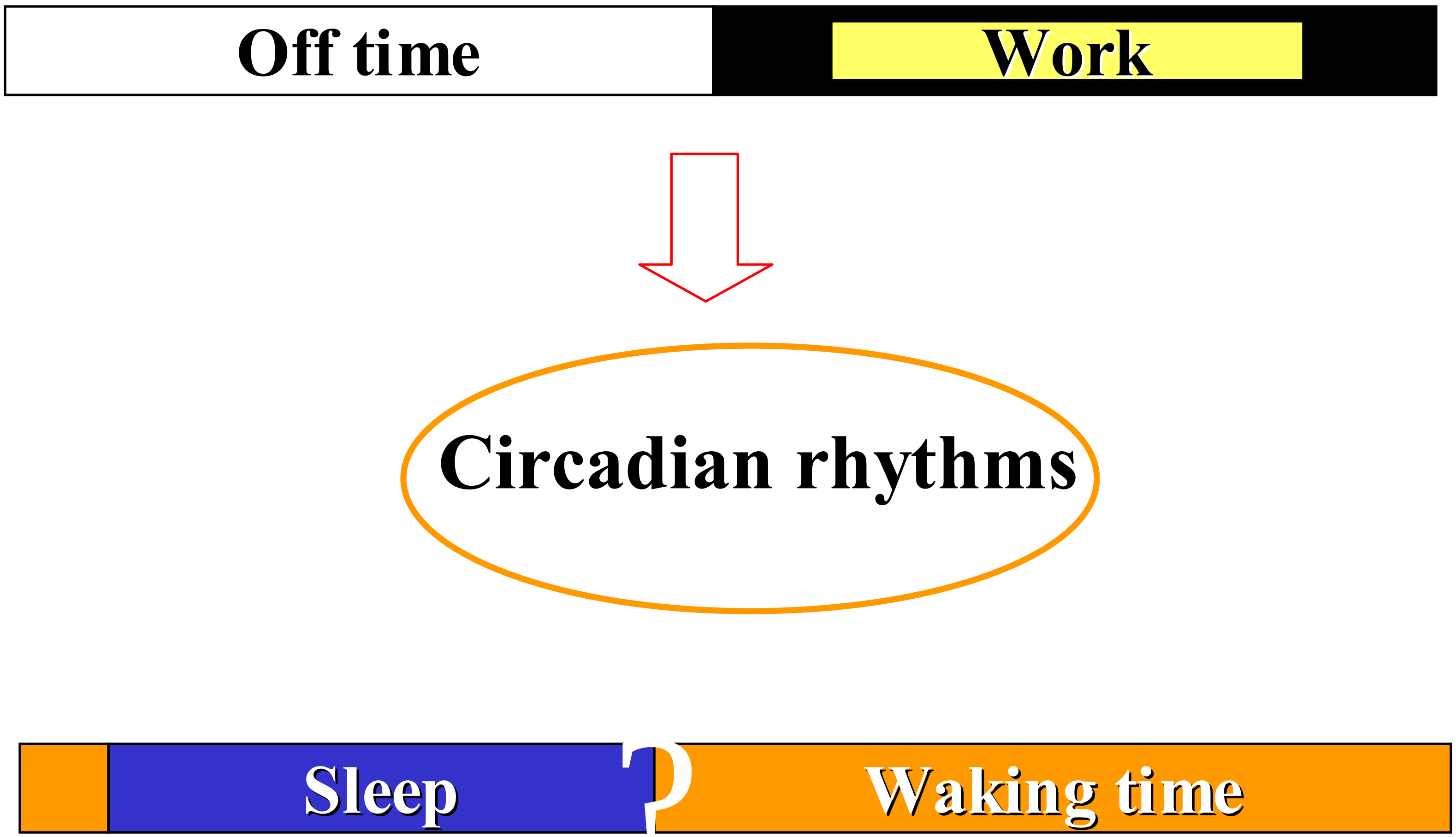
Usual Temporal Organization: Day work during diurnal activity span



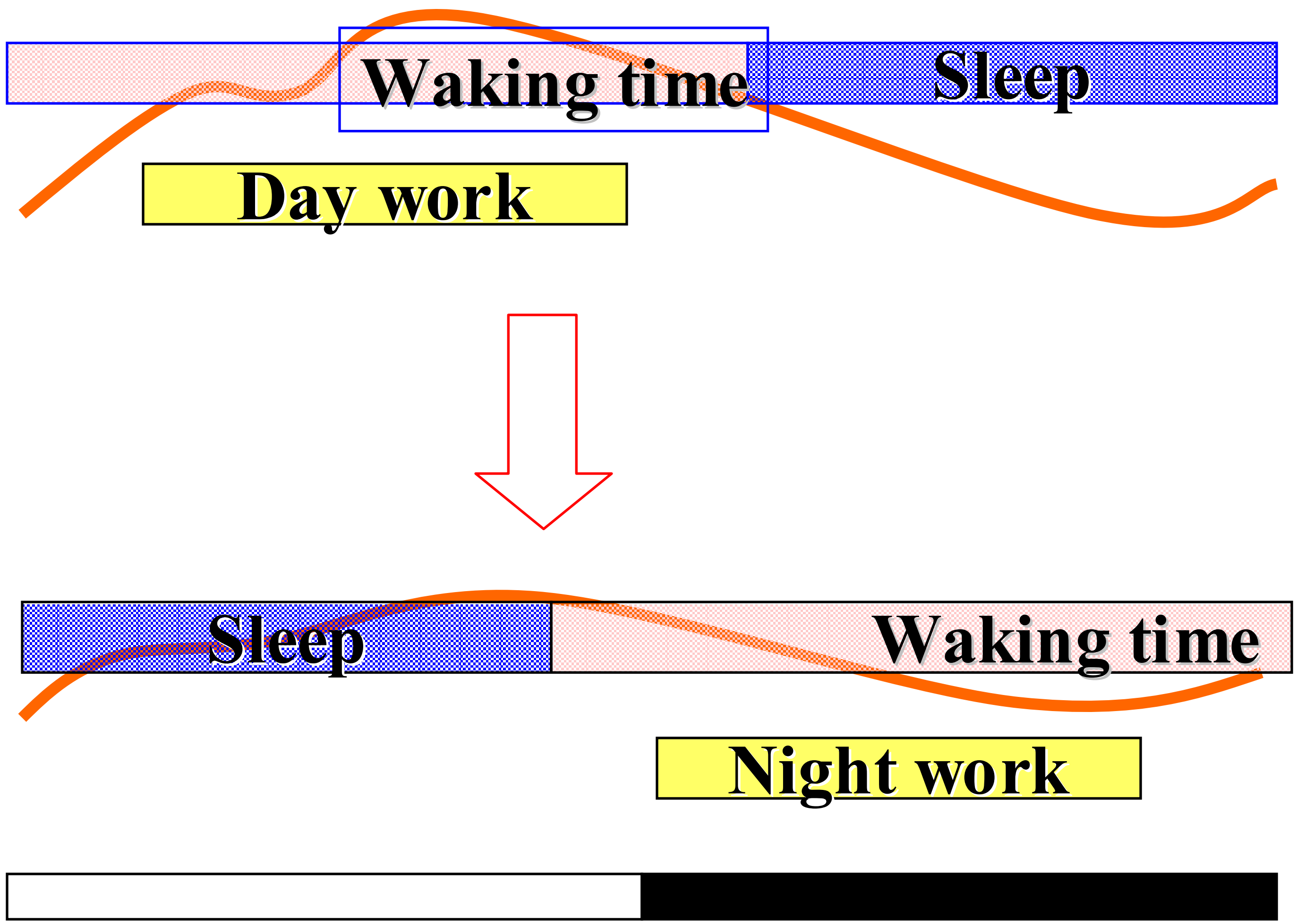
Night & rotating shift work schedules demand:

Workers perform at night and out of phase with the astronomic (day-night) and social surrounding

Temporal challenge of night work: Night work during usual night sleep span



Conflicts between night-shift work & circadian rhythm staging



Night & Rotating Shift Work

- **USA: Estimated 14-20% of Americans engaged in night/shift work**
- **USA: Only 29.1% work 5 day/wk fixed day schedules of ≤ 40h/wk (Presser, 1999)**
- **Developing Countries: Between 15-30% of labor force engaged in night/shift work**
- **European Union: Only 24% of work force exempted from weekend, night, shift, <10hr/day and >40 hr/wk (Costa et al., 2004)**

Circadian rhythm & sleep problems caused by rotating & permanent night shift work schedules

I. Each rotation between day & night-shift work results in disruption of the circadian time structure

Abrupt shift in synchronizer phase (e.g., shift from day to night work)

- **Followed by gradual phase shift of the clock oscillators over several days**
- **Central brain clock (SCN) oscillator shifts faster than peripheral clock oscillators -- Consequences:**
- **(1) transient (several-day) uncoupling of central & peripheral clocks**
- **(2) internal disruption of circadian time structure (internal desynchronization) PLUS**
- **(3) Disparity between phasing of internal circadian rhythms & cyclic demands of external environment (external desynchronization)**

Shift Rate of all variables (mean)

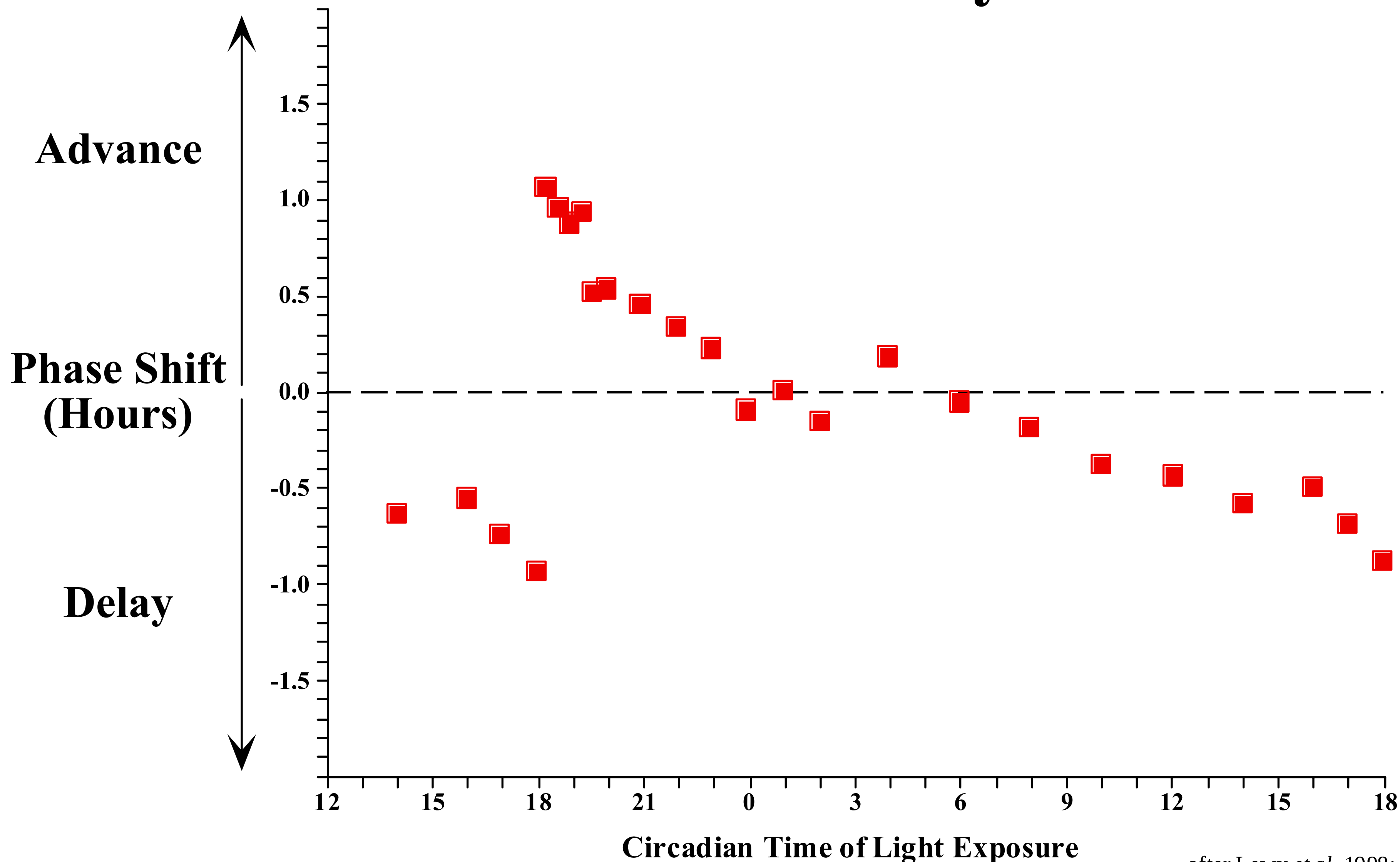
- Westbound Flight 92 min/day
- Eastbound Flight 57 min/day

(Speed varies: Most rapid during first 24 hrs and then decreases exponentially)

Aschoff *et al*, 1975

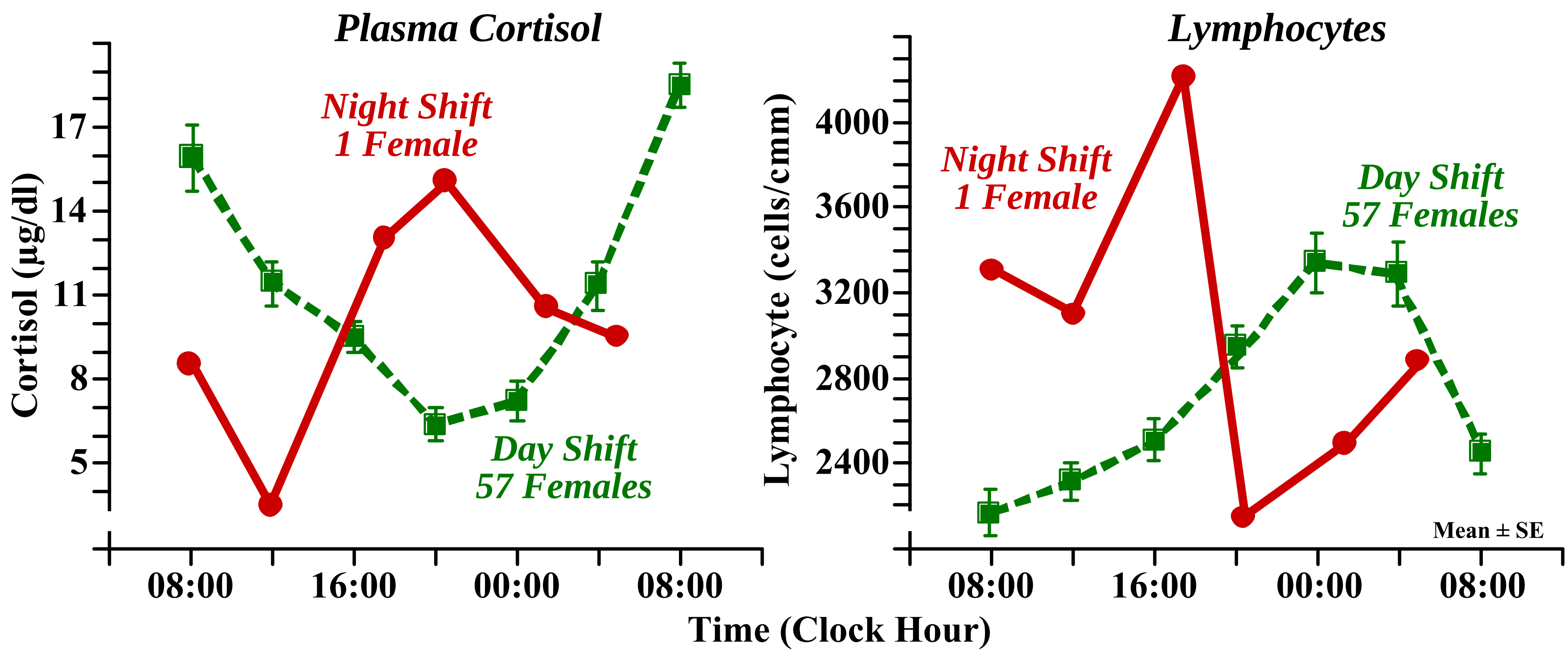
Klein and Wegmann, 1974

Time of Light Exposure Determines Phase Shift of Melatonin Rhythm



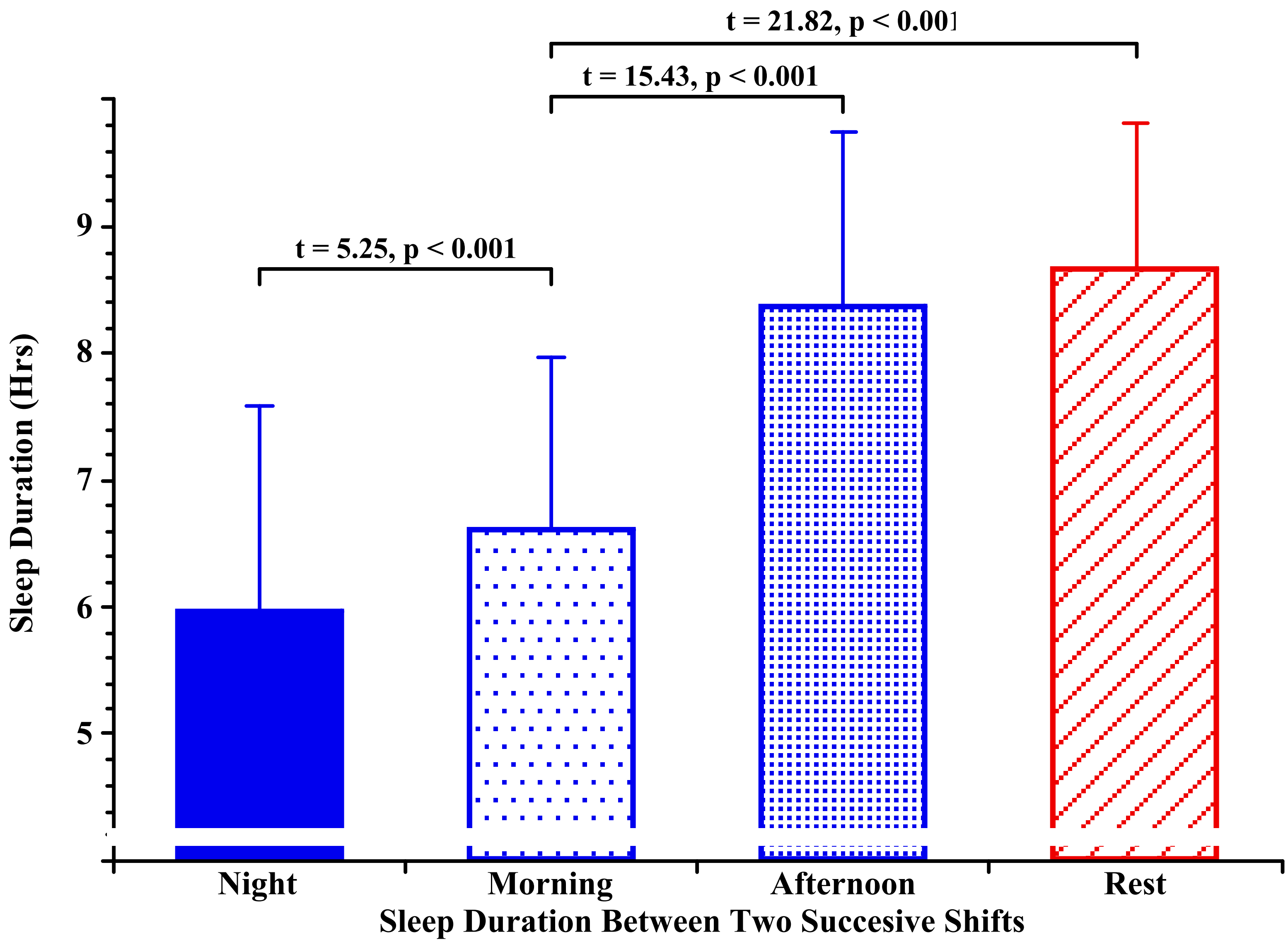
after Lewy *et al*, 1998;
Chronobiology International, 15(1):71-83

Circadian Variation in Circulating Lymphocytes & Plasma Cortisol in Medical Technologists on Day Shift (08:00 - 16:30) vs. Night Shift (00:00 - 08:30)



II. Rotating shift & night work schedules associated with sleep disruption & compromised quantity & quality

Sleep Duration Between Two Successive Shifts of the Same Kind or of Rest Days (N= 297 Workers)



after Folkard and Barton, 1993
Ergonomics, 36:85-91

Night work, sleep deprivation & alertness

Night work

↓

Acute sleep loss

↓

Chronic sleep deprivation

↓

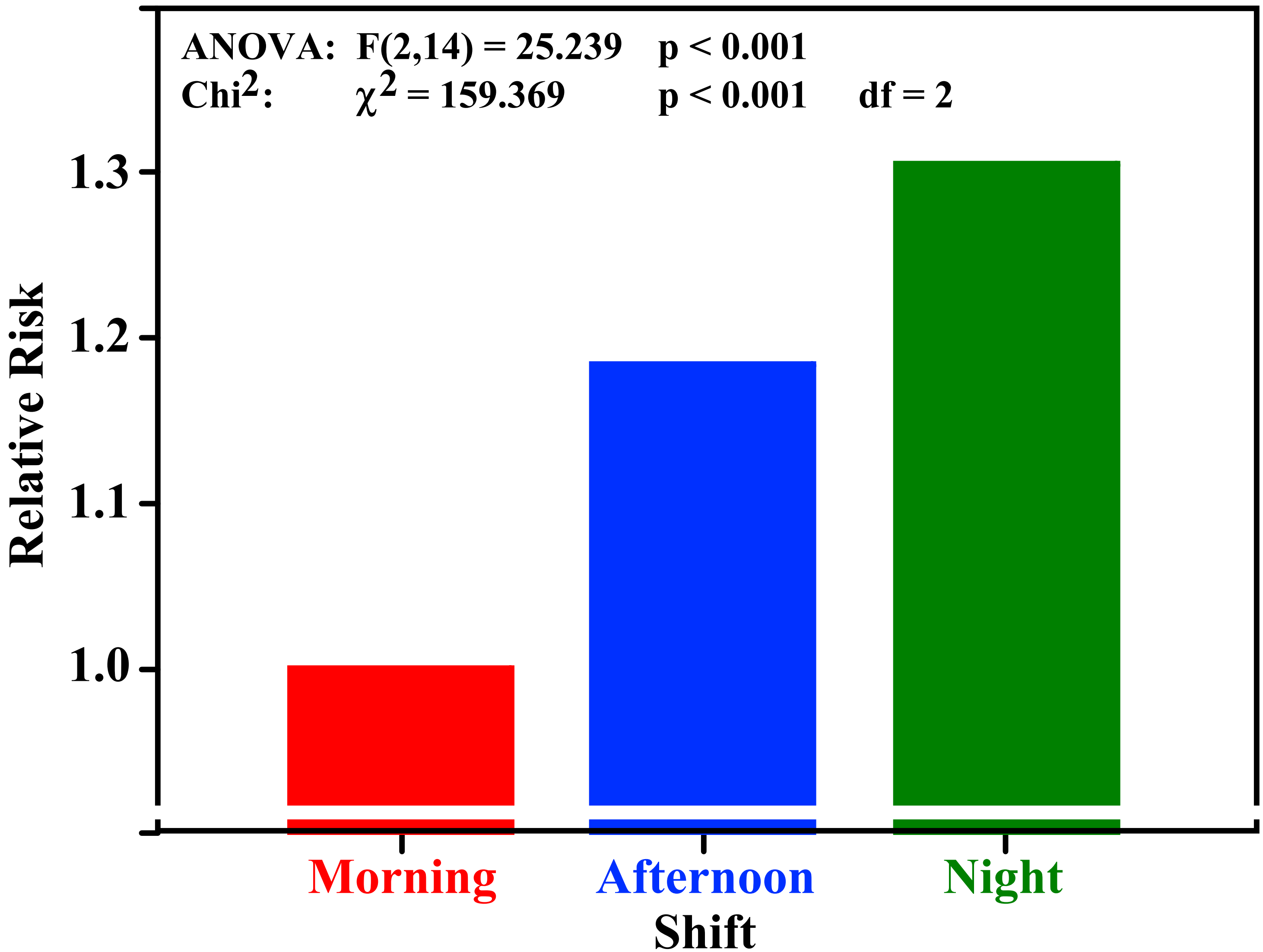
Micro-sleeps, lapses, sleepiness

↓

Impaired performance/Fatigue

Tepas, 1982

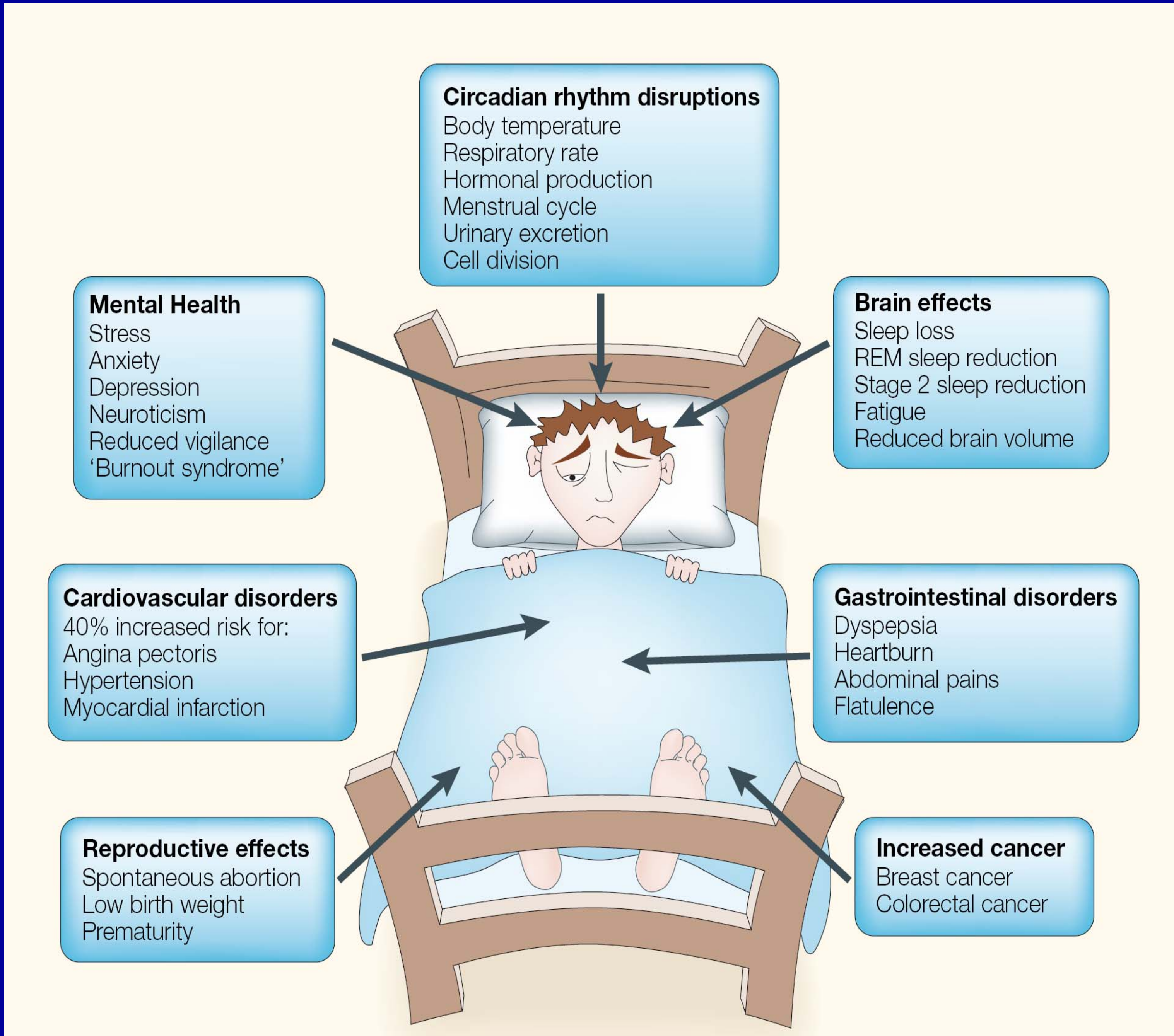
Relative Risk of Accident and Injury Incidence Across Three Shifts



after Folkard and Akerstedt, 2004
Aviation, Space, and Environmental Medicine 75(3):A161-A167

Greater risk of accidents during night than day shift

- Three-Mile Island Nuclear Plant (USA)
- Chernobyl nuclear disaster (Russia)
- Gopal, India (deadly chemical release)
- Exxon Valdez oil spill (Alaska, USA)
- Needle sticks of medical personnel (HIV exposure)
- Highest rate of worker compensation typically for night shift



Foster e Wulff, Nat. Ver. Neurosc, 2005

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IARC – Monograph 98
Shiftwork – Circadian Disruption
December, 2007

IARC – Monograph 98
Shift work – Circadian Disruption

- **Cancer in Humans:**
  - **There is *limited evidence* in humans for the carcinogenicity of shift work that involves night duty**
- **Cancer in Experimental Animals:**
  - **There is *sufficient evidence* in experimental animals for the carcinogenicity of light during the daily dark period (biological night)**
- **Overall Evaluation**
  - Shift **work that involves circadian disruption with light exposure at night is probably *carcinogenic to humans***

Breast Cancer in Female Shift Workers

Prospective Cohort Studies

I. Nurses Health Study: 78,562 Women, 10 yr follow-up, 2,441 BC

Years of Rotating Night Work	Relative Risk RR	Relative Risk 95% CI
1 - 14	1.08	0.99 – 1.18
15 – 29	1.08	0.90 – 1.30
>30	1.36	1.04 – 1.78

II. Nurses Health Study II: 115,022 Women, 12 yr follow-up

Years of Rotating Night Work	RR	95% CI
≥20	1.79	1.06 – 3.01

Schernhammer et al, 2001, 2006

Breast Cancer - Retrospective Studies:

		RR (95% CI)
Hansen 2001:	All night work	1.5 (1.3 – 1.7)
7,565 cases with	Nurses only	1.3 (1.2 – 1.4)
matched controls	>6 yrs	1.7 (1.3 – 1.7)
	yrs shift work	
Lie et al 2005:	0	1.00
537 cases, 1:4 controls	1 - 14	0.95 (0.67 – 1.33)
Norwegian Nurses	15 - 29	1.25 (0.82 – 2.02)
	30+	2.21 (1.10 – 4.45)
Davis et al 2001:		1.6 (1.0 – 2.5)
813 cases, 793 controls		

Other cancers in night-shift workers

Prospective Cohort Studies

		RR (95% CI)
Prostate:		
Kubo et al 2006	Fixed Night	2.3 (0.6 – 9.2)
14,052 men, 31 cases	Rotating Shifts	3.0 (1.2 – 2.7)
Endometrial:		
Viswanathan et al 2007	1 – 9 yrs	0.89 (0.74 – 1.08)
53,487 nurses	10 – 19 yrs	1.06 (0.76 – 1.49)
515 cases	≥20 yrs	1.47 (1.03 – 2.10)

Other cancers in night-shift workers

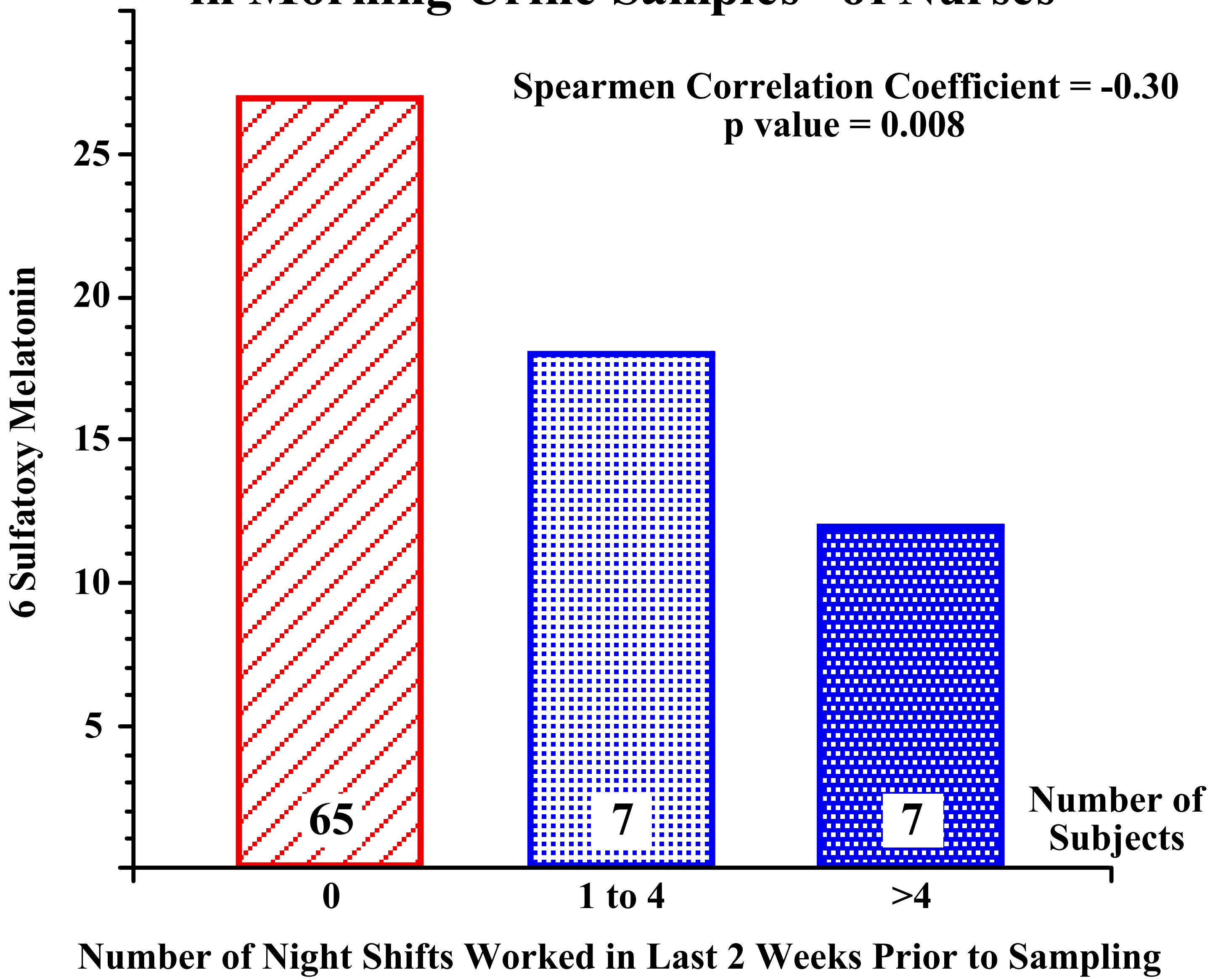
Prospective Cohort Studies:

		RR (95% CI)
Colorectal:		
Schernhammer et al 2003	1 – 14 yrs	1.00 (0.84 – 1.19)
78,586 nurses, 602 cases	≥15 yrs	1.35 (1.03 – 1.77)
Colon:		
Schernhammer et al 2003	1 – 14 yrs	0.93 (0.74 – 1.16)
78,586 nurses, 347 cases	≥15 yrs	1.37 (0.97 – 1.95)
Rectum:		
Schernhammer et al 2003	1 – 14 yrs	0.87 (0.57 – 1.33)
78,586 nurses, 103 cases	≥15 yrs	1.54 (0.75 – 3.16)

Summary: Significant Positive/NO of Studies per Type of Model/Protocol in Experimental Studies of Effect of Circadian Rhythms Disruption on Cancer Incidence & Growth

Study Type / Experimental Focus	No Other Exposure	Chemical Initiation / Promotion Models	Chemical Transplacental Carcinogenesis Models	Tumor Cell or Graft Transplantation Studies	Total
Alterations in Light Exposure	2/3	5/6	1/1	10/10	18/20
SCN Lesions	---	---	---	1/1	1/1
Chronic Experimental Jet Lag	---	---	---	2/2	2/2
Pinealectomy – Induced Melatonin Suppression	---	2/8	---	11/13	13/21
Direct Manipulation of Melatonin	---	---	---	5/5	5/5
Clock Gene Mutations	1/1	1/2	---	---	2/3
Circadian Timing of Carcinogen Administration	---	4/4	---	---	4/4
Total	3/4	12/20	1/1	29/31	45/56

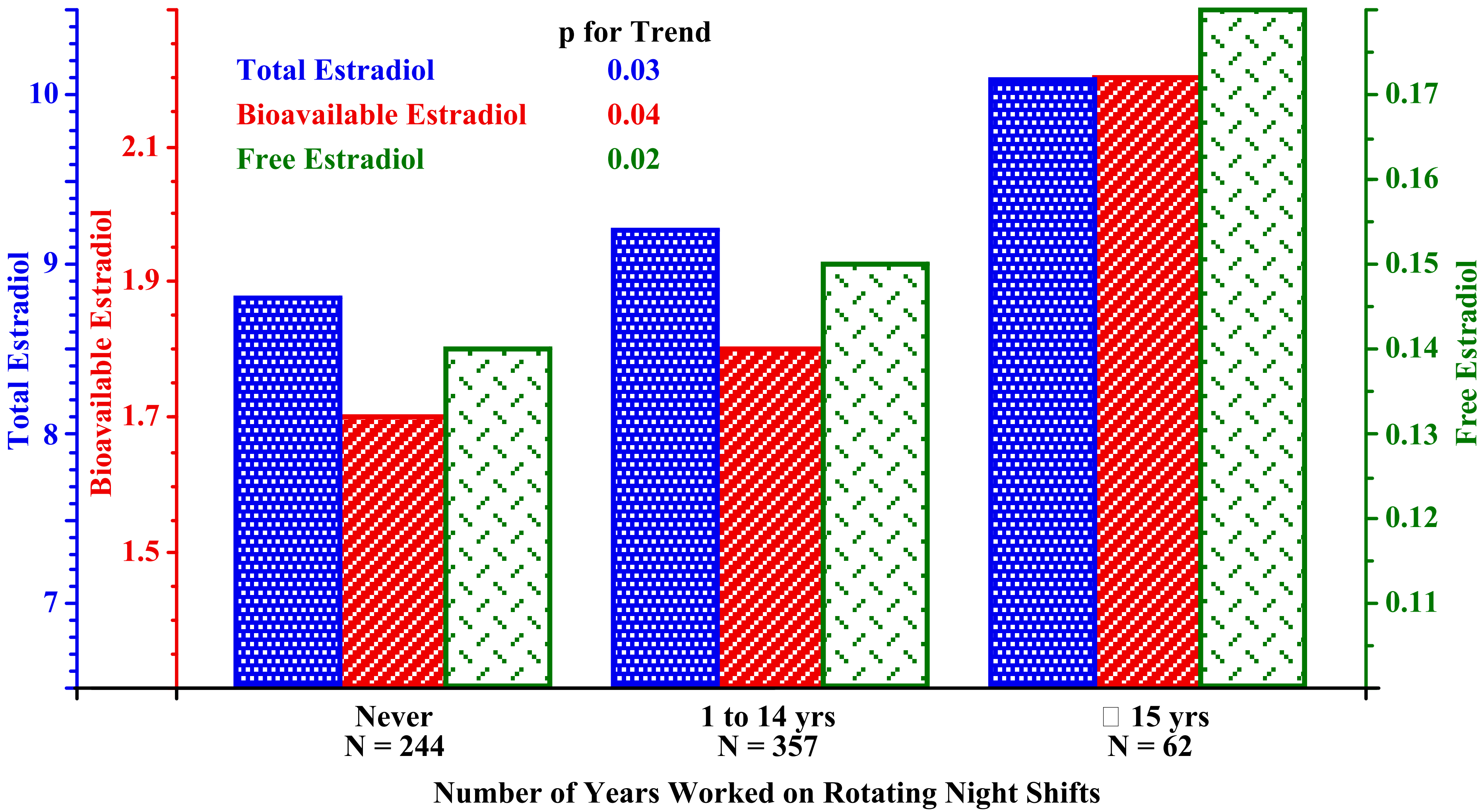
Urinary Creatinine Adjusted 6 Sulfatoxy Melatonin (6SO-MT) in Morning Urine Samples* of Nurses



*Mean of 3 Samples each

after Schernhammer et al, 2004
Cancer Epidemiol Biomarkers Prev 13(6):936-943

Geometric Mean Plasma Estradiol Concentrations in Postmenopausal Women by Number of Years Working Rotating Night Shifts



after Schernhammer et al, 2004
Cancer Epidemiol Biomarkers Prev 13(6):936-943

Sleep Duration of Adults: United States, 2002-2004:
National Center for Health Statistics

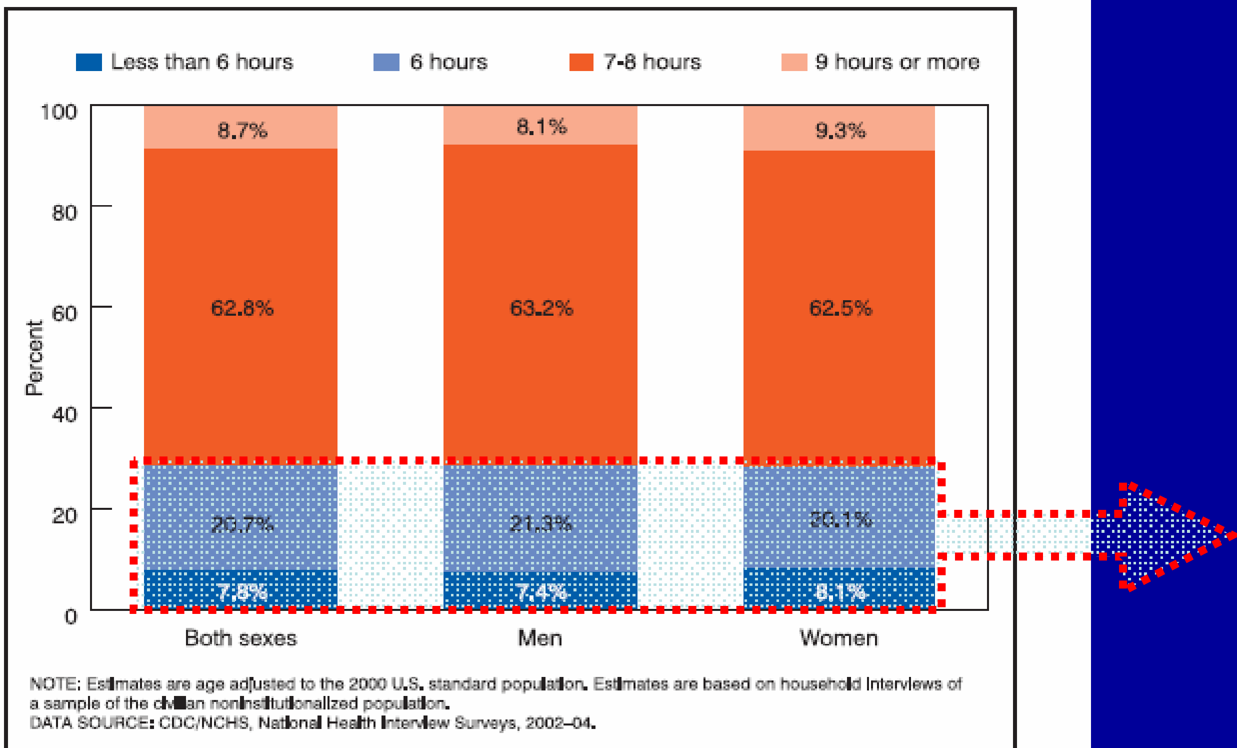
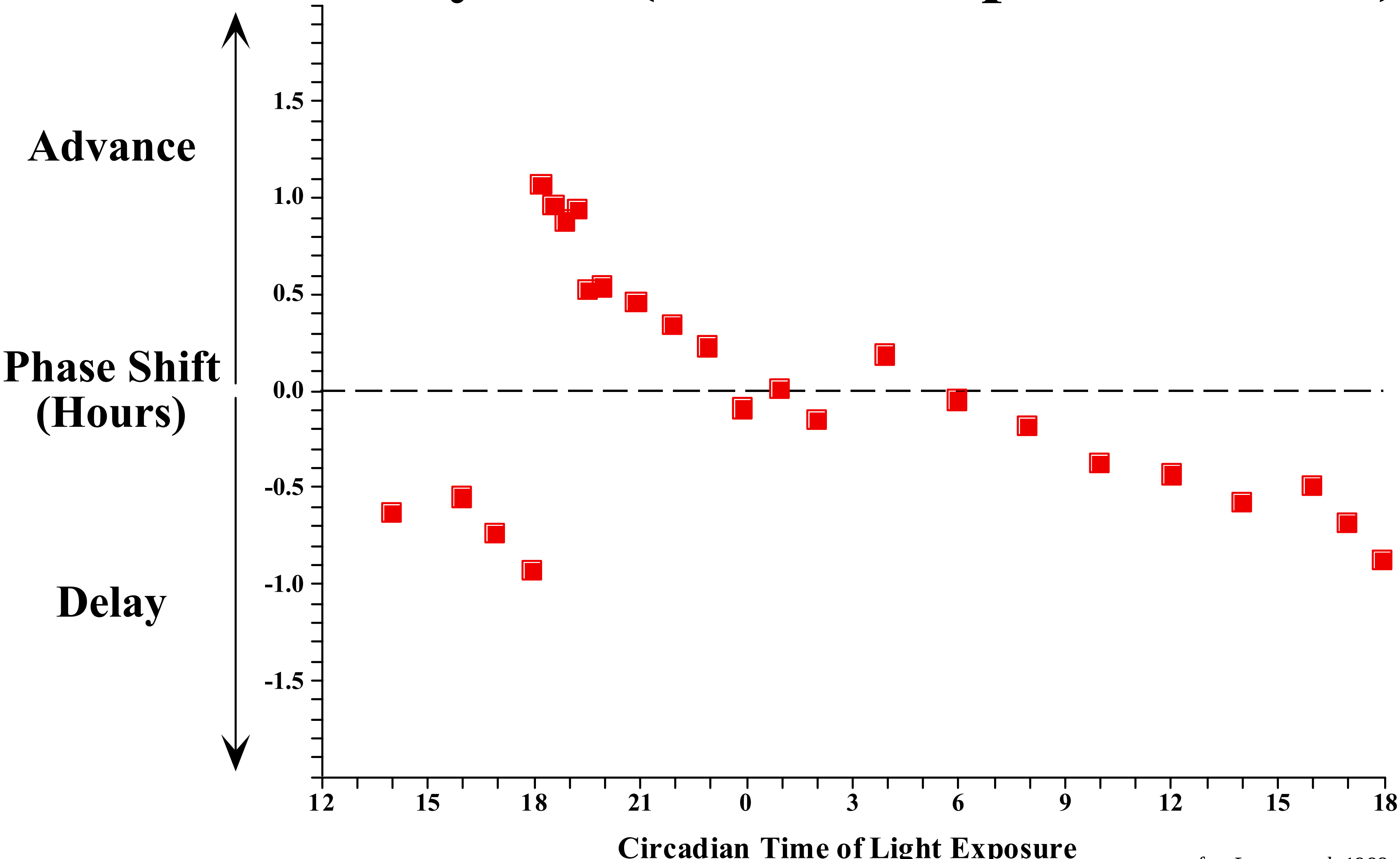


Figure 7.1. Percent distributions of hours of sleep in a 24-hour period, by sex: United States, 2004

28% of U.S. adults sleep 6 hours or less each night

Vital and Health Statistics, Series 10, Number 230: Data From the National Health Interview Survey, DHS Publication No. (PHS) 2006-1558

Time of Light Exposure Determines Shift of Melatonin Rhythm (Phase-Response Curve)



after Lewy *et al*, 1998;
Chronobiology International, 15(1):71-83

Staying up late, nighttime room light, melatonin & breast cancer?

- Bojkowski et al, 1987: Moderate light (300 lux) 30-min pulse at night inhibits melatonin
- Glickman et al, 2002: <1 lux monochromic (446-484 nm) light elicits significant melatonin suppression
- Oleary et al, 2006: Women who turn on room lights during usual sleep hrs ≥2 nights/wk or ≥2 times/night associated with breast cancer risk? (OD=1.65; 95% CI 1.02-2.69)

Chronic Sleep Deprivation

- A risk factor for:
  - Insulin resistance
  - Impaired glucose regulation
  - Obesity
- And favors development of:
  - "Metabolic syndrome"
  - Type 2 diabetes mellitus
  - & maybe risk for cancer ???

Conclusions

- Human beings prefer diurnal activity & nighttime sleep as a species
- Rotating & permanent night-shift work schedules result in repeated disruption of circadian rhythm & melatonin inhibition by nighttime light exposure
- Health consequences are many, perhaps even cancer?
- Consequence of sleep deprivation with nighttime light exposure in everyday life requires further assessment, even in non-shift workers, for circadian disruption & health risks, including possibility of cancer