Sleep Deprivation, Fatigue and Effects on Performance – The Science and Its Implications for Resident Duty Hours

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Fatigue and its role in medical errors are now regarded as a challenge to providing quality medical training and care.

- **Fatigue**: Health care is a 24 / 7 industry that relies on shift work, prolonged work hours, and on-call to meet expectations.

- **Performance**: Delivery of health care relies heavily on human cognition and executive functions (judgment, logic, complex decision making, detection, working memory, procedural memory, vigilance, information management, communication, etc.)

- **Human Error and Accidents**: Unintentional human error in the workplace is the most frequently identified cause of accidents, contributing significantly across industries to $\approx 70\%$ of accidents.

- **Tradition of Evidence-Based Change**: The health care and the biomedical communities have a tradition of using science (I) to discover the effects of **specific lifestyle practices** that compromise human health and safety, and (II) to discover effective interventions for mitigating adverse effects.

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ACGME Resident Duty Hours (2002)

**monthly limit on work**

320 h to 352 h
Maximum monthly limits on Federally-regulated duty hours vary greatly across work modalities and countries

Comparative monthly (30 days) working hours

<table>
<thead>
<tr>
<th>Country</th>
<th>Hours</th>
<th>Regulation</th>
</tr>
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<tbody>
<tr>
<td>USA LH</td>
<td>100</td>
<td>14 CFR 121</td>
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<tr>
<td>EU</td>
<td>260</td>
<td>49 CFR 395</td>
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<tr>
<td>USA LH CMV</td>
<td>263</td>
<td>CMV HOS Regulations, 1994</td>
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<td>Canada CMV</td>
<td>312</td>
<td>Road Transport (Driver Fatigue) Regulations,</td>
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<td>Australia LH</td>
<td>360</td>
<td>46 USC 8104</td>
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<tr>
<td>USA Small</td>
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<tr>
<td>Maritime</td>
<td>432</td>
<td>49 USC 11</td>
</tr>
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</table>

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The public’s tolerance for risk: 
42,000 highway fatalities vs 420 commercial aviation fatalities in a year

The public’s tolerance for adverse outcomes due to human error depends in part on the perception of risk, which is influenced by perceived control and perceived lethality.

Industries in which people perceive adverse events as being beyond their control (i.e., in the hands of others) and having high risk (e.g., lethality), are often publicly required to limit work hours for the purpose of minimizing adverse events from human error (e.g., commercial pilot, physicians in training).

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Basic Science Overview

• Homeostatic need for sleep (S) and its interaction with the endogenous circadian pacemaker (C).

• Regulation of wakefulness, alertness and performance by sleep need, sleep inertia, and the circadian system.

• Neurocognitive performance changes engendered by sleep loss, night work, and inadequate recovery sleep.

• Fatigue management and countermeasures.
Sleepiness and Fatigue:
Conceptual and operational overlap

Sleepiness
• acute sleep loss (e.g., on call for 30 hours)
• chronic sleep restriction (e.g., sleeping less needed for recovery)
• circadian displaced waking (e.g., night shift work, jet lag)
• pathology of sleep (e.g., obstructive sleep apnea; pain)
• pathology of wakefulness (e.g., narcolepsy)
• sleep/waking altered by medications/drugs (e.g., sedation)

Fatigue
• physical/cognitive demands without recovery (e.g., prolonged work)
• psychological exhaustion (e.g., “burnout”)
• pathology (e.g., infections, etc.)
• physical injury/trauma
Fatigue can alter performance via interaction of the circadian pacemaker and homeostatic drive for sleep.
Sunset over North America 2-1-03

Slides courtesy of David F. Dinges, Ph.D.—Do not publish or reproduce without author's written permission.
Earth’s daily rotation on its axis relative to the sun is the fundamental orbital mechanic that underlies endogenous (molecular) circadian rhythms, and their daily regulatory influence on neurobehavioral, cognitive and physiological functions.

Sleeping easy. The organization of the circadian pacemaker. Circadian rhythms are genetically determined through gene expression in a feedback loop which, in mammals, occurs in neurons of the suprachiasmatic nucleus (SCN) (A). These neurons are individual oscillators that are coupled to form a pacemaker (B), which is connected to effector systems under pacemaker control (C). For the sleep-wake cycle the effector system is the neocortex, which receives critical input from the hypothalamus and thalamus (D). In the upper right-hand corner, the behavioral sleep-wake rhythm is shown entrained for 10 days (solid line represents waking, dashed line, sleep) in a light-dark cycle, and free-running with a period greater than 24 hours under constant light conditions.

(from Moore, Science, 1999)
Human circadian secretory profiles of melatonin (top graph) and cortisol (bottom graph) are present when sleep is taken (closed blocks) and when sleep is missed (open blocks). There is a phase difference in secretion of melatonin and cortisol.

from Dinges et al. (1999)
Fatigue based in sleep and circadian drives and their interaction with endogenous and exogenous modulators

Increased behavioral capability

HOMEOSTATIC DRIVE FOR SLEEP

Reduced behavioral capability

ENDOGENOUS FACTORS (e.g., stress, anxiety, urgency, motivation?)

neurobehavioral, neuroendocrine, (neuroimmune?) functions
(e.g., physiological alertness, cognitive performance, feeling fatigued, somatic “perceptions,” psychological effort, etc.)

EXOGENOUS FACTORS (e.g., caffeine, noise, workload, physical activity)

CIRCADIAN DRIVE FOR WAKEFULNESS

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Cognitive performance is temporally dynamic via the interaction of three neurobiological processes

- circadian timing system
- sleep-wake homeostasis
  - prolonged wakefulness (>20 hr)
  - chronic sleep restriction (sleep debt)
  - inadequate recovery sleep duration / days
- sleep inertia

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Sleep and Chronobiology Laboratory is a time- and environmental-isolation facility (and GCRC satellite), for intensive monitoring of human sleep, waking and circadian physiology and neurobehavioral functions over many days. SCL experiments involve >1,000 24-h protocols per year.

24-h EEG, EOG, ECG, EMG
24-h blood draws
24-h core body temperature
24-h infrared monitoring
24-h neurobehavioral testing

24-h behavioral monitoring

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Sleep Inertia = The hypnopompic disorientation, confusion and cognitive dysfunction that occurs upon awakening from sleep, especially deep NREM sleep (SWS), and/or sleep in the middle of the night, and/or sleep following sleep deprivation.

- Can be a serious problem for physicians on call.
- Adversely affects a wide range of cognitive performance functions.
- Occurs with as little as 30 minutes sleep.
- Amnesia for the “awakening” and cognition that occurred during it.
- Up to 2-hour duration--rate of recovery is exponential.
- Increased metabolic activity reduces it (e.g., exercise, caffeine).
Sleepiness = propensity to fall asleep physiologically

- Awakened: low voltage, random, fast
- Drowsy: 8 to 12 cps-alpha waves
- Stage 1: 3 to 7 cps-theta waves
- Stage 2: 12 to 14 cps sleep spindles and K complexes
- Delta Sleep: 1/2 to 2 cps-delta waves > 75 μV
- REM Sleep: low voltage, random, fast with sawtooth waves

EEG hypersynchrony

Sleep latency across 24-hr period

- Sleep latency with progressive sleep deprivation

Circadian phase (0° = melatonin onset)

From Carskadon
Cognitive performance is temporally dynamic via the interaction of three neurobiological processes:

- circadian timing system
- sleep-wake homeostasis
  -- prolonged wakefulness (e.g., awake 20 to 36 hours)
  -- chronic sleep restriction (sleep debt) (e.g., 5h sleep per night for 5+ nights)
  -- inadequate recovery sleep duration / days (e.g., 1 day off in 7, with only 8h sleep)
- sleep inertia

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Neurobehavioral functions across 40 hours of wakefulness

Sleepiness, cognitive errors and slowed reaction times are worse between 6 AM and 10 AM, a few hours after the circadian minimum in core body temperature (solid vertical line) and 12 hours before the end of the 40-hr vigil. This illustrates the interaction of sleep homeostatic and circadian processes in regulating sleepiness.

From Van Dongen & Dinges (2000)

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Lapses of attention by healthy adults as a function of time awake

from Van Dongen & Dinges (2000)
Fatigue studies have also been undertaken in simulator and field experiments, such as those performed by the NASA Ames Fatigue Countermeasures Program.
Prolonged human habitation of space poses both circadian and sleep loss challenges to performance and safety.
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Neurobehavioral effects of sleep loss

- Voluntary and involuntary sleep latencies shorten
- Microsleeps intrude into wakefulness (state instability)
- Behavioral lapsing (errors of omission)
- False responses (errors of commission)
- Time-on-task decrements (fatigue)
- Cognitive speed / accuracy trade-off
- Learning and recall deficits
- Working memory and related executive functions decline
Wake state stability and instability

Stable responses after an 8-hr sleep opportunity

Unstable responses after a night without sleep

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Performance becomes unstable with sleep loss

From Doran et al. (2001)

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Severe sleep attacks during laboratory performance

Failures to respond for 30 sec on a vigilance task across 42 hours of total sleep deprivation

From Konowal et al. (1999)

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Drowsy driving and fall asleep crashes:
Frequency histogram of time of day of 4,333 highway crashes in which the driver was judged to be asleep but not intoxicated.

Time of peak occurrence
8:00 a.m.

100,000 drowsy driving crashes per year (source US DOT)

From Pack et al. (1995)
Fall asleep crashes on the highway (red) versus 30-sec sleep attacks (blue) during performance in the laboratory.

Red from Pack et al. (1995)
Blue from Konowal et al. (1999)
Increases in lapsing and false responses as sleep loss progresses over 88 hr (○) relative to controls (■).

Sleepiness induces errors of omission (lapses).

Compensatory effort results in errors of commission (false responses).

From Doran et al. (2001)
Logical reasoning performance:
Effects of 1 and 2 nights without sleep on

From Heslegrave et al. (1995)

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Sleep loss results in widespread cognitive performance declines that are modulated by the circadian pacemaker.

Cognitive throughput decreases

Probed memory recall decreases

Vigilance lapses increase

Optimal reaction times increase

Slides courtesy of David F. Dinges, Ph.D.—Do not publish or reproduce without author’s written permission.
Vigilance decrement functions from experimentally-induced, medically-induced, and occupationally-induced sleep loss

1. Experimental sleep loss

2. Obstructive sleep apnea

3. Long-haul flight crews

1. Dinges et al. (1994)
2. Kribbs et al. (1993)
3. Rosekind et al. (1994)

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PET study of sleep-deprived healthy adults. Relative to normal wakefulness, sleep deprivation was associated with decreased metabolism in thalamus, prefrontal cortex, and inferior parietal cortex.

Slide courtesy of Tom Balkin, WRAIR, USAMRMC (data from Thomas et al., J Sleep Res 2001)
Subcortical mechanisms involved in wakefulness

Excitatory influences in the forebrain:

• Acetylcholine (LDT, PPT, thalamus)
• Serotonin (ascending raphe)
• Histamine (posterior hypothalamus)
• Norepinephrine (locus coeruleus)
• Orexin (medial hypothalamus)

slide courtesy of Saper & Scammell, 1999
There are substantial individual differences in cognitive response to sleep loss. Some people (type 3 responses) are severely affected, while others (type 1 responses) are less affected.

Despite large individual differences in cognitive responses to sleep loss, subjects appear to be unaware of their differential responses (type 1 = type 3 responses)

Dinges et al. (2000)
Least square regression lines fit to the relationship between PVT SD and mean RT across total sleep deprivation

From Doran et al., 2001

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Very different claims / predictions regarding effects of chronic sleep loss
Dose-response experiments on the neurobehavioral and physiological effects of chronic sleep restriction at all circadian phases.
Neurocognitive effects of chronic sleep restriction: PVT performance (behavioral alertness)

**PVT lapses**

*Differences among conditions*

\[ p = 0.036 \]

*Curvature (SEM)*

\[ \theta = 0.78 \pm 0.04 \]

*Effect sizes*

- 4 hr vs 8 hr: 1.45
- 6 hr vs 8 hr: 0.71
- 4 hr vs 6 hr: 0.43

Van Dongen et al. SLEEP (2003)

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Neurocognitive effects of chronic sleep restriction:
KSS ratings (subjective sleepiness)

KSS sleepiness

Differences among conditions
\( p = 0.001 \)

Curvature (SEM)
\( \theta = 0.16 (0.03) \)

Van Dongen et al. SLEEP (2003)

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Proportion of healthy adults experiencing severe sleep attacks (30s) during cognitive performance as a function of 3 dosages of chronic sleep restriction.

Cumulative failures to respond as a function of days of sleep restriction for 4h, 6h, and 8h time in bed (TIB) per night.

Hazards model p = 0.0025

4h time in bed (TIB) per night (46%)

6h TIB (23%)

8h TIB (0%)

Day of sleep restriction

Cumulative failures to respond

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Coping with fatigue from prolonged work hours: A non-exhaustive list of “countermeasure” categories

✓ education / training in “fatigue management”
✓ limit prolonged work (wake) periods (no 24h+ duty periods)
✓ protect recovery sleep periods (24h+ off duty)
✓ strategic use of nap sleep (prophylactic or “power” napping)
✓ strategic use of caffeine and food
✓ optimal working and sleeping environments
✓ fitness for duty discussions and periodic checks
✓ monitor error rates (know thyself)
✓ adjust performance parameters (e.g., avoid time pressure)
✓ reduce non-essential performance tasks
✓ inculcate a culture of shared responsibility
Managing fatigue and enhancing cognitive performance: Countermeasures

- **Enhance sleep** (onset, maintenance, duration, quality, timing, frequency)
  - identify and treat sleep disorders
  + ensure adequate daily and weekly recovery sleep
  + employ strategic prophylactic napping
  - judicious use of hypnotics
  + optimal work-sleep environments

- **Enhance circadian adjustment**
  - strategic use of bright light
  - melatonin and other phase-shifting drugs
  + exercise / activity / diet?

- **Enhance waking alertness/performance**
  + judicious use of caffeine (for those who can and do use it)
  - wake-promoting compounds
  - fitness for duty technologies
  - personal on-line monitoring technologies
  - system technologies (e.g., human-machine interaction)
  - environmental technologies
  + biomathematical models predicting cognitive capability

† may be useful in physician training

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Sleep, Fatigue, and Medical Training:
Setting an Agenda for Optimal Learning and Patient Care

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Sleep Research Society  
American Medical Association  
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National Heart, Lung, Blood Institute
National Institute of Nursing Research
National Institute of Aging
National Center for Research Resources

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Army Research Office
Office of Naval Research

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