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Organization of Behaviour
• Daily Organization
– Foraging, resting, courtship, hatching
– Terms: nocturnal, diurnal, crepuscular
• Annual Organization
– Migration, breeding, hibernation
• Other Cycles
– e.g. tidal rhythms, lunar cycles

Biological Rhythms
• **Biological rhythms** are regular fluctuations in a living process
• **Circadian rhythms** have a rhythm of about 24 hours
• **Ultradian rhythms** such as bouts of activity, feeding, and hormone release repeat *more than* once a day
• **Infradian rhythms** such as body weight and reproductive cycles repeat *less than* once a day
  • e.g. menstrual cycle, annual cycle

Circadian Sleep Cycles
• Circadian rhythms – "about a day"
• Virtually all physiological, biochemical, and behavioral processes show some circadian rhythmicity

Do Endogenous Clocks Exist?
• Hold animals in constant conditions
– Exhibit **free-running** rhythms
– Slightly longer than 24 hours
– Individuals have slightly different rhythms, and become de-synchronized
– Thus, must be endogenous control

Circadian Clock
• Synchronized by environmental cues – time-setters or zeitgebers
– E.g. light, food availability
• Large shifts of clock can take several cycles to entrain

Jet Lag and Shift Work
• **Jet lag** – zeitgebers are accelerated or decelerated
• **Shift work** – zeitgebers unchanged, but sleep-wake cycle must be altered
• Both produce a variety of deficits
• Can the effects be prevented or minimized?

Reducing Jet Lag
• Gradually shift sleep-wake cycle prior to travel
• Administer post-flight treatments to promote the needed shift

– Exposure to zeitgebers will lead to more rapid entrainment
- Bright sunlight
- Exercise
- Meals

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Experimental 'Jet Lag' Inhibits Adult Neurogenesis and Produces Long-Term Cognitive Deficits in Female Hamsters

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Abstract

Background: Circadian disruptions through frequent transmeridian travel, rotating shift work, and poor sleep hygiene are associated with an array of physical and mental health maladies, including marked deficits in human cognitive function. Despite anecdotal and correlational reports suggesting a negative impact of circadian disruptions on brain function, this possibility has not been experimentally examined.

Methodology/Principal Findings: In the present study, we investigated whether experimental 'jet lag' (i.e., phase advances of the light:dark cycle) negatively impacts learning and memory and whether any deficits observed are associated with reductions in hippocampal cell proliferation and neurogenesis. Because insults to circadian timing alter circulating glucocorticoid and sex steroid concentrations, both of which influence neurogenesis and learning/memory, we assessed the contribution of these endocrine factors to any observed alterations. Circadian disruption resulted in pronounced deficits in learning and memory paralleled by marked reductions in hippocampal cell proliferation and neurogenesis. Significantly, deficits in hippocampal-dependent learning and memory were not only seen during the period of the circadian disruption, but also persisted well after the cessation of jet lag, suggesting long-lasting negative consequences on brain function.

Where is the endogenous circadian clock?
- Many tissues exhibit endogenous rhythms.
- Suprachiasmatic nuclei (SCN)

– Master clock in mammals

Where is the clock?
- Many tissues exhibit endogenous rhythms.
- Suprachiasmatic nuclei (SCN) – master clock in mammals
- Lesion SCN leads to arrhythmia
- Transplant SCN reinstates normal rhythm
- Transplant mutant SCN (approx. 20 h cycle) instates mutant rhythm

SCN
- Is the SCN the master clock in humans?
- Patient A.H. received SCN damage during surgery

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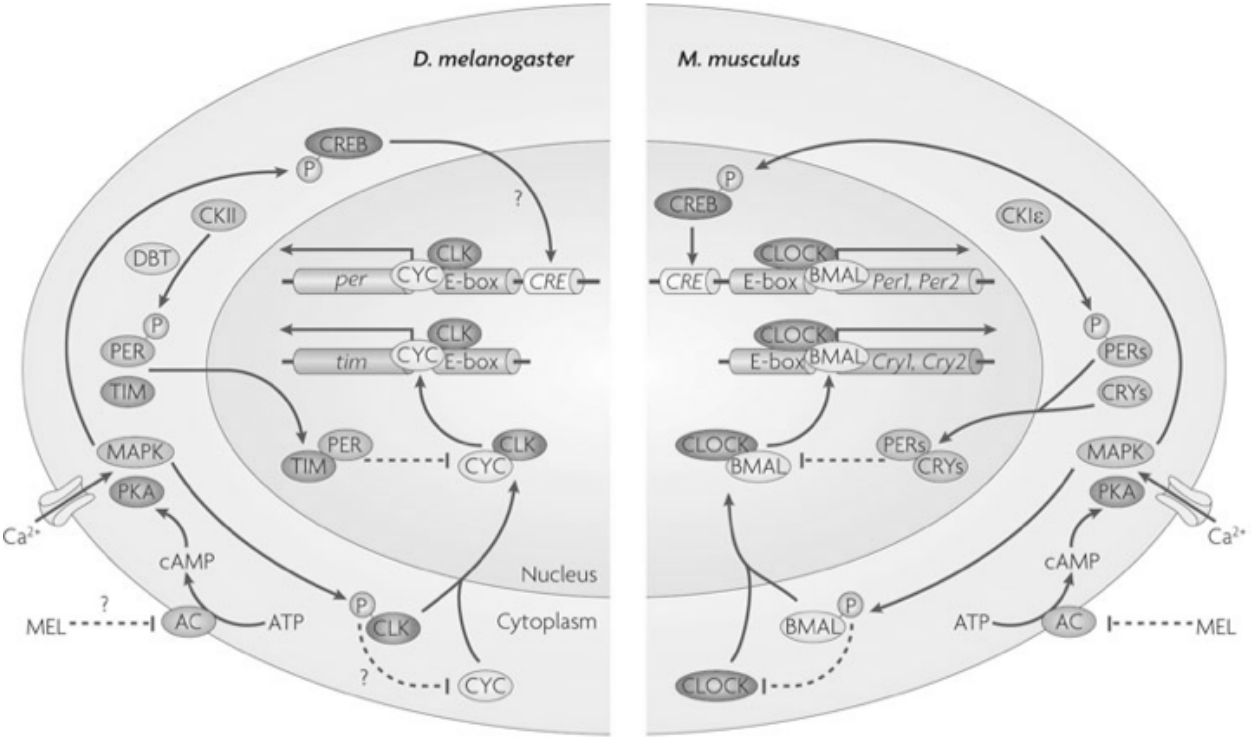
Neural mechanisms of entrainment
• In mammals (but not other animals)
– Light from the eyes entrains circadian rhythm
– NON-visual photoreceptive cells project via retinohypothalamic tract to SCN
– A form of retinal ganglion cells with melanopsin as photopigment

Molecular basis of the clock
• Highly conserved between fruit flies and mammals
• *period* (PER) and *timeless* (TIM) genes key players



Nature Reviews | Neuroscience

Molecular Basis of the Clock
• BMAL and CLOCK genes activate other genes (PER and CRY)
• Protein products of PER and CRY dimerize, reenter nucleus, inhibit further transcription of BMAL and CLOCK
• Protein products turn off their own production

Endogenous clock and sleep
• Endogenous clock > 24 hrs
• Typically we want to stay up later and sleep in
• Explains why phase delay has more rapid entrainment

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Stages of Sleep

• How is sleep measured?

– In 1950s discovered there are eye movements in certain stages of sleep, and varying EEG activity

– Combined measures in sleep labs typically include EEG, EOG, EMG

Three Standard Physiological Measures of Sleep

• **Electroencephalogram** (EEG) – Reveals "brainwaves"

• **Electrooculogram** (EOG)

– Records eye movements seen during rapid eye movement (REM) sleep

• **Electromyogram** (EMG)

– Detects loss of activity in neck muscles during some sleep stages

Stages of sleep

• Alert: low voltage, high frequency waves

• Going to sleep: appearance of alpha waves

• Enter sleep: EEG has higher voltage, lower frequency

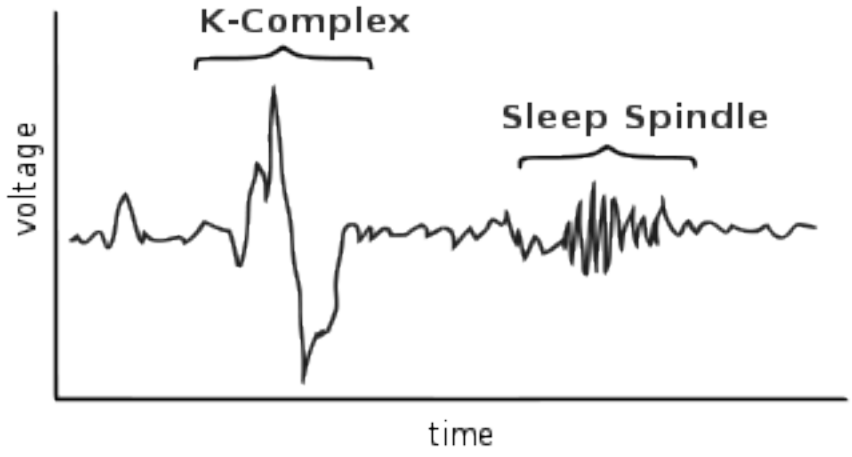
Stages of Sleep

• Stage 1

– Higher amplitude and lower frequency

• Stage 2

– Punctuation of sleep spindle and K- complex wave forms



• Stage 3

– Occasional delta waves

• Stage 4

– Dominated by delta waves

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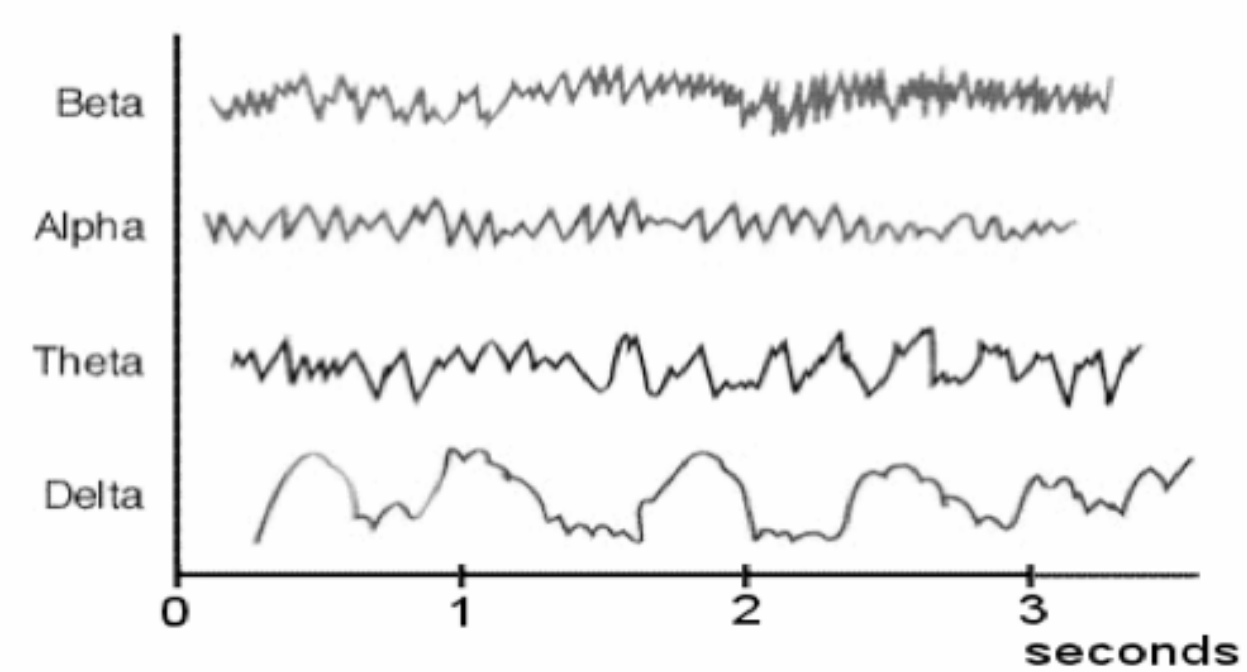

• Rest of night spent going back and forth between stages 1 to 4
• Re-entering stage 1 associated with REM (rapid eye movements) but deeply relaxed muscles
• **REM sleep:** emergent stage 1 EEG sleep
• **Slow-wave sleep (SWS):** stage 3-4 sleep

REM Sleep and Dreaming
• 80% of awakenings from REM yield reports of story-like dreams
• External stimuli may be incorporated into dreams
• Dreams run on real time
• Everyone dreams
• Penile erections are not a result of erotic dreams
• Sleepwalking and talking are less likely to occur while dreaming

Interpretation of Dreams
• Freud postulated dreams are caused by repressed desires
– But no evidence to support this (or most of Freud's other ideas....)
• Activation Synthesis Hypothesis
– Brain-stem circuits active in REM sleep
– Information supplied to cortex is largely random
– Dreams a result of cortex trying to integrate and make sense of largely random input

Why Do We Sleep?
• We are highly motivated to sleep, but why?
• A variety of hypotheses
1) Recuperation theories
2) Adaptation theories

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Recuperation Theories
• Idea that sleep is required to restore homeostasis and recuperate from being awake
– E.g. restore energy levels?

Adaptation theories
• Part of a circadian activity cycle
• Imposes rest at times of day as a result of adaptation
– E.g. diurnal animals sleep at night to avoid injury or predation, and/or to conserve energy
• Adaptation theories posit we should be highly motivated to sleep even if we don't need it to survive (like sexual behaviour)

Comparative Studies
• Sleep differs from torpor and hibernation
• Torpor and hibernation involve lowered metabolic rates
– Often animals come out of hibernation to sleep!
• Though few species studied it looks like all birds and mammals sleep
– But varied amounts (Table 14.1)
• Sleep may serve an important recuperative or other function
• Animals balance costs and (potential) benefits of sleep
• Prey animals like ungulates sleep very few hours
• Dolphins do not exhibit REM sleep, and only half of the brain engages SWS at a time
– Risk of drowning? http://www.youtube.com/watch?v=3DEE3gapfT0
• Birds also have unilateral sleep
– Potential adaptation to avoid predation or long-distance migratory flight?
• Because some species sleep very little, extended sleep may not be critical to survival
• Species' sleep times appear adapted to energy use and ecology, but recuperative function of sleep still not clear

Effects of Sleep Deprivation
• It is difficult, if not impossible, to separate the effects of **stressors** used to prevent sleep from the effects of lost sleep
• Recuperation theories predict:
– Long periods of wakefulness will result in disturbances
– Disturbances will get worse as deprivation continues
– After deprivation, much of the missed sleep will be regained

Sleep-Deprivation Case Studies
• Sleep-deprived students
– By the third night, subject found desire for sleep overpowering
Randy Gardner
– Stayed awake for 11 days
– Only slept 14 hours the first night after the study

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Experimental Studies
• Even moderate sleep deprivation has effects:
  1) Increased sleepiness!
  2) Negative affect (cranky)
  3) Reduced vigilance/ alertness
• Other effects less consistent
  1) Various cognitive tests
  2) Executive function

Sleep Deprivation
• Various physiological effects
– Body temperature, blood pressure
– Potential effects on immune function
– BUT hard to separate effects of stress
• Eventual onset of microsleeps
– 2-3 second microsleeps

Sleep Deprivation and REM
• Deprivation of REM sleep leads to REM rebound (see Fig 14.6)
– More than usual amount of REM sleep
• Compensation of REM sleep suggests independent regulation from SWS

REM Sleep and Memory
• Several hypotheses that REM is important for explicit memory consolidation
• But this idea not fully supported
– E.g. patients on antidepressants may have suppressed REM but no amnesia

REM default theory
• REM may not function in and of itself
• But alleviates extended SWS sleep
• Subjects who were made awake instead of REM exhibited no REM rebound

Sleep Efficiency
• Sleep deprivation leads to increased sleep efficiency
– Higher proportion of SWS
• Longer sleepers have proportionally less SWS
• Naps without SWS don't increase sleep that night
• Sleep deprivation training leads to reduced stage 1,2 sleep

Neural basis of sleep
• Patient case studies indicated both anterior and posterior hypothalamus were involved in sleep
• Animal studies indicate importance of reticular formation
– Low levels of activity associated with sleep
– High levels of activity associate with wakefulness

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Reticular REM-Sleep Nuclei

• Similarities between REM and wakefulness suggest that the same brain area might be involved in both

• REM sleep is controlled by nuclei in the caudal reticular formation, each controlling a different aspect of REM

Drugs That Affect Sleep

• Drugs that increase sleep (**hypnotic drugs**): benzodiazepines – Valium, Librium

– Most commonly prescribed hypnotic drugs

– Effective in the short term

– Complications

- Tolerance
- Cessation leads to insomnia
- Addiction
- Use leads to next day drowsiness
- Increase of stage 2 sleep while decrease of stage 4 and REM

• Drugs that decrease sleep (**antihypnotic drugs):** stimulants and tricyclic antidepressants

– Both increase activity of catecholamines

– Act preferentially on REM – may totally suppress REM with little effect on total sleep time

– Side effects

- Loss of appetite
- Addiction

Melatonin

• Synthesized from serotonin in the pineal gland

• Melatonin levels follow circadian rhythms controlled by the SCN

– Produced in dark phase of the day

• Pineal gland triggers seasonal reproductive changes in fish, birds, reptiles, and amphibians

• Normally secreted at night (in dark)

• Light exposure at night can decrease secretion

• Melatonin can entrain clock in mice and birds

• Some evidence of entrainment in humans

– Use as jet-lag remedy

– Entraining free-running blind people

Melatonin and sleep

• Mixed results for use of melatonin as sleep aid

• Appropriately timed dose may lead to consistent sleep for some clinical populations

• For normal sleepers melatonin may decrease sleep latency and increase sleep efficiency, but small effect size

– “Clinically insignificant” –a few minutes

• Only benefit for delayed phase sleep disorder, not general insomnia

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Melatonin
• Effects on hamster, which suppress reproduction on short days of winter
• Receptors throughout CNS
• Effects on
– Reproductive physiology
– Immune function

Sleep Disorders
• **Insomnia** – disorders of sleep initiation and maintenance
• **Hypersomnia** – disorders of excessive sleep or sleepiness
• REM-sleep dysfunctions

Insomnia
• Iatrogenic – physician-created – e.g., consequence of sleeping pill use – Alternative treatment: sleep restriction
• Sleep apnea – stop breathing during the night leads to repeated awakenings. Two types:
  • Obstructive – obstruction of respiratory passages by muscle spasms or atonia
  • Central – CNS fails to initiate breaths
– Most commonly seen in males, the overweight, and the elderly

Hypersomnia – Narcolepsy
• Severe daytime sleepiness and repeated brief daytime sleeping - "sleep attacks"
• **Cataplexy** – loss of muscle tone while awake
• **Sleep paralysis** – paralyzed while falling asleep or upon waking
• **Hypnagogic hallucinations** – dreaming while awake
• Appears to be an abnormality in the mechanisms that triggers REM
– Narcoleptics enter directly into REM
– Dreaming and loss of muscle tone while awake
  – Suggest REM intruding into wakefulness
– May be due to genetic orexin (hypocretin) deficiency

Effects of Long-Term Sleep Reduction
• Differences between short and long sleepers?
– No consistent differences
• Long-term reduction of nightly sleep?
– When reduced to 6h/night subjects often reported daytime sleepiness
– Otherwise no ill effects
– Overall sleep was more efficient
• Effects of napping?
– Some evidence that polyphasic sleep is more efficient

Effects of Shorter Sleep Times on Health
• Some evidence suggests that 5-7 hours/night of sleep is correlated with greater longevity