Panel 1:
Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload

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Maladaptation to 23.5-h sleep wake schedule space shuttle flight STS-90 in dim light

Dijk et al., Am J Physiol. 2001
The problem
Lack of entrainment to 23.5-h and 24.6-h sleep wake schedule in dim light

‘Shuttle day’
23.5 h

T-Cycle = 23.5 Hr
Relative Clock Time (Hr)

Earth Sol
24.0 h

T-Cycle = 24.0 Hr
Relative Clock Time (Hr)

(close to) Martian
Sol 24.6 h

T-Cycle = 24.6 Hr
Relative Clock Time (Hr)

Wright Jr et al., PNAS. 2001
**Countermeasure:** Properly timed light can cause entrainment at normal phase angle

Scheer et al., PLoS One. 2007

*Martian Sol: 24.65-h T-cycle*

*Shuttle day: 23.5-h T-cycle*
Circadian desynchrony

Poor lighting
Non-24h T-cycles
Slam shifts

Disrupted sleep
Noise
Temperature
Confined space

Impaired cognitive function
mood

Disrupted neuroendocrine function
Adverse health consequences

Diagram showing the relationship between various factors and their effects on circadian desynchrony, disrupted sleep, and impaired cognitive function and mood.
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1. How well risk understood? Major disagreement in literature?

2. Report: Sufficient evidence, risk context, and concern for long-term space missions?

3. Report: Evidence that gaps most critical? Additional gaps?

4. Report: Interactions among risks?

5. Report: sufficient breath of literature?
Additional Gaps

Risk for Adverse Health Outcomes

1. Decreased sleep duration and quality:
   a) Decreased glucose tolerance
   b) Changes in energy metabolism
   c) Increased cardiovascular risk factors
   d) Changes in immune system

2. Circadian misalignment:
   a) Decreased glucose tolerance
   b) Changes in energy metabolism
   c) Increased cardiovascular risk factors
   d) Changes in immune system
Additional Gaps

Risk for Adverse Health Outcomes

1. Decreased sleep duration and quality:
   a) Decreased glucose tolerance
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   d) Changes in immune system
Short sleep lowers leptin and lowers glucose tolerance

less sleep more
sleep and cardiometabolic health

Decreased sleep quantity and/or quality

- Decreased insulin sensitivity
  - Insufficient beta-cell compensation
  - Decreased glucose tolerance

- Extra energy expenditure to stay awake

- Increased ghrelin/
  - Decreased leptin (on isocaloric diet)
  - Increased hunger &
  - Appetite

- Decreased physical activity

- Immune activation
  - Increased blood pressure
  - Changed sympathovagal balance

Energy intake exceeds increased energy expenditure
  - Altered food choices

Increased body weight

Diabetes ↔ Obesity ↔ Cardiovascular diseases

Nedeltcheva & Scheer. Curr Opin Endocrinol Diabetes Obes, 2014
Additional Gaps

Risk for Adverse Health Outcomes

1. Decreased sleep duration and quality:
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2. Circadian misalignment:
   a) Decreased glucose tolerance
   b) Changes in energy metabolism
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   d) Changes in immune system
Circadian misalignment impairs glucose tolerance

Scheer et al., PNAS 2009

+6%

+22%

Diabetic

Pre-diabetic

P=0.025

99 mg/dL

132 mg/dL

Scheer et al., PNAS 2009
• Circadian disruption plus sleep restriction impairs glucose tolerance with decreased insulin concentrations; indicating impaired beta-cell function (Buxton et al., STM 2012)

• Circadian misalignment with similar sleep loss impairs insulin sensitivity beyond effects of sleep restriction (Leproult et al., Diabetes 2014)

• Circadian misalignment after simulated 12-h slam shift impairs glucose tolerance (Morris et al., PNAS 2015) and worsens cardiovascular risk factors including inflammatory markers (Morris et al., PNAS 2016)

• Circadian misalignment after simulated 12-h slam shift impairs glucose tolerance also in chronic shift workers (Morris et al., JCEM 2016)
Pathological changes might feedback and re-enforce further changes, creating a vicious cycle.
Circadian Misalignment

Misalignment of environmental/behavioral cycles relative to the endogenous circadian system

- Environment misaligned with SCN
- Behavior misaligned with SCN

Misalignment within the endogenous circadian system

- Peripheral clocks misaligned with SCN
- Desynchrony among clock genes

Behavioral cycles

- Rest/activity
- Misalignment of specific behavioral cycle

Peripheral clocks

- Fasting/feeding
- Sleep/wake

Desynchrony among organs

Desynchrony among cells

Qian & Scheer, Trends Endocrinol Metab. 2016
Conclusions

Beyond performance decrements

• Effects of decreased sleep quantity and quality, and circadian desynchrony on adverse health outcomes (e.g., cardiometabolic, immune, energy balance) for both short-term and long-term space missions requires further attention.

• Effects can be seen very rapidly, and with maintained effect after repeated exposure and, e.g., in chronic shift workers.

• Circadian desynchrony effects need to consider complexity of circadian system, i.e., not merely compare timing of central clock with sleep/wake cycle, but recognize peripheral oscillators and other behavioral cycles (e.g., fasting/feeding).