

Ritmi spanja in Nobelova nagrada

Leja Dolenc Grošelj

Teden
možganov 2018

Na sanjah
svet stoji



VZAJEMNA
zdravstvena zavarovalnica

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SLOVENIAN NEUROSCIENCE ASSOCIATION



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The Nobel Assembly at Karolinska Institutet has today decided to award the

2017 NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE



Jeffrey C. Hall
Michael Rosbash
Michael W. Young

"for their discoveries of molecular mechanisms controlling the circadian rhythm"

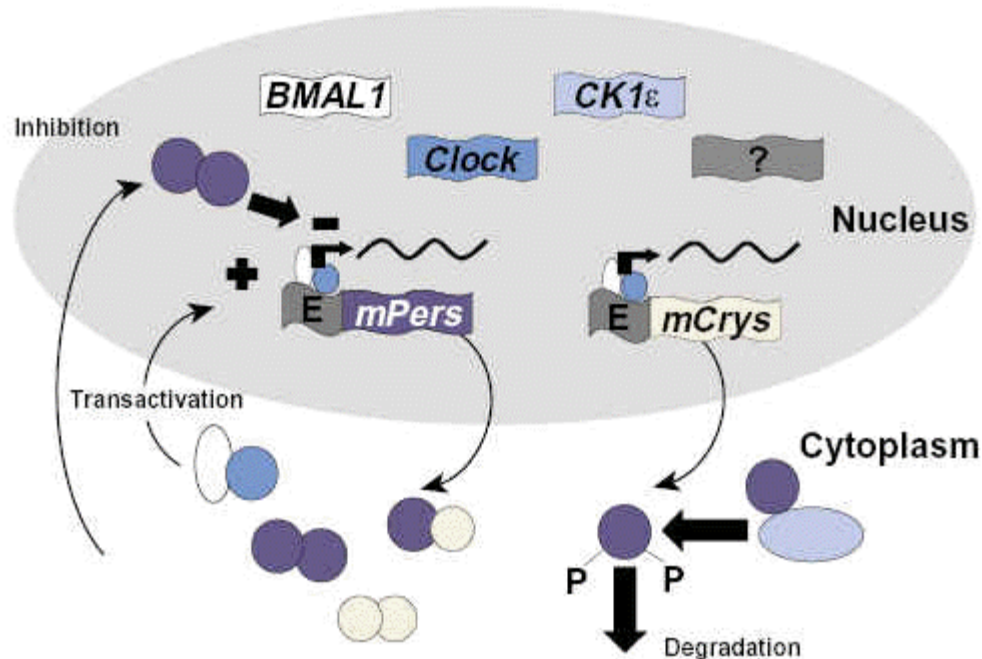
NOBELOVA NAGRADA ZA ODKRITJE CIRKADIANIH RITMOV

- Njihovo raziskovanje cirkadianih ritmov se je začelo v sedemdesetih letih prejšnjega stoletja, ko so pri vinski mušici preučevali cirkadiano nihanje izražanja genov
- Pojav sta prvič opisala Hall in Rosbash leta 1984. Odkrila sta pomen periodnih genov za vzdrževanje notranje biološke ure, ki jo sinhronizirajo cirkadiani ritmi, nihajoči v ritmu 24 ur

Zehring, W.A., Wheeler, D.A., Reddy, P., Konopka, R.J., Kyriacou, C.P., Rosbash, M., and Hall, J.C. (1984).
P-element transformation with period locus DNA restores rhythmicity to mutant,
arrhythmic *Drosophila melanogaster*.
Cell 39, 369–376.

CIRKADIANI RITMI PERIODNIH GENOV

- Raziskovanje periodnih genov je vodilo v odkritje periodnih proteinov, katerih sinteza je odvisna od 24-urnega cikla: periodni geni vplivajo na sintezo omenjenih proteinov, ki nato blokirajo periodne gene za nadaljnjo sintezo, ta proces pa poteka v 24-urnem sinusnem nihanju



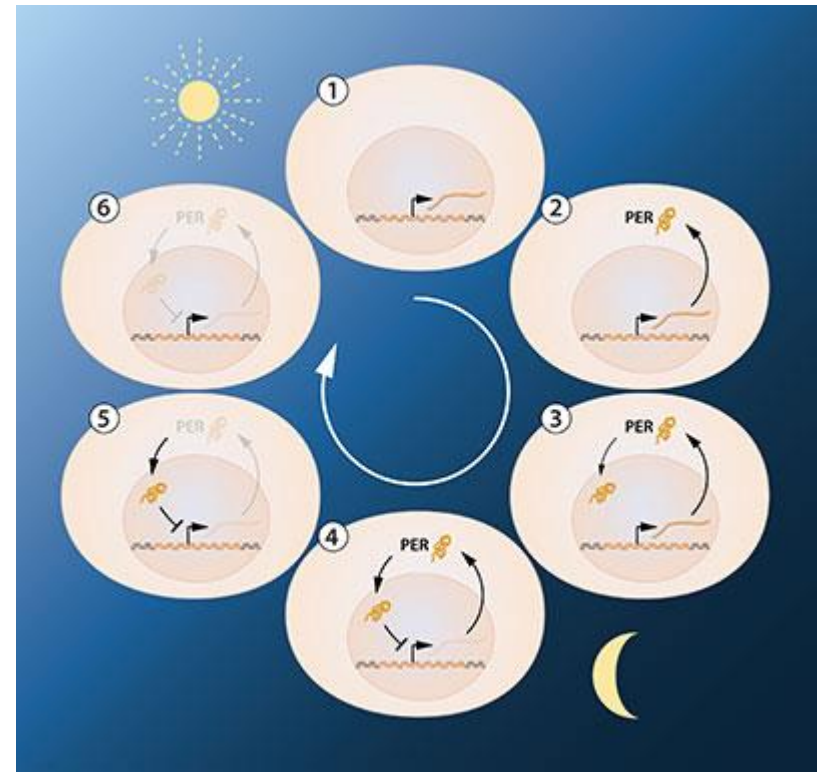
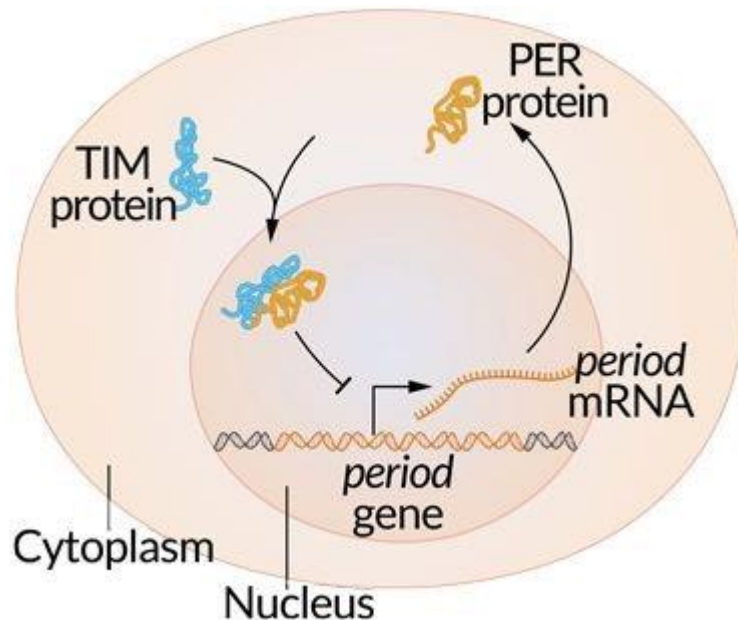
Hardin, P.E., Hall, J.C., and Rosbash, M. (1990).

Feedback of the *Drosophila* period gene product on circadian cycling of its messenger RNA levels.

Nature 343, 536–540.

PERIODNI GENI IN SINTEZA PROTEINOV

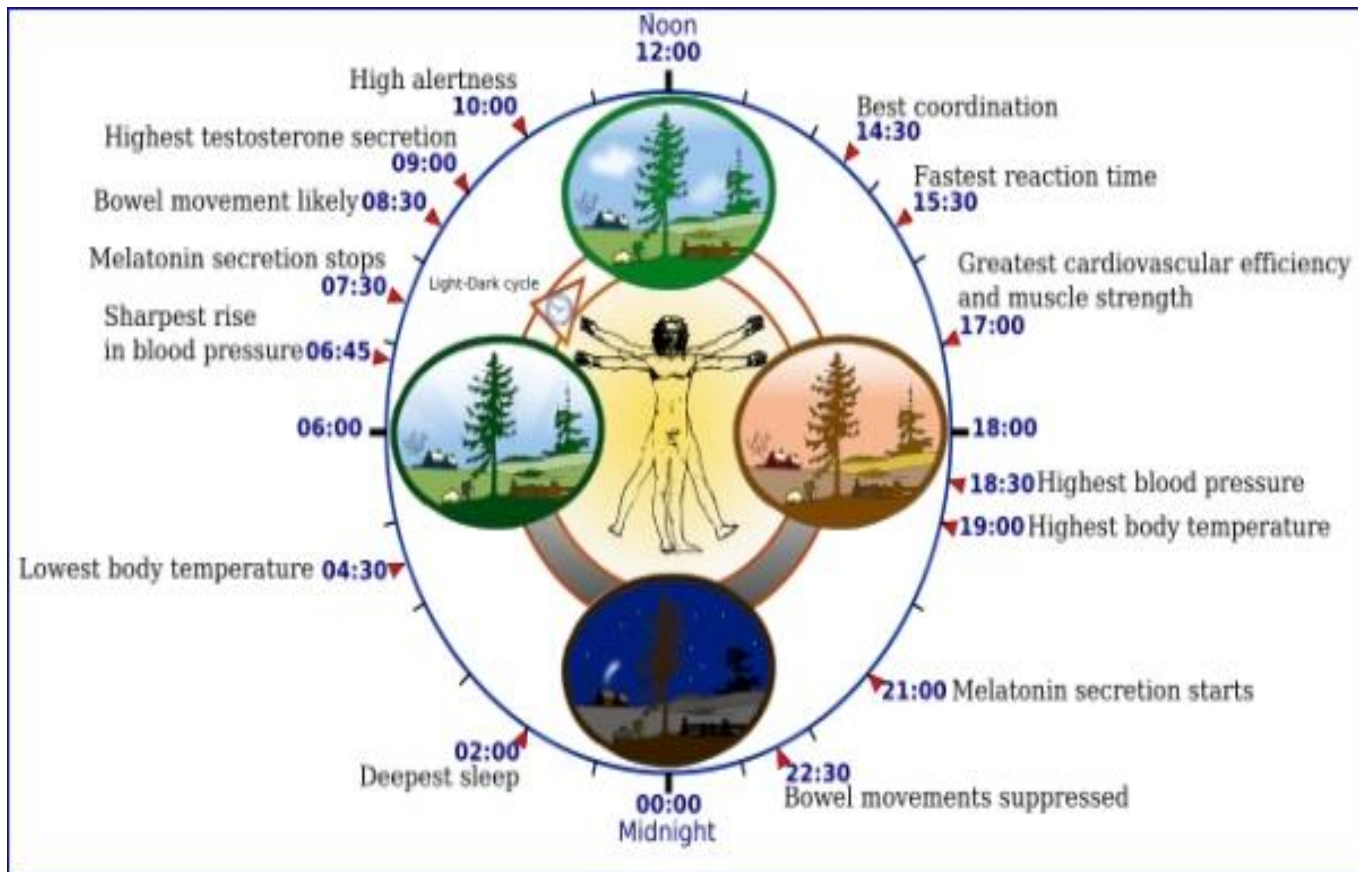
- Odkritje »periodnih« genov (ang. *period genes*) pri vinski mušici nam omogoča razumevanje kopičenja proteinov v celicah ponoči in njihove razgradnje podnevi

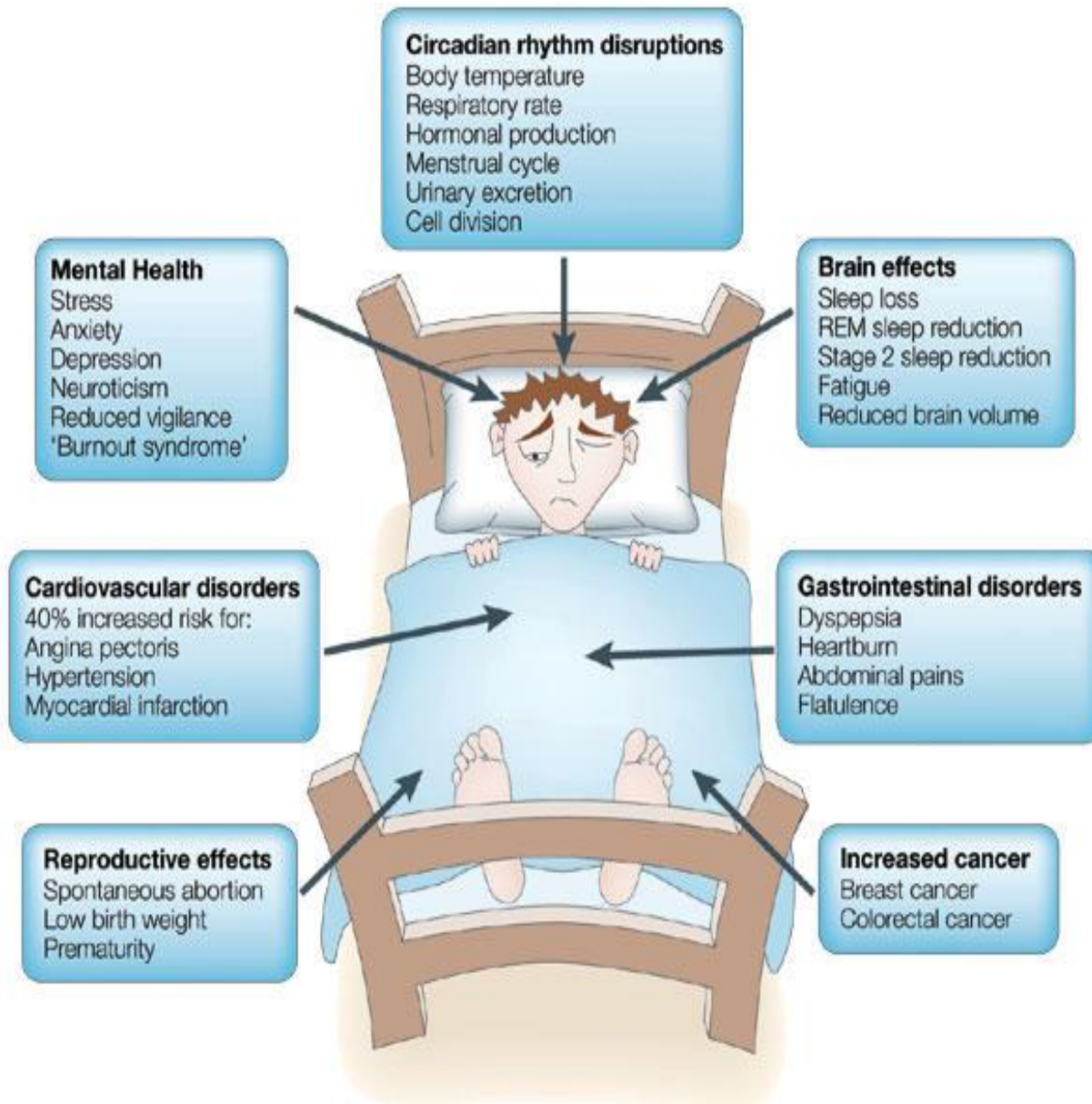


Bargiello, T.A., Jackson, F.R., and Young, M.W. (1984).
Restoration of circadian behavioural rhythms by gene transfer in *Drosophila*.
Nature 312, 752–754.

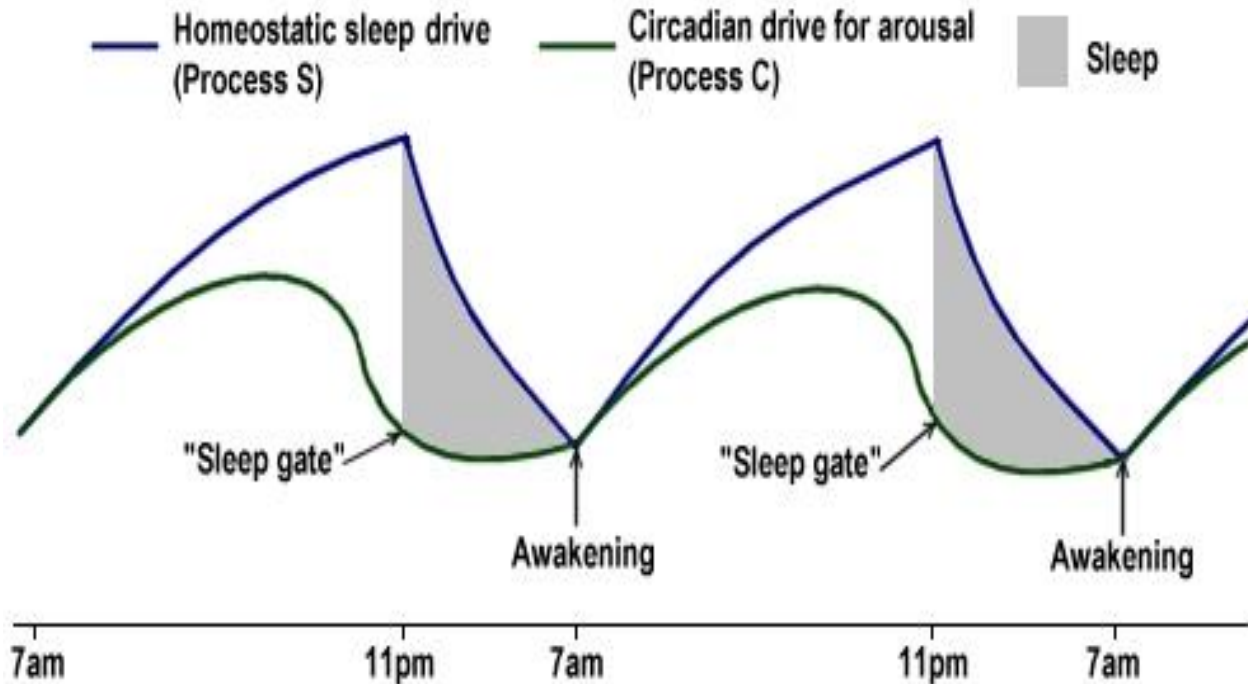
POMEN NOBELOVE NAGRADE

- Odkritje nihanja periodnih genov je pomembno za razumevanje bioloških ritmov živih bitij, ki so usklajena s 24-urnim dnevnim ciklom, kot so: ritem spanja in budnosti, telesna temperatura, krvni pritisk, izločanje nekaterih hormonov (melatonin in kortizol) ter cirkadiani ritmi vedenja

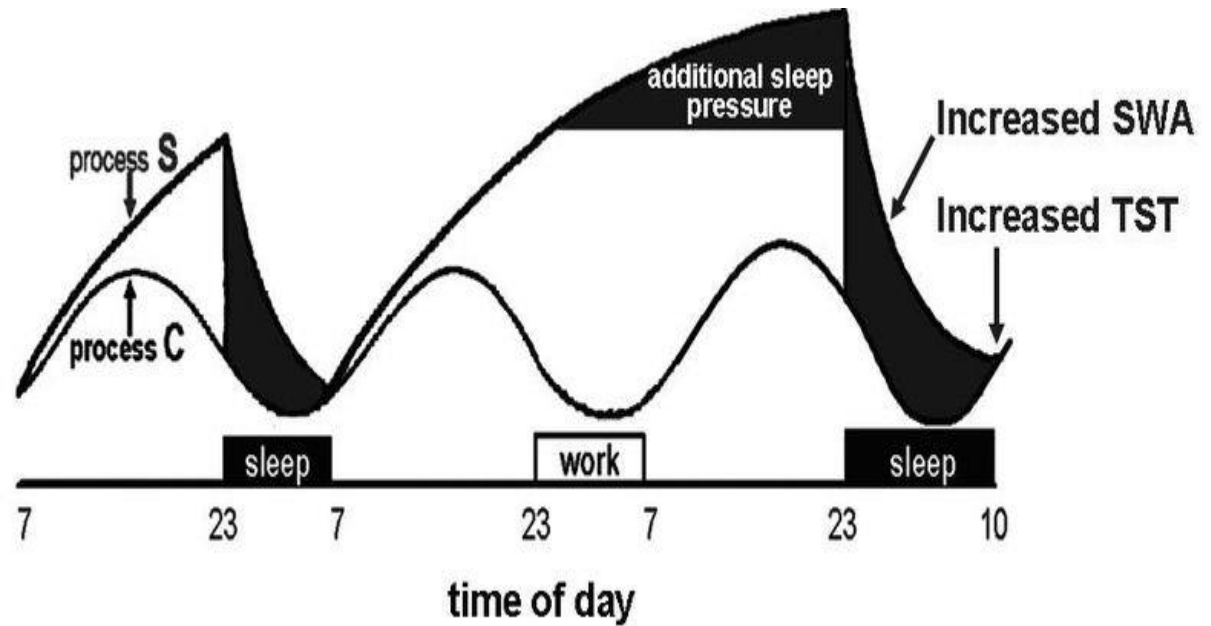
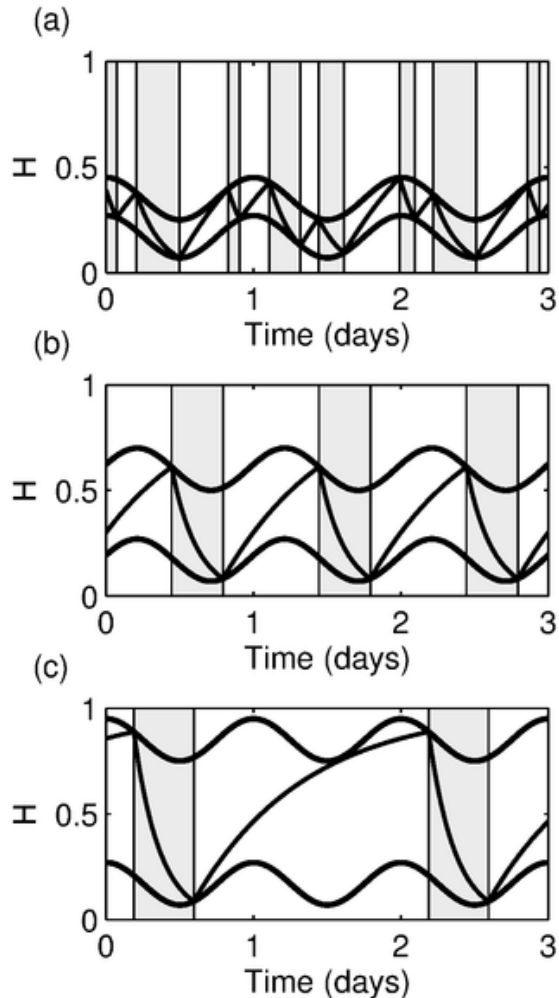




CIRKADIANI PROCES IN SPANJE

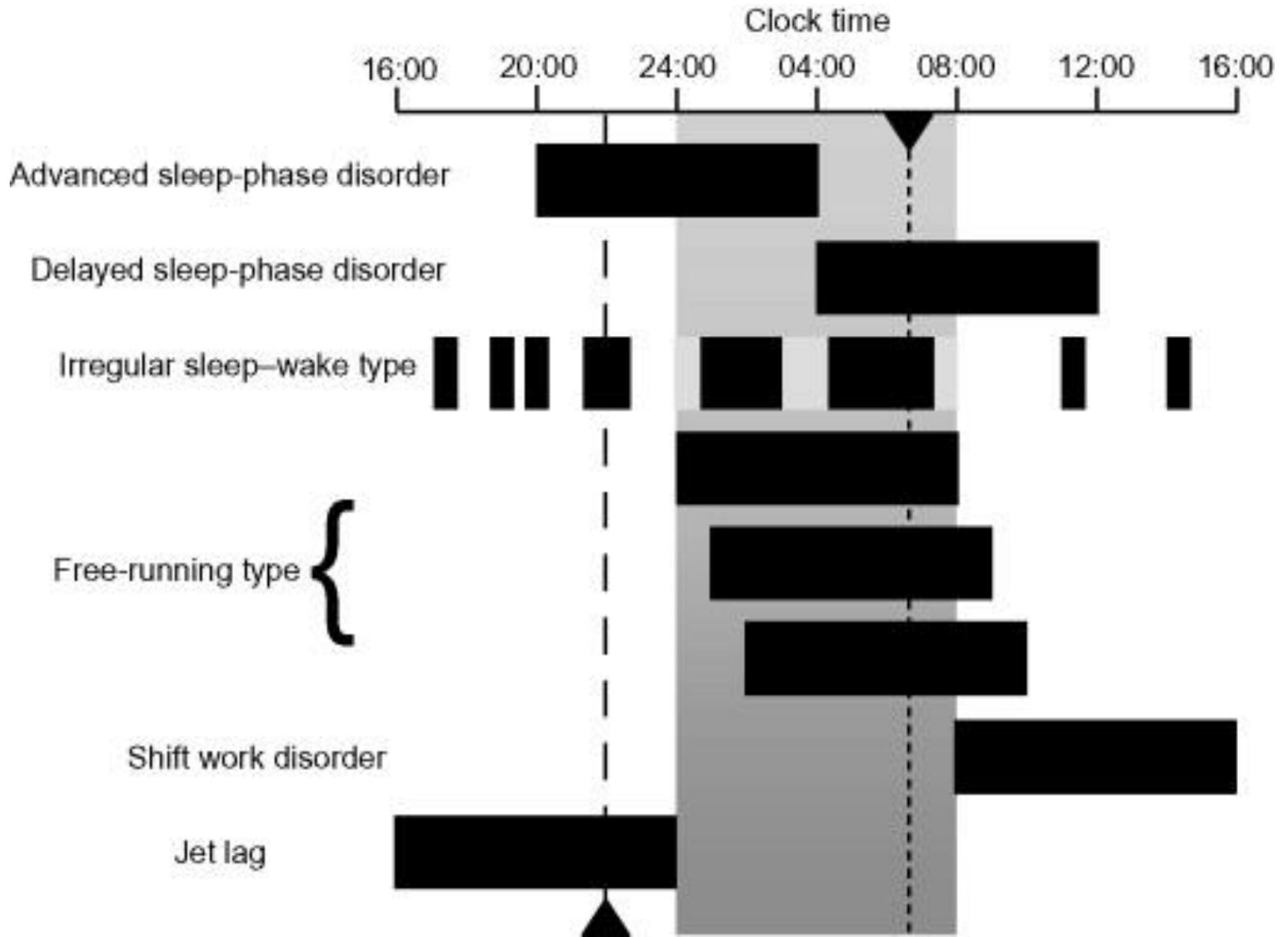


MATEMATIČNI MODEL SPANJA IN BUDNOSTI



Borbély AA, Achermann P.
Sleep homeostasis and models of sleep regulation.
In: Kryger MH, Roth T, Dement WC, editors.
Principles and practice of sleep medicine.
Elsevier Saunders; 2005. pp. 405–417

CIRKADIANE MOTNJE SPANJA



ZDRAVLJENJE CIRKADIANIH MOTENJ SPANJA

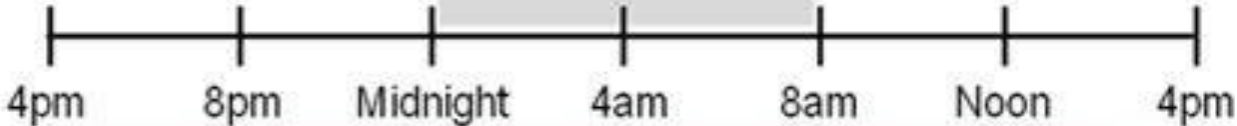
Normal Sleep Phase



Advanced Sleep Phase

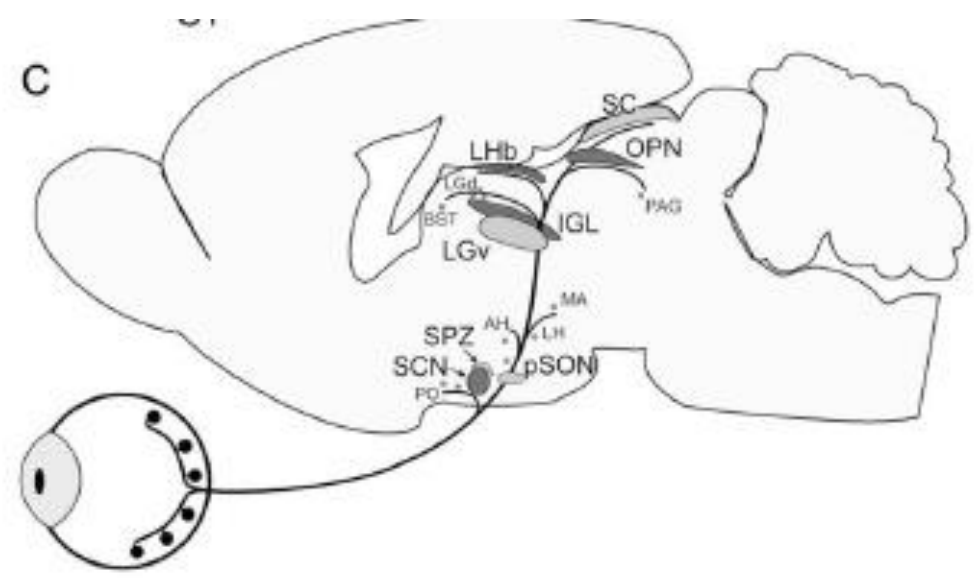
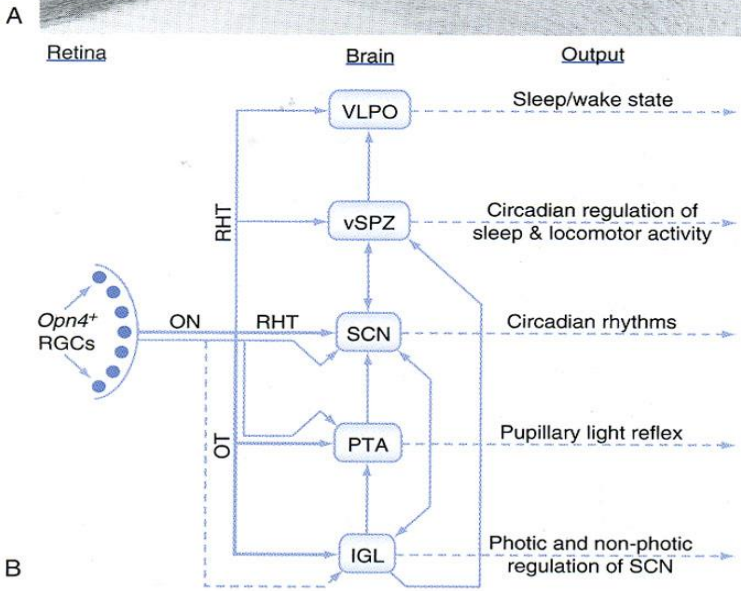
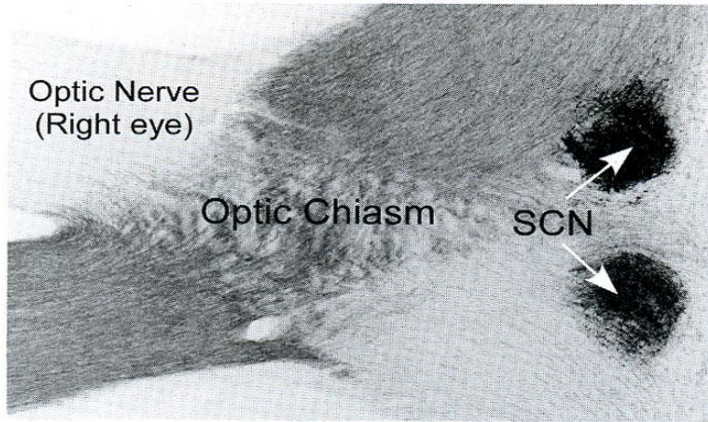


Delayed Sleep Phase



	Dim light melatonin onset		Bright light therapy
	Minimum core body temperature		Melatonin

NE-OPTIČNE POVEZAVE MELANOPSINKIH GANGLIJSKIH CELIC



VPLIV MODRE SVETLOBE NA SPANJE

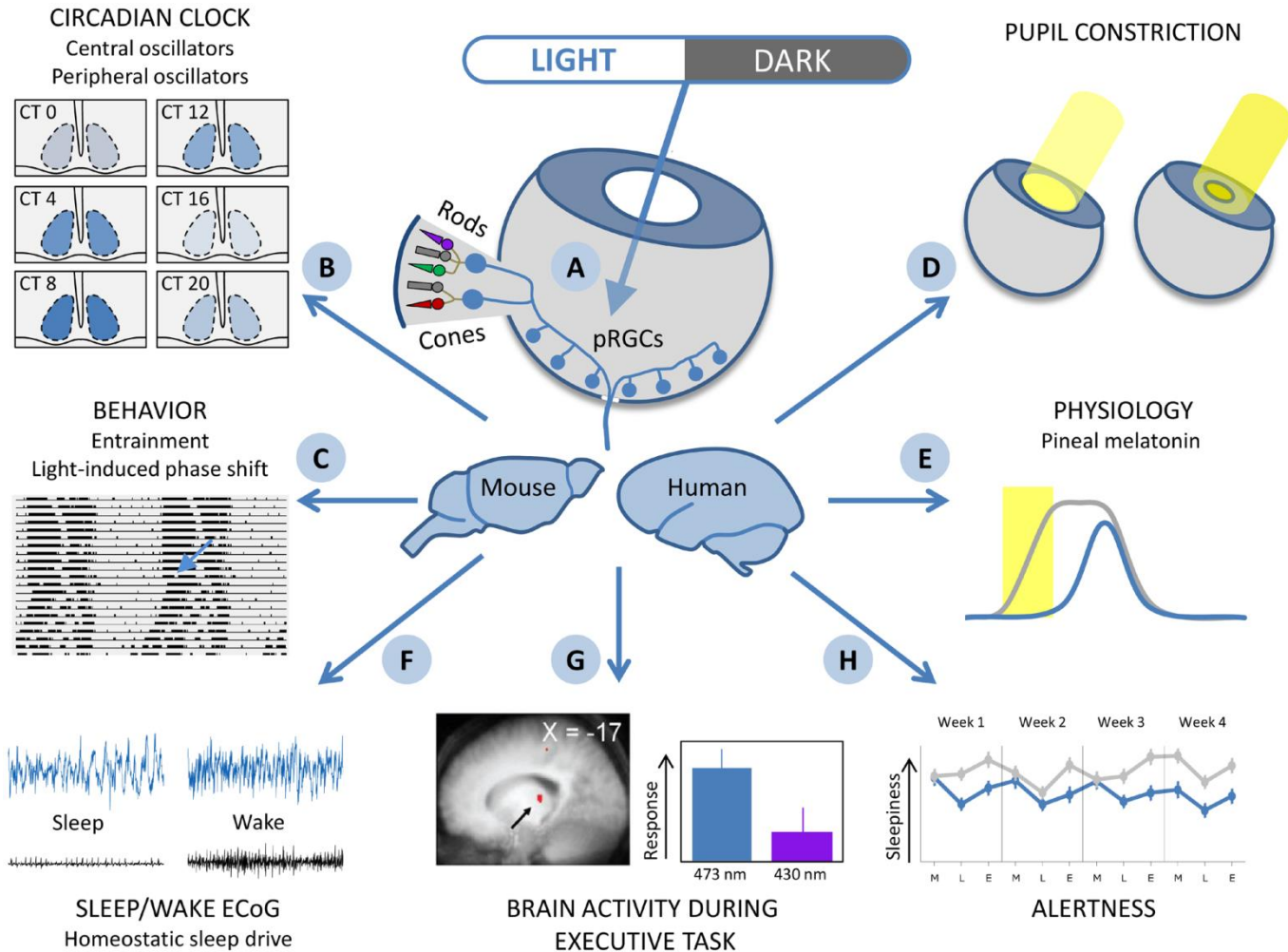
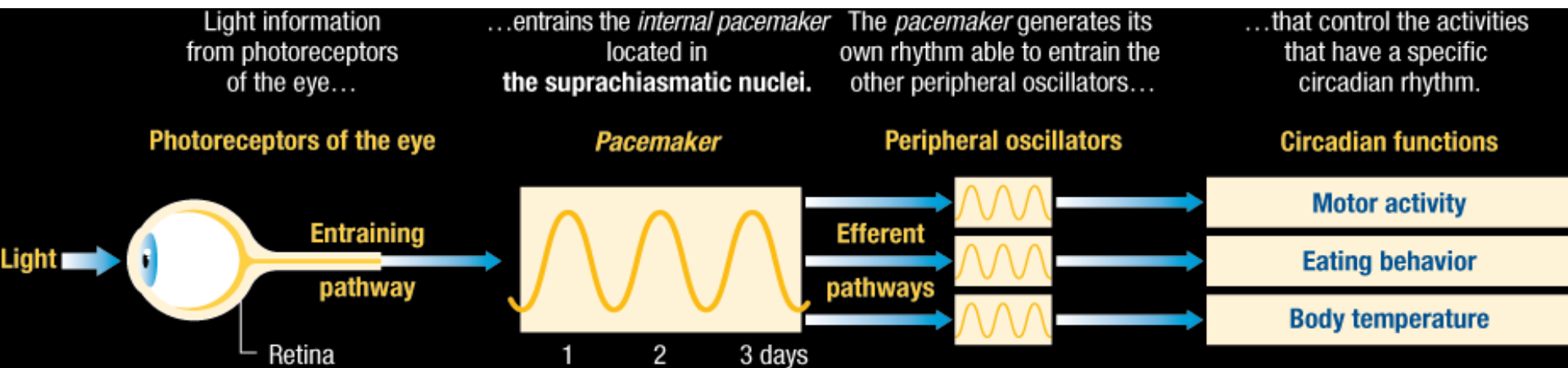


Figure 1. Summary of pervasive effects of light. A diffuse network of photosensitive retinal ganglion cells (pRGCs), which also receive input from rods and cones, are maximally sensitive to blue light between 470 and 480 nm (A). These cells have direct connections to the central circadian oscillator in the SCN where depending on the time of day (circadian time, CT) light induces changes in gene expression (B). pRGCs also mediate the synchronisation to LD cycles of locomotor activity, and light-induced phase shifts (C). pRGC connections to the olivary pretectal nucleus mediate light-sensitive pupil constriction (D), and indirect input via the SCN regulates the light-sensitive suppression of melatonin production in the pineal (E). The pRGC network has direct connections to sleep regulatory structures such as the VLPO and thereby modulates sleep and the ECoG during wakefulness (F). Blue light can modify brain responses to an executive task, as measured using fMRI (G) (figure adapted from [33], with permission), and can improve alertness (H) during the morning, lunch time, and early evening (figure based on data published in [32]).

VLOGA CIRKADIANIH RITMOV PRI ČLOVEKU



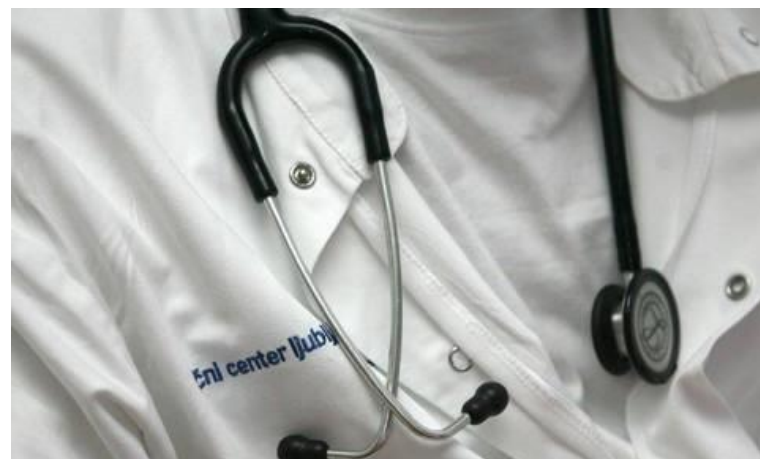
CIRKADIANI RITMI IN MOTNJE SPANJA

- V današnjem svetu vsaj 20% ljudi dela v nočnem oziroma izmenskem turnusu, kar posledično poruši cirkadiane ritme in vodi v:
 - hude motnje spanja in budnosti
 - prekomerna zaspanost vodi v nesreče na delu, doma in v prometu
 - metabolne bolezni
 - povečano tveganje za srčno-žilne bolezni
 - nekatere vrste rakavih obolenj (karcinom dojke, karcinom debelega črevesja in prostate)
 - ter celo v prezgodnjo smrt

POSLEDICE NESPANJA IN IZMENSKEGA DELA

FlyDubai: the crash was due to the pilots being disoriented, a phenomenon known as “somatogravic illusion.”

According to several Flydubai staff members captain 38-year-old Aristos Sokratous, decided to leave the airline mainly because of fatigue and lifestyle issues.



MOTNJA SPANJA ZARADI IZMENSKEGA DELA

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Revised

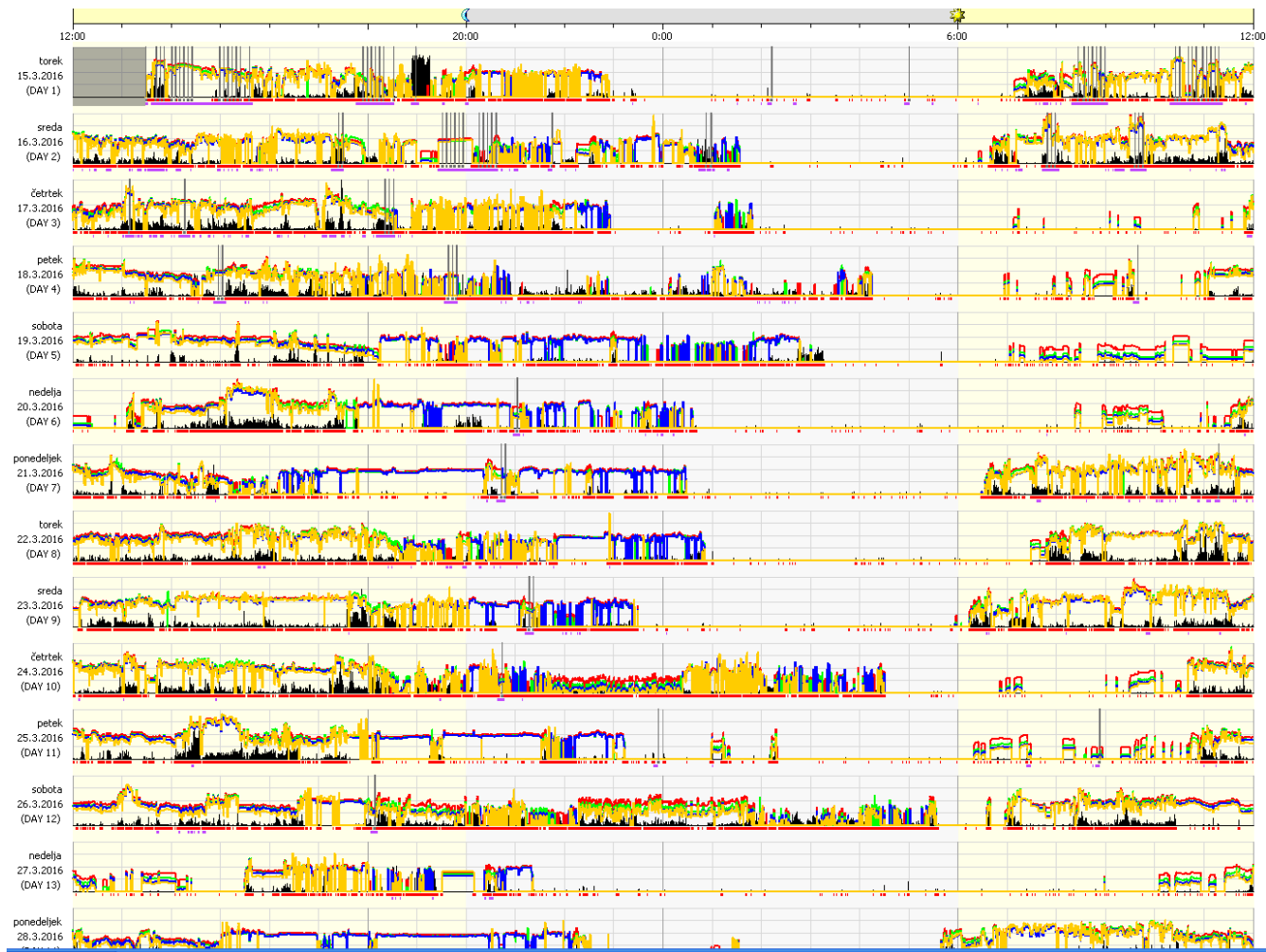
Valerie J. Gawron, Ph.D.
Megan A. Kaminski
Mitchell L. Serber
Cass M. Flynn
Michael Hadjilovchev, Ph.D.
William M. Jarratt
Steven L. Eiler
Thomas A. Neal II, MD, MPH

June 2011

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CAASD

PRIMER BOLNIKA Z NESPEČNOSTJO AKTIMETRIJA



CIRKADIANE MOTNJE SPANJA IN POVEČANO TVEGANJE ZA RAZVOJ RAKA

Cancer

“Exposure to light-at-night [is] associated with an increased risk of breast cancer” (Davis & Mirick 2006)¹⁹.

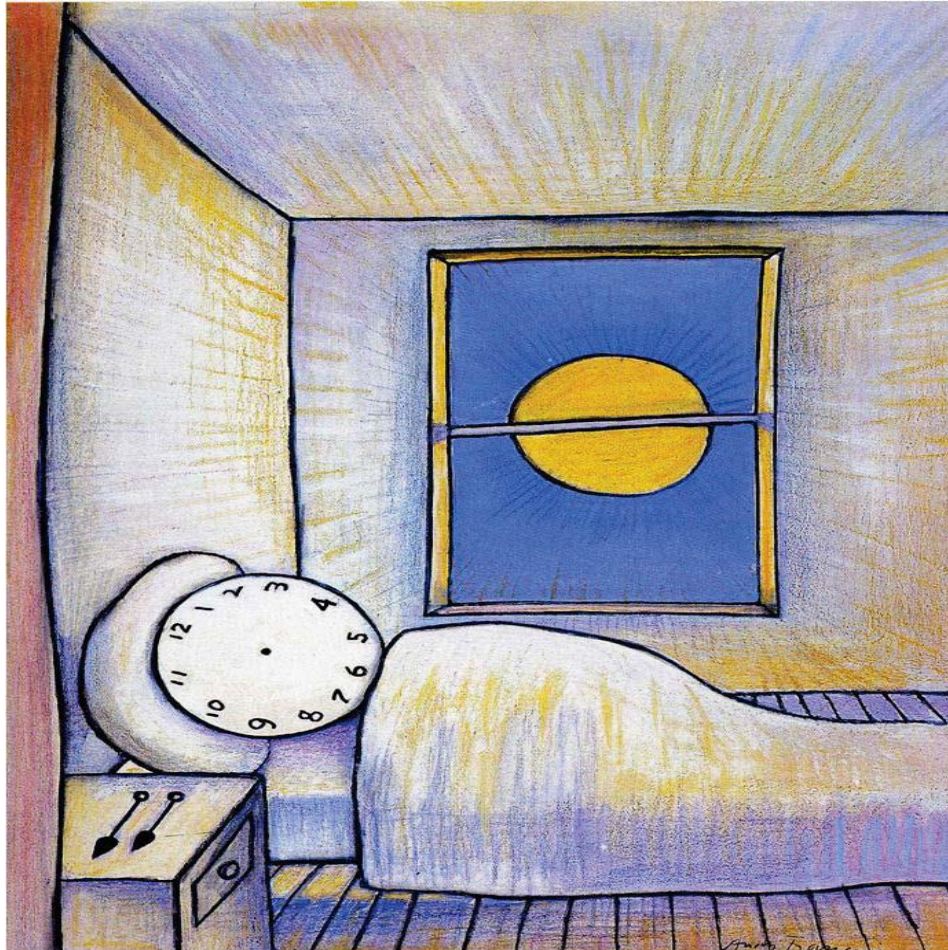
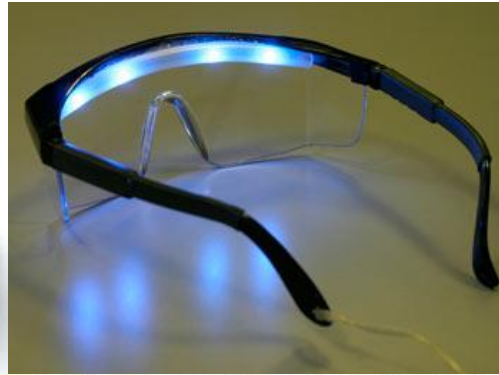


A WHO agency recently concluded that shift work is carcinogenic due to circadian disruptions and their link to cancer²¹.

POMEN NOBELOVE NAGRADE

- Letošnja Nobelova nagrada je pomembna za razumevanje molekularnih mehanizmov periodnih genov ter cirkadianih motenj različnih fizioloških funkcij organizma.
- Nagrada je hkrati zelo aktualna za zavedanje cirkadianih motenj budnosti in spanja, problema sodobne družbe, ki z nočnim in izmenskim delom ruši biološke mehanizme človeškega organizma.





André François
Grasse matinée, 1971

HVALA!