Circadian Rhythms, Sleep, and Performance in Space

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Maintaining optimal alertness and neurobehavioral functioning during space operations is critical to enable the National Aeronautics and Space Administration's (NASA's) vision "to extend humanity's reach to the Moon, Mars and beyond" to become a reality. Field data have demonstrated that sleep times and performance of crewmembers can be compromised by extended duty days, irregular work schedules, high workload, and varying environmental factors. This paper documents evidence of significant sleep loss and disruption of circadian rhythms in astronauts and associated performance decrements during several space missions, which demonstrates the need to develop effective countermeasures. Both sleep and circadian disruptions have been identified in the Behavioral Health and Performance (BH&P) area and the Advanced Human Support Technology (AHST) area of NASA's Bioastronautics Critical Path Roadmap. Such disruptions could have serious consequences on the effectiveness, health, and safety of astronaut crews, thus reducing the safety margin and increasing the chances of an accident or incident. These decrements oftentimes can be difficult to detect and counter effectively in restrictive operational environments. NASA is focusing research on the development of optimal sleep/wake schedules and countermeasure timing and application to help mitigate the cumulative effects of sleep and circadian disruption and enhance operational performance. Investing research in humans is one of NASA's building blocks that will allow for both short- and long-duration space missions and help NASA in developing approaches to manage and overcome the human limitations of space travel. In addition to reviewing the current state of knowledge concerning sleep and circadian disruptions during space operations, this paper provides an overview of NASA's broad research goals. Also, NASA-funded research, designed to evaluate the relationships between sleep quality, circadian rhythm stability, and performance proficiency in both ground-based simulations and space mission studies, as described in the 2003 NASA Task Book, will be reviewed.

Keywords: circadian rhythms, sleep, alertness, fatigue, performance, human space operations.

NASA'S VISION "to extend humanity's reach to the Moon, Mars and beyond" requires research that focuses on how to manage and/or overcome the challenges of human space travel. The challenges not only exist in technical limitations of equipment but also in the physiological limitations of humans. The environment in which astronauts are required to work and live during space exploration can present challenges and place unique demands on human physiology that affect one's ability to adapt, perform, and live in space. Maintaining optimal levels of performance and alertness during human space missions, both short- and long-term, is critical to mission safety and success. Therefore, NASA is focusing research on the development and implementation of countermeasures and strategies that would allow crewmembers to maintain optimal performance capacity during space operations. The impact of this challenging environment on human physiology must be quantified before effective and valid countermeasures can be developed for implementation during future space exploration.

Astronaut fatigue, alertness decrements, and performance failure have all been identified as critical risk factors during extended spaceflight. The loss of the 24-h light/dark cycle, circadian disruption, microgravity, confinement, and workload demands make sleep difficult in space. Operational demands often require astronauts to override their internal biological clock (i.e., circadian pacemaker that programs them to be awake during the day and asleep at night), thus resulting in sleep and circadian disruption. Ground-based research, both basic and flight simulation studies, has demonstrated that such misalignments can result in performance decrements, subjective and objective sleepiness, decreased alertness, and sleep disruptions (4,5,46,49,52,154). As a result, crewmembers can experience fatigue when trying to perform mission-critical tasks and insomnia when trying to sleep, thus compromising the mission and increasing the risk of accidents and possible mission failure.

NASA's Office of Biological and Physical Research specifically addresses physiological and biomedical challenges associated with human space travel. The research focuses on the development of countermeasures and technologies that will help overcome the risks associated with crew health, safety, and performance during space missions. These risks are identified and assessed through implementation of the Bioastronautics Critical Path Roadmap (BCPR), a framework initiated in 1997 by the Johnson Space Center's Space and Life Sciences Directorate, to help guide NASA's bioastronautics research (109). The discussion of the paper will focus on research relevant to Risks #29 and #30 within NASA's BCPR. Risk #30, which states "human performance failure due to disruption of circadian phase, amplitude, period or entrainment and/or human performance failure due to acute or chronic degradation of

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TABLE I. BIOASTRONAUTICS CRITICAL PATH ROADMAP (BCPR) RISKS THAT ADDRESS SLEEP, CIRCADIAN, ALERTNESS AND PERFORMANCE ISSUES.*

Crosscutting Area	Discipline	Risk Number: Title Addressed
Behavioral Health & Performance (BH&P)	Behavior & Performance	# 30: Human Performance Failure Due to Sleep Loss and Circadian Rhythm Problems # 29: Mismatch between Crew Cognitive Capabilities and Task Demands
Advanced Human Support Technology (AHST)	Space Human Factors Engineering (SHFE)	# 29: Mismatch between Crew Cognitive Capabilities and Task Demands

*NASA's Office of Bioastronautics addresses research to overcome the risks of human spaceflight, making it both safe and productive. The research is guided by the implementation of the Bioastronautics Critical Path Roadmap (BCPR), which addresses the risks by identifying enabling questions within specific crosscutting areas and disciplines. Presented in the table above are those risks (Risk #29 & #30) that specifically address sleep, circadian, alertness, and performance issues with identification of the crosscutting area and discipline under which they fall.

sleep quality or quantity," focuses on the development of countermeasures for the challenges associated with sleep and circadian disruptions. Similar sleep and circadian challenges are also addressed by Risk #29, which includes research on "human performance failure due to inadequate accommodation of human cognitive limitations and capabilities" (**Table I**).

The current NASA Task Book (110) lists several research programs designed to evaluate the relationship between sleep quality and quantity, circadian rhythm stability, and performance proficiency in ground-based simulations and space mission studies. NASA funds this research both directly through NASA grants and indirectly through the National Space Biomedical Research Institute (111).

In this paper, we review the literature on circadian rhythms, sleep, and performance in space, and current countermeasure research directed at ameliorating the adverse consequences of circadian rhythmic disruption, sleep loss and disruption, and performance deterioration, all of which have been documented in several space missions. Following an overview of the basic principles of circadian rhythmicity, sleep, and performance, the history of circadian rhythm research in the space environment is reviewed along with a description of individual characteristics which may impact circadian rhythms and performance in space. The nature of light exposure in space and the use of lighting regimens as a countermeasure to circadian rhythm disruption, sleep disturbance, and performance decrements in space are then discussed. The effects of altered work/rest schedules and shift work on sleep and performance in space are examined, along with current investigations in sleep modeling and countermeasures. Finally several other variables that can affect circadian rhythmicity and sleep in space are reviewed, including microgravity, noise, exercise, workload, social isolation, space motion sickness, and miscellaneous operational flight variables.

Circadian Rhythms, Sleep, and Performance: An Overview

The circadian and sleep systems, two physiological processes, interact in a dynamic manner to regulate changes in alertness, performance and timing of sleep (22,75,144). The circadian component is controlled by an endogenous biological clock, the circadian pacemaker, which is located in the suprachiasmatic nucleus of the hypothalamus (79,104,135). The circadian pacemaker contributes to the control of waking alertness and performance in a sinusoidal fashion of approximately 24 h throughout the day. There exists a regular pattern of peaks and troughs, in alertness and performance, throughout the 24-h day. On a 'typical' 24-h cycle, with sleep nocturnally placed, performance and alertness variables reach their low point around 03:00–05:00 and 15:00–17:00 (18,102). The effect of circadian rhythmicity on performance increases as the amount of central processing or vigilance necessary for performance increases. The circadian trough in performance and body temperature associated with a decline in arousal and alertness, and reduced motivation can be defined as fatigue (56,146). However, when a circadian variable becomes desynchronized, it no longer follows a regular 24-h pattern and becomes unpredictable. The measurement of fluctuations in core body temperature or melatonin levels are two commonly used methodologies for measuring circadian rhythms (10,25). The sleep drive, a homeostatic process of exponential form, is primarily responsible for the timing of sleep and waking (22,144). The drive to sleep is at its lowest point in the morning, on awakening, and as the day progresses, the drive to sleep increases. Once sleep is initiated, this drive gradually decreases until awakening. Sleep/wake cycles in a field environment, in which subjects are ambulatory, can be reliably assessed through completion of sleep/wake diaries in combination with actigraphy, the detection and measurement of relative activity levels using a wrist-worn miniature microprocessor unit (29,73,74,83,100,118).

Fatigue, alertness, and performance levels are not only influenced by internal systems of circadian rhythms and the homeostatic sleep drive, but may also be affected by exogenous factors. Exogenous factors or zeitgebers (i.e., time givers) can include environmental factors such as the light/dark cycle, level of social interaction, and work duty demands. Although the inherent rhythm of the circadian pacemaker tends to be ~24.2-h (36), under free running conditions, it is the 24-h light/dark cycle that is largely responsible for entraining circadian rhythms to a 24-h day. Light information is received via retinal ganglion cells of the eye and is then transmitted through the hypothalamic tract to the suprachiasmatic nucleus of the hypothalamus, which is the location of the circadian pacemaker

(105,128). Following this neural pathway, light acts as a powerful stimulus in the regulation of circadian rhythms, contributing to a stable phase relationship between circadian rhythms and the sleep/wake cycle (38). Light can also aid in shifting circadian rhythms to an earlier (phase advance) or later (phase delay) time within the biological day. Additionally, use of bright light during nighttime can result in significant improvement in performance and alertness levels (26,39,68). The degree to which light regulates circadian rhythms is dependent on the duration, intensity, and frequency of light exposure as well as the phase of the circadian rhythms at which the light is received by the eye (38). Research has also suggested that the wavelength of the light is equally critical, with shorter wavelengths having a greater effect on the pacemaker compared with longer wavelengths (86). Therefore, in order to achieve the desired effects of light as a countermeasure, it is necessary to completely understand the spectral characteristics of light in the regulation of circadian rhythms and sleep/wake patterns.

Circadian Rhythms in Space

Operational demands require shifted work schedules and irregular sleep/wake cycles in flight crews during space operations. These shifts can induce a misalignment between the phase of the circadian pacemaker and the sleep/wake cycle, resulting in circadian disruption. Consequently, there is a dissociation between the timing of circadian physiological and performance rhythms. The consequences, as demonstrated in ground-based studies, can be increased sleep disruption, malaise, performance errors, uncontrollable sleep periods intruding into waking hours, a more negative mood and decrements in social interaction, inefficient communication, and accidents (69,151). This overall impairment of performance proficiency results from the shifting of performance times to an unfavorable phase of the performance circadian rhythm. It was not until 1967, during the Gemini Program, that the first evaluation of human circadian rhythms in space occurred (16). Although no circadian rhythm disturbances were reported, this and subsequent spaceflight studies were not specifically designed to evaluate circadian rhythms; and the presence of circadian rhythmicity was only passively observed in physiological data collected in other investigations. However, in animal studies, circadian rhythms were documented for the first time, during spaceflight, in an instrumented rhesus monkey on the Biosatellite III mission in 1969 (66). It was not until almost 30 yr later that the first studies focusing specifically on circadian rhythms were conducted, in macaque monkeys (2) and rats (58), under rigorous environmentally controlled conditions during spaceflights. Changes in circadian rhythmicity, such as significant changes in free-running periodicity, changes in circadian rhythm phase, waveform and internal phase relations were observed.

Collection of reliable human circadian rhythm data in space, which requires regular sampling intervals over a 24-h period, is often compromised by operational constraints, altered work/rest schedules, certain medications, exercise regimens, and exposure to highly variable light intensities. Therefore, the first comprehensive acquisition of human circadian rhythm and sleep data was not conducted until the 1988/89 Mir mission (63) and the first comprehensive study of human circadian rhythms, sleep, and performance in space was not completed until 1996 during the STS-78 Spacelab mission (98,100). Circadian rhythms, as assessed by core body temperature, were similar in phase and amplitude to those on the ground, with a slight reduction in amplitude in flight, but showed little evidence of free-running. The temperature rhythm waveform was more of a sawtooth shape, which was not observed in ground-based (head-down tilt bed rest) studies, but was reported in a subsequent flight study (43). Monk and colleagues (100) concluded that the circadian system was resilient to the mission environment, despite an operationally imposed 23.6-h sleep/wake cycle and that the morning reveille wake-up was a powerful signal and possible zeitgeber for the circadian rhythms of the crew. Although the authors found that circadian rhythms in space appeared to be very similar in phase and amplitude to those on the ground, and were appropriately aligned for the required work/rest schedules, data collected in other spaceflights indicated the presence of circadian rhythm disturbances during spaceflight. Gundel and colleagues found circadian rhythms of body temperature and alertness to be phase delayed 2–3 h with no change in amplitude in one astronaut over an 8-d mission (64). However, due to the short duration of the flight, it was not possible to determine whether the phase delay represented a circadian phase shift or free-running periodicity. In a subsequent Mir space station mission, three of four astronauts exhibited a phase shift of 2 h with evidence of reduced circadian amplitude in core body temperature compared with baseline data collected on Earth (65). According to the investigators, the phase shifts in these studies were attributed to later bed times and reduced zeitgeber strength. In more recent studies of STS-85 and STS-90 crewmembers, in-flight mood and performance deterioration was associated with progressive decreases in the circadian body temperature rhythm amplitude and a phase delay in the cortisol rhythm relative to sleep onset (43,112). Shorter than 24-h rest-activity schedules and exposure to light/dark cycles inadequate for optimal circadian synchronization may have contributed to these disturbances (112). In fact, it is not uncommon, due to operational constraints, for several consecutive sleep episodes to be scheduled on a 22.5-h day, as opposed to a 24-h, which can induce sleep onset insomnia (34). Very few studies have documented the long-term effects of spaceflight on circadian rhythms. Circadian rhythms, measured by oral temperature and alertness ratings, were evaluated in one astronaut on a 122-d Mir mission (103). During the last 12 d, disruptions in sleep occurred in association with reduced circadian amplitude. In another long-duration flight, circadian rhythm fluctuations stabilized considerably on the 120th day of flight and remained stable over the rest of the flight (7). However, another study showed that, in one cosmonaut during a 438-d

Mir flight, circadian body temperature rhythm phase was delayed, relative to baseline, by 2:52 h (first 30 d of mission), 3:25 h (mission days 183–215), and 1:34 h (mission days 395–425), but this change was attributed to changes in zeitgeber strength and structure on Mir (63).

There are several individual characteristics that may affect performance in the space environment. Certain individuals are more susceptible to sleep loss or to the debilitating effects of shifted work/rest cycles (133), which may be dependent on individual circadian rhythm chronotypes (3,143). Prior experience as subjects in simulated microgravity (bed rest) studies enhances adaptation to the simulated space environment (41). Gender differences have been documented in cognitive abilities (67) and psychomotor performance (54,94).

Differences in circadian chronotype may differentiate the capacity to adjust to altered sleep/wake schedules. A number of individual circadian rhythm indices, including morningness-eveningness (ME), rhythm phase, amplitude, and stability, have been evaluated as predictors of adaptability to circadian phase shifts (95). There is a continuum of individual behavioral and physiological circadian rhythm phase differences in humans under entrained conditions which range from morning types to evening types (51,71,140). These individual differences in circadian rhythm characteristics suggest that there will be significant differences in the capacity of a given space crewmember to maintain adequate sleep and physiologically adapt to work/rest schedule shifts and shortened sleep/wake cycle schedules. The effect of space environmental factors on performance is likely to vary idiosyncratically among crewmembers based on individual performance, physiological and circadian rhythm characteristics, prior spaceflight experience, and gender. A ground-based research study was recently completed that investigated the extent to which individual performance responses to extended duration mission demands were a function of recent sleep/wake history, trait-like neurobehavioral vulnerability, and/or sensitization or adaptation as a consequence of previous exposure (145). The results revealed that there were differences in performance among individuals, but performance responses were not related to sleep/wake history or previous exposure, and there appeared to be trait-like characteristics within the individual for performance responses. Prior knowledge of individual performance responses to sleep deprivation conditions can provide predictive reliability for the capacity of a given crewmember to adjust to the altered work/rest schedules encountered during space missions.

Light Exposure in Space

Astronauts in space are exposed to variable light levels due to the non-24-h orbital cycle (day/night) of space operations, such as the 90-min orbital cycle of the Space Shuttle. Additionally, light levels in the space environment can be variable. Field data have shown that light levels aboard spacecraft can be as low as 10 lux during the highest activity portions of the day and as high as approximately 80,000 lux on the flight deck (43). Therefore, highly variable light intensity exposure (43) and reduced sensitivity to zeitgeber strength during space missions can further contribute to circadian disruption (59). The Soviets recommended 400–500 lux of full spectrum light for work on spacecraft (20) and results demonstrated an improvement in performance when the location of lights on Salyut-7 was changed to maximize lighting (19).

NASA currently uses light treatment to facilitate adaptation of the circadian timing system in preparation of missions, allowing the astronauts to be physiologically alert when critical tasks are required (33). The timed use of bright light to facilitate circadian phase shifts was effective in the STS-35 mission, the first mission requiring both dual shifts and a night launch. Subjective reports indicated that they were able to obtain better quality sleep during the day and remain more alert during the night after using the bright light exposure to facilitate their in-flight schedule adaptation prior to the launch dates (35). Another ground-based experiment evaluated a 7-d protocol combining bright-light exposure with sleep shifting in eliciting a 12-h phase-shift delay in eight U.S. Space Shuttle astronauts before launch. By the 4th to 6th day of the 7-d protocol, seven of the eight crewmembers showed phase delays in melatonin, cortisol, and 6-hydroxy melatonin sulfate, falling within 2 h of the expected 11- to 12-h shift (149).

With NASA's renewed support of a manned mission to Mars, the effects of a Mars light/dark cycle must be investigated to determine the ability of the human to adapt to a Mars cycle and its impact on physiological alertness. In support of the manned mission to Mars, ground-based research is being conducted to evaluate the ability of the human circadian pacemaker to entrain to a period outside the 24-h period of Earth (**Table II**; Czeisler). The research is also assessing intermittent light exposure as a countermeasure approach. The Martian day, otherwise known as a sol, is approximately 39 min longer than an Earth day (sol period = 24.6 h). Although this period length is well within the circadian range of entrainment according to previous studies conducted in relatively bright light (23–27 h; 11), preliminary laboratory results have suggested that in dim light conditions, such as found indoors, humans cannot reliably entrain to a 24.6-h Mars sol; and those who have periods shorter than 24 h, which is about 25% of the population, will have the greatest challenges in entraining to a Mars sol (37). The results will benefit NASA in developing procedures for light manipulation approaches to maximize alertness and consolidated sleep times during a manned mission to Mars.

Ground-based research is currently in progress to aid in the development of light countermeasure regimes (Table II; Brainard). The research is focusing on the influence of different wavelengths in the regulation of circadian rhythms by studying their effects on the production and secretion of melatonin in healthy human subjects. The wavelengths include those greater than 600 nm (Mars' atmosphere) and less than 440 nm [International Space Station (ISS) and Space Shuttle], since they are likely to be encountered by astronauts in space

TABLE II. NASA'S OFFICE OF BIOLOGICAL AND PHYSICAL RESEARCH (OBPR) TASKBOOK PROJECTS FOCUSING ON SLEEP, CIRCADIAN, ALERTNESS AND PERFORMANCE ISSUES.*

Research Title	Principal Investigator	Institution	Funding Source	Research Type
Optimizing Light Spectrum for Long Duration Space Flight	George C. Brainard	Thomas Jefferson University	NSBRI	Ground
Performance and Sleep Consequences of Repeated Phase Shifts Within Appendix K Guidelines	Timothy H. Monk	University of Pittsburgh Medical Center	99-HEDS-03	Ground
Circadian Entrainment, Sleep-Wake Regulation and Performance during Space Flight	Charles A. Czeisler	Brigham and Women's Hospital, Harvard Medical School	NSBRI	Ground
Countermeasures to Neurobehavioral Deficits from Partial Sleep Loss	David F. Dinges	University of Pennsylvania School of Medicine	NSBRI	Ground
Sleep-wake Actigraphy and Light Exposure during Spaceflight	Charles A. Czeisler	Brigham and Women's Hospital, Harvard Medical School	98-HEDS-02	Flight
Astronaut Scheduling Assistant: Biomathematical Model of Neurobehavioral Performance Capability	Melissa M. Mallis	NASA Ames Research Center/Fatigue Countermeasures Group	AHST SHFE	Ground

*The Office of Biological and Physical Research (OBPR) task book is an online, searchable database that includes descriptions of all peer-reviewed and internal NASA research activities funded by OBPR. Yearly completion of the database, which includes an annual report and the status of the research, is required for all Investigators. Presented in the table above are those research projects, from the 2003 task book, that are focusing on the relationships between sleep quality, circadian rhythm stability, and performance proficiency in humans.

environments. These data will allow for the determination of the best spectral characteristic required for the development of effective light tools to help both crewmembers and ground controllers maintain stable circadian rhythm and sleep/wake cycles and inform design specifications for light and transmission levels of space vehicles and habitats.

Altered Work/Rest Schedules in Space

Significant decrements in performance can occur if work times are scheduled several hours before or after peak circadian performance levels, which could occur with large shifts in sleep/wake schedule times. Staggered sleep schedules, in which one crewmember sleeps while another crewmember works can result in a shift in sleep and circadian rhythms and have been a major cause of sleep disturbances in space, especially in earlier missions such as Gemini and Apollo (16,17, 34,60,62,113,129,130,132,139). Around-the-clock operational tasks often require splitting crews into two separate shifts, requiring half the crew to invert their sleep/wake cycles (34). A procedure called "slam shifting," which involves abrupt shifts of up to 12 h, is now used to align the sleep/wake schedules of Space Shuttle and ISS crews on docking (112). Staggered sleep schedules on an 8-d mission did not work since the crew tended to retain ground-based work/rest cycles and the schedules resulted in increased fatigue and irritability (17). On a 1-yr flight, where sleep times for docking operations were shifted by 4.5 to 5.0 h 14 times, asthenia, end of day fatigue, and sleep disruptions were documented (62). Several space missions [Soviet Salyut-4, Salyut-6, and Soyuz (6,85,3); Space Shuttle STS-90 and STS-95 missions (43,112)] have used shortened (23.33–23.66-h) work/rest schedules. Cosmonaut Sevast'yanov reported the regime to be a real "scourge" during the Salyut-6 mission (6) and deteriorations in sleep and workload performance were associated with shifted sleep/wake schedules and 23.5-h work/rest cycles in Salyut-4, Salyut-6, and Soyuz missions (6,85,3). However, when regular 24-h sleep/wake schedules are maintained in ground-based, head-down bed rest studies and performance tests are administered during waking hours from 1–2 h after awakening to 1–2 h before sleep onset, no significant diurnal variation in most performance test metrics is found (42,78). Current astronaut crew scheduling guidelines allow for astronauts' schedules to be lengthened by no more than 2 h (phase delay) and shortened by no more than 30 min (phase advance) within a given day (108). Schedules can be lengthened only if there is an operational requirement. For example, if the shuttle is going to dock with ISS during a time that the ISS crew is scheduled to be sleeping, operations would require the ISS crew to shift to a new schedule in the days preceding, in order to be awake and alert for the docking. If the ISS crew needed to awaken at 04:00 when their normal waking time is 06:00, they would require a phase advance of 2 h of their sleep cycle. This could be accomplished by either phase advancing or delaying in the days preceding the docking, in accordance with Appendix K guidelines (108). Although Appendix K scheduling guidelines allow for the crew to adapt to a new schedule, such schedule changes can occur repeatedly over consecutive days, thus worsening circadian disruption. Ground-based research is currently documenting the effects of repeated phase shifting on the circadian pacemaker, specifically examining the effects on sleep, physiological alertness, objective performance, and mood. Specific to Appendix K scheduling guidelines, the research is aimed to determine if shifting to an earlier schedule (phase advances of 30 min) is more beneficial than shifting to later times (phase delays of 2 h) (Table II; Monk). Preliminary data collected on 10 individuals in the phase delay condition suggested that the circadian pacemaker is not able to entrain to repeated 2-h phase delays, implying that the guidelines outlined in Appendix K be reevaluated for the effects of circadian shifting on physiological alertness, neurocognitive functioning, and mood.

It is not only astronauts traveling to Mars who will be challenged by the inability of the circadian pacemaker to entrain to a Mars sol, but ground control personnel involved in Mars-related space missions will also be challenged by circadian and sleep disturbances. Demands of the recent Mars Exploration Rover (MER) operations required personnel to perform mission-critical tasks in accordance with a 24.6-h Mars sol. In other words, the Mars schedule required a daily shift in which individuals went to sleep and reported back to work approximately 39 min later every day, while still being exposed to the 24-h light/dark cycles of Earth. MER personnel volunteers participated in data collection for a NASA Fatigue Countermeasures Group-led study to document the sleep/wake schedules and alertness levels during actual operations (greater than 90 d).

This was the first time adaptation of the sleep/wake cycles of individuals on Earth to a Mars sol was documented in the field while being exposed to 24-h Earth time cues. Performance data were also collected daily on a subset of the volunteers, but only during the last week of working on a Mars sol schedule. These data analyses will be informative for the development of procedures and scheduling techniques for operating on Mars time, such as for NASA's Mars Smart Lander project and for the manned mission to Mars. Missions Operations Directorate personnel at Johnson Space Center provide around-the-clock coverage of critical tasks during operations. They are also subject to the effects of shift work and erratic schedules on alertness and performance, further supporting the need for additional data collection in ground crew support of space operations.

Sleep in Space

Although NASA scheduling requirements recommend a preferred sleep period of 8 h, with a minimum of 6 h, for both single and dual shift space missions (108,129), significant sleep loss and disturbances have been reported during most space missions. It has been documented that nightly sleep durations of astronauts in orbit are about 6 h, with some obtaining less than 4 h (77), as compared with an average of 8 h on the ground. This has been documented in numerous studies involving polysomnographic measurements (1,35,43,64,65,98, 100,101,136,137), actigraphy, and subjective reports (35,43,63,98,100,103).

Sleep/wake cycles can be either longer or shorter than 24-h cycles due to operational demands, resulting in further misalignment between the phase of the circadian pacemaker and the sleep/wake cycle. Overall, sleep reduction observed during the shortened sleep/wake schedules may result from scheduled bed times that coincide with the wake maintenance zone, the time when the circadian rhythm programs wakefulness, which could lead to sleep disruption (43). Crewmembers can also experience insomnia due to sleeping during an adverse circadian phase. For example, a sleep/wake cycle that is longer than 24 h can occur when the shuttle or ISS Progress is scheduled to dock with the ISS 3 h after scheduled bedtime, thus forcing astronauts to lengthen their day. This extended wake time can contribute to a sleep debt and increasing levels of fatigue.

The first sleep documented to occur in space was during 1961 and was that of the Soviet cosmonaut Titov of the Vostok-2 mission (60,131). The first attempt to sleep for consecutive nights (four) occurred in Vostok-5 in 1963 (132,139). Gordon Cooper was the first astronaut to sleep and nap in space (Mercury mission; 139). The Gemini VII mission marked the first instance of electroencephalographic (EEG) recordings (55 h from astronaut Borman) of sleep in space (1). Astronauts on the Apollo missions reported that sleep generally was intermittent and was more difficult the first night but normal in 3–4 d. A few instances occurred of no sleep during the first night in space, primarily in the early missions (130). Only minor sleep problems were reported on Skylab (57) and on Salyut-6, 7, which were 96- to- 175-d missions (20) where a 24-h schedule and planned workloads were maintained (57).

Although reductions in total sleep time may have been strictly due to operational constraints (e.g., mission length, uncomfortable sleeping environment) during the earlier missions, sleep difficulties and reductions in sleep times continue to be reported in more recent space operations. Reports collected during a flight debriefing survey of 58 astronauts found astronauts reported daily sleep to be 6.03 h in space compared with 7.9 h while on the ground (129). This comprehensive study was conducted in response to the numerous reports of sleep problems during space missions. It was found that sleep disruption was a common occurrence on shuttle missions, particularly on critical first (duration = 5.7 h) and last (duration = 5.6 h) mission days. On other days, sleep durations were reduced 1.7 h during flight relative to 7.9 h preflight. Many crewmembers had fewer than 5 h sleep on some nights and some had 2 h or less. In another comprehensive study, sleep was recorded from five astronauts and cosmonauts from the NASA/Mir Program during preflight (26 nights), flight (24 nights) and postflight (14 nights) and they found that in-flight sleep time was reduced by 27% (136). Partial sleep deprivation was scientifically documented on later shuttle flights, where sleep data were collected. Sleep decreased from 6.5 h preflight to 6.1 h during flight (STS-78) and sleep durations were $<$ 5 h on 11 crewmember nights (98). On STS-90 and STS-85 missions, average sleep duration was reduced from 7.0 to 6.6 h (43). The authors concluded that sleep loss was a strongly reproducible finding and common occurrence of living in space for about 2 wk. Soviet space missions have also documented several instances of sleep problems (82).

The first polysomnographic study of sleep occurred on the 1988/89 MIR mission (63) while the first study of sleep in conjunction with circadian rhythms and performance in space occurred on the STS-78 mission (100). Polysomnographic studies of sleep in space have shown changes in sleep architecture including severely diminished rapid eye movement (REM) sleep, decreased REM latency, redistribution of slow wave sleep from the first to the second sleep period (63,65), general decrease of slow wave sleep (100), increased sleep movement arousals (97), reduced sleep efficiency (89% preflight to 63% in flight; 136) and reduced subjective sleep quality (136). Observed decreases in delta activity during slow wave sleep are of concern since this sleep is considered the deepest and most restorative sleep stage (100). Alterations in sleep architecture have also been documented in other Mir flights (97,137). These findings of changes of sleep architecture in space suggest that in addition to total sleep time reduction in space, there is a disruption of process S, the restorative component of sleep (22). Such chronic reductions of total sleep time and the restorative component of sleep during spaceflight raise concerns about the cumulative adverse effects such factors may have on neurobehavioral performance and physiological alertness since achieving adequate levels of sleep is the only way to maintain maximal alertness and performance levels.

Sleep medication use is further evidence of the existence of in-flight sleep loss and disruption during spaceflight. A recent evaluation of pharmaceutical use on 79 space shuttle missions (120) found that, of 219 person-flight records examined, 45% indicated consistent medication use for sleep disturbances. This confirmed the earlier findings of a 1994 study in which 30% of astronauts were reported to request sleep medication (113). Also, Santy found a 50% sleep medication use in dual-shift missions and 19.4% use in single-shift missions (129). These numbers are more than threefold greater than the percentage of Americans estimated to use sleep hypnotics in a given year, which indicates that crewmembers' sleep in space is seriously disturbed (34). Dual shift operations, which require half the crew to invert their sleep/wake cycles, result in 2.5 times as many crew individuals resorting to sleep medication as on single shift missions (129). The benzodiazepines used in sleep medications are effective as hypnotics, but their adverse side effects include carryover sedation, performance impairment, anterograde amnesia, and alterations in sleep EEG activity (36). As an alternative, 0.3 mg of melatonin exhibited appropriate hypnotic properties for treating sleep disruption without significant side effects in ground-based spaceflight simulations, but no beneficial effects of 0.3 mg of melatonin were found when used as a countermeasure during the STS-90 Neurolab mission (112).

A countermeasure alternative to sleep medications is the use of naps when operational demands during space operations will not allow for a consolidated 8-h period of sleep. Ground-based research is being conducted to determine optimal scheduling approaches for crewmembers to obtain total sleep times that would allow for maximum levels of neurobehavioral functioning (Table II; Dinges). The investigators are examining whether varying amounts of anchor sleep and nap sleep can be used as a countermeasure to prevent physiologically based performance and alertness decrements. Preliminary results suggest that nighttime anchor sleep, in combination with daytime nap sleep, does increase neurobehavioral functioning; however, the effects of the partial sleep restriction are still apparent in performance measures (4,87). Results have also shown that it is not only the duration of the nap that determines the magnitude of effect on performance, but the placement of the nap within the circadian cycle, as well as the time at which the nap is taken relative to beginning of the sleep restriction period (123). Overall, the data indicate that nap/split-sleep schedules may help maintain cognitive performance in the face of chronic sleep restriction in space (50). The data will allow NASA to develop sleep/wake schedules that will maximize sleep times through the proper circadian placement of anchor and nap sleep periods, which will result in optimal performance and alertness levels during future space operations.

The documentation of sleep quality and quantity continues in field-based research (Table II; Czeisler). There are 16 crewmembers who have volunteered from various shuttle flights and the Soyuz mission to participate in data collection using actigraphy to determine the effects of both short-term and long-term missions on sleep and circadian disruption. Ambient light levels are also being recorded, through a light sensor on the actiwatch devices, to further document the extent of variance in light exposure among astronauts and its effects on circadian and sleep disruption. Data collection also includes baseline and recovery data collected on Earth to document the differences of sleep quality and quantity pre-, during, and post-mission. The data collected will be used to help develop countermeasures to manage and prevent further sleep disturbances and associated performance and alertness decrements during space operations.

Sleep Loss, Fatigue, and Performance

The circadian rhythm is a major source of performance variability (56,146) and performance proficiency levels on future space missions could be dependent on the phase of the performance rhythms. In a simulation of space crew tasks, the most demanding task (conversion of digital symbols to words) had very low efficiency between 00:00 and 07:00–08:00 in the morning, which has negative implications for night work efficiency during piloted space missions, even when it is planned as a single event in piloted space missions (134). Performance variability from circadian disruption is of concern during extended space operations where astronauts' biological clocks would not be entrained and could potentially free-run at their endogenous period. As a result, alertness and performance can be impaired due to trying to maintain neurobehavioral functioning at an adverse circadian phase. This is further complicated by trying to obtain sleep when the body is programmed to be awake, resulting in sleep disruptions in both quality and quantity. Further research is necessary to evaluate circadian rhythm changes in space and to develop countermeasures to circadian disruption.

Individuals must be able to maintain a high level of alertness and performance to operate complex technology as well as to make critical task decisions. Any loss of awareness or decrease in maximum performance levels can have catastrophic outcomes. Most individuals are often unaware of their increasing fatigue levels and the accompanying performance deficits (44,72,127,135,155). The challenge in the identification of fatigue is that there are no biochemical markers of fatigue or sleepiness, and although unobtrusive fatigue monitoring technologies might have potential in the detection of fatigue, their feasibility in a space environment remains unproven (47,88).

The space performance literature indicates that decrements do occur, most commonly in association with sleep loss, altered work/rest schedules, and heavy workload. The transition to cosmonaut-managed workloads with rest days, establishment of psychological countermeasures, and adherence to stable 24-h sleep/wake schedules has reduced performance errors and improved workload performance on Soviet flights (20). The more definitive recent studies (e.g., 15,28,93) indicated that in the absence of significant sleep loss, workload demand, or alterations in work/rest schedules, cognitive performance is maintained but performance involving neuromotor-coordinated movement is impaired.

Sleep deprivation effects were documented as early in the space program as the 4-d Gemini mission, in which the command pilot became increasingly fatigued over several days and the crew felt some irritability and loss of patience during the last 2 d (17). Instances of emotional stress were accentuated or provoked by lack of sleep on several space missions (20). In the STS-78 mission, alertness declined from early to late flight in all crewmembers (100). Operational performance errors have been directly attributed to sleep loss on a Soviet 211-d flight (84). In a recent sleep study during an 8-d Mir spaceflight, a sleep period of 4.2 h was associated with a distinct drop in alertness and a significant decrement in a tracking test (64).

Cognitive performance test decrements occurred among the five crewmembers in the STS-90 and STS-85 missions in association with reduced sleep duration (43). During STS-78 (98) and Mir 23/24 (23,99,103) missions, performance ratings indicated that performance decrements resulted from disturbed nights of sleep with durations less than 5 h. During the last 12 d of the Mir mission, disruptions in sleep were associated with a decline in reasoning accuracy on a reasoning task (103). During one cosmonaut's 438-d Mir mission, the first 3 wk in space and postflight readaptation were associated with tracking performance decrements, elevated workload, and impairment in subjective mood. The tracking performance decrements were attributed to a fatigue-related reduction in attention and microgravity-related disturbances of sensorimotor processes (92). During the STS-78 Space Shuttle mission, performance decrements in one of four astronauts were associated with elevated subjective fatigue scores, but performance deterioration in two of the four crewmembers could not be directly attributed to fatigue without appropriate ground-based control groups for microgravity effects (53).

The time period immediately following awakening from sleep ("sleep inertia") can also result in performance task impairment and/or disorientation. This phenomenon lasts for at least 5 min in non-sleep deprived subjects (44,48) to more than 2 h after awakening (76). Performance decrements, as a result of sleep inertia, can occur during awakenings from a warning alarm noise during emergencies in spaceflight (80,119). Sleep restriction experienced by astronauts (i.e., less than 6 h sleep per night) raises safety concerns because it has been documented in multiple ground-based studies that such levels of sleep deprivation affect neurobehavioral functioning such as increased reaction times, memory difficulties, cognitive slowing, and increased lapses of attention (21,27,45,46,70,107,147). When restriction continues over successive days, significant decrements in performance can appear in less than 1 wk (14,49,145).

In recognition of the occurrence of performance decrements during space operations, NASA is focusing efforts on the development of scheduling software that will help to identify the vulnerable periods in performance functioning. The "Astronaut Scheduling Assistant" (ASA) is being developed under NASA's Space Human Factors Engineering program for use in space operations (Table II; Mallis). The ASA is a biomathematical modeling tool that combines and expands elements of currently available models of alertness based on the neurobiology of sleep/wakefulness and circadian rhythms (22,75). The biomathematical model being developed for the ASA incorporates mathematical equations predicting neurobehavioral function as affected by the homeostatic and circadian components, as well as cumulative sleep loss. In addition, interindividual variability is accounted for by the biomathematical model (89). The software tool will aid in schedule development by predicting the specific effects of sleep/wake/work schedules on individual astronaut's performance, and ultimately optimize safety for the crew within mission goals and constraints. It features a user-centered design that allows it to be useful for mission schedulers, flight surgeons, and crewmembers.

Other Variables Affecting Circadian Rhythms and Sleep

Although the focus of the current review has been on how the human physiology of sleep and circadian systems respond to the operational demands and varying light levels imposed during space operations, there are other factors that can also affect sleep patterns and the stability of circadian rhythms. According to Fowler and Manzey (55), there are two theories to account for the frequent occurrence of sleep loss and disruption in space and the subsequent performance decrements: 1) the direct effects of microgravity on the brain via vestibular or motor systems; and 2) responses to the multistressor environment. Although hundreds of factors exist that can potentially affect sleep quality/quantity and circadian rhythms disruption, only the most common variables including the effects of microgravity, environmental factors, exercise, workload, and motion sickness will be discussed below.

Microgravity: A number of factors related to microgravity itself can affect sleep quality: 1) fluid shifts; 2) absence of pressure on the body; 3) back pain; 4) reduced motor activity; 5) spacesuit discomfort; and 6) space motion sickness (132). Ground-based simulations of microgravity by bed rest and water immersion studies (73 subjects in 36 studies; 106) resulted in sleep reduction from 7.5–8 h to 6.5 h, longer sleep latencies, more frequent awakenings, and subjective impairment of sleep. Sleep deterioration in these studies was attributed to boredom. Long-duration space missions, simulated by isolation and confinement, resulted in an increase in daytime napping with a decrease in nighttime sleep by 100-min (96). However, these ground-based studies, in which boredom and monotony are common complaints, may not be adequate simulations of the space mission environments, in which excessive workloads are the common complaints (30,60,98,100, 119,132,139).

Noise: The primary environmental stressor responsible for sleep disturbance is spacecraft noise resulting from spacecraft equipment, from crewmember activities (16,17,31), and from emergency or warning alarms (80,119). Noise increases irritability and contributes to insomnia, particularly at the end of long missions, and can lead to frustration, resulting in a decrease in work productivity (20). A survey of 33 shuttle astronauts indicated that over half of the respondents reported that noise disturbed their sleep up to 5–8 times per night (150) and some crewmembers have even reported wearing earplugs during both waking and sleeping periods (8,9,80,81,114,115).

Exercise: Strenuous exercise regimens of 2 to 2.5-h duration on 3 consecutive days followed by a rest day were employed on Soviet spaceflights (20) to counteract cardiovascular deconditioning and muscle atrophy. It is expected that such exercise countermeasure regimes will be incorporated in future spaceflight mission schedules. In a simulated microgravity study, a group participating in a strenuous exercise regimen exhibited worsened mood levels relative to control and non-strenuous exercise groups (42) which was indicative of overtraining fatigue or excessive total workload. Although exercise can have adverse effects on sleep, it can also induce phase shifts in the melatonin circadian rhythm, in which late afternoon or early evening exercise regimens induced phase advances and late evening exercise induced phase delays (24,52). Repeated exposure to appropriately timed exercise sessions during space missions could be used to facilitate the adaptation of human circadian rhythmicity (13,24) and thus serve as a countermeasure.

Workload: Excessive workload has been a problem in space missions since the onset of the space program. This is in part due to the operational philosophy that astronauts must adjust to the mission rather than the mission adjusting to the astronauts. Accumulated workload fatigue is associated with sleep difficulties (139) and increased performance speed but also increased errors (124). Several instances of sleep disruption, due to mission workload demands, have been documented (16,23,30,99,119,132,139). Overloading effects are most likely to emerge during the first 2–6 wk in space, when the astronauts have to adapt to new environmental conditions and cope with a considerable workload. Excessive workload associated with sleep loss and fatigue were thoroughly documented by the flight commander of the Mir-23 mission in 1997 (23). This cosmonaut was tired from staying up past midnight most nights repairing coolant leaks and his fatigue was subsequently aggravated by a 12-night sleep study, in which his nighttime sleep was interrupted by intrusive instrumentation and awakenings for blood draws. By his own reckoning, he had not had a full night's sleep in weeks before the sleep study and had received only 2 d off in the previous 4 mo. His level of exhaustion was of such concern to flight controllers that they raised concerns to the flight doctors about his fitness to perform a spacecraft docking exercise.

Isolation environment: The spacecraft environment subjects astronauts to the potential stressors of isolation, confinement, and perception of mission-associated risks. Confinement and monotony have been implicated in sleep disruptions during long-duration space operations (132). Ground-based simulations of these conditions have been conducted using analogue environments such as Antarctic missions, isolation facilities, bed rest studies, submarines, and underwater habitats. In bed rest studies, subjects may exhibit performance decrements (12,156), improvement (41,42), or no change (138,152). Depression, irritability, and hostility are commonly reported in Antarctic missions (116), and some cognitive impairment has been documented (116). However, in submarines, the reported incidence of psychiatric illness is lower than in the rest of the Navy, and few performance decrements are reported, which was attributed to careful crew selection (148). Some have argued that maintenance of high motivation is the key to preventing performance deterioration in isolation (61,131). Therefore, in a relatively short spaceflight incorporating a highly select and motivated crew, isolation and confinement stressors are not likely to affect performance, except in a susceptible crewmember.

Motion sickness: Motion sickness results in the "sopite" syndrome, which is characterized by drowsiness, malaise, irritability, disinclination for physical or mental work, and illusions of position and motion (141), all of which would be expected to produce a detrimental effect on performance. Episodes of space motion sickness have been identified as a contributor to sleep loss or disruption (113,128,131). The effect of motion sickness on performance among individuals varies with some astronauts demonstrating performance decrements and others remaining stable (122,140). Intra-muscular injections of promethazine were first used during a shuttle flight in March 1989 and have been used on 14 other occasions since then (40). The use of anti-emetic medications by space crew to combat space motion sickness may have significant effects on performance (32,117,121,153).

Other flight variables: Several other spaceflight environmental factors have been identified as contributors to sleep loss or disruption, such as unshielded bright light sources, ambient temperature changes, spacecraft vibration, elevated CO_2 levels, and cosmic radiation [30,60,91,98,100,132,139,142; Atkov O. Personal communication; 1992 (Soviet manned space program: experience as cosmonaut-physician aboard Salyut 7; Seminar presented at NASA Ames Research Center; March 5, 1992); Goldwater D. Personal communication; 1981]. Sleep disruption attributed to physical discomfort has been reported (60,98,100,132,139) and attributed to uncomfortable or unfamiliar sleep environments or uncomfortable space suits (132,139). Sleep disruption has also been attributed to a need to void (98,100). Psychological factors have also been implicated in sleep disruption, including excitement, emotional tension, monotony, and confinement during long space missions [113,129,132,139; Atkov O. Personal communication; 1992 (Soviet manned space program: Experience as cosmonaut-physician aboard Salyut 7; Seminar presented at NASA Ames Research Center; March 5, 1992)].

NASA Takes a Comprehensive Approach in the Management of Alertness and Fatigue During Space Operations

In order to ensure safety and efficiency during space operations, NASA has taken the critical step in funding research that will allow for the planning and implementation of successful missions by understanding and considering the role that sleep and circadian physiology play in the regulation of alertness, performance, and sleep in a challenging space environment. However, in order to achieve the goal of safety, a comprehensive approach in the management of fatigue and alertness needs to be employed, which includes: 1) educational efforts; 2) effective scheduling policies and procedures; and 3) implementation of specific fatigue remedies and countermeasures (125). In recognition of the challenges of sleep and circadian disruption associated with the operational demands of space operations, NASA has already begun to address all steps of a comprehensive approach to help manage fatigue among ground personnel and during the recent Mars Exploration Rover (MER) mission. NASA invited experts to provide advice, based on scientific research, on scheduling and fatigue countermeasure approaches to be implemented during MER operations. Additionally, fatigue education training workshops on the physiological mechanisms and regulation of fatigue and alertness, countermeasure application, and schedule development, were presented. These workshops were tailored specifically for MER operations and were based on the original Fatigue Education and Training Module developed by the NASA Ames Fatigue Countermeasures Group (126). Approximately 200 MER team members were educated on the challenges associated with working a Mars day prior to the landing of the two rovers. Understanding the physiological challenges associated with working a Mars sol schedule and providing knowledge to MER personnel about fatigue, countermeasure approaches, and scheduling techniques allowed the MER team to implement approaches to help them maintain their sleep quantity and quality during different phases of their circadian cycle, with the ultimate goal of maintaining high levels of performance for the cognitively demanding tasks required for the MER project.

SUMMARY

In summary, sleep loss during space missions is a common occurrence and is associated with deterioration in sleep quality, manifested by reduced REM sleep and REM latency, increased movement arousals, and reduced and shifted slow wave sleep. Sleep loss in space results primarily from altered work/rest schedules and circadian rhythm phase shifts, uncontrolled mission workload demands, emergency alarms, and environmental conditions such as noise and physical discomfort. Total sleep deprivation, however, is relatively uncommon since only a few instances have been reported and its occurrence seems confined to the first night in space on earlier missions. However, there is substantial evidence that sleep loss and disruption during space missions is directly associated with increased use of sleep medications and deterioration in cognitive and operational performance and mood states, which could have a deleterious effect on mission safety and the achievement of mission objectives. The sleep and motion sickness medications have adverse side effects, including decreased alertness and reduced cognitive performance proficiency, which suggests the need for better countermeasures. The known effects of sleep inertia on alertness and performance proficiency continues to present a problem for the performance of space crews in response to emergency alarms.

Alterations in circadian rhythm phase, amplitude, period length, and waveform have now been documented in several spaceflights and have been associated with disturbed sleep, fatigue, performance decrements, and undesirable physiological changes in several instances. These problems have been exacerbated by the employment of dual shifts, slam-shifting, and workload demands which promote circadian rhythm instability and necessitate task performance near the nadir of circadian rhythms in arousal, performance, and motivation. Given the uncontrolled effects of schedule shifts, medications, exercise regimens, and erratic light exposure, it has not been possible to evaluate the direct effects of microgravity on circadian rhythms in humans and to determine if true incidences of rhythm disruption from external synchronizers (free-running rhythms) have occurred in space. However, results from controlled animal studies have documented direct microgravity effects on circadian period length, phase, and internal rhythmic phase relationships.

The effects of spaceflight on sleep quality, circadian rhythm stability, and performance may depend on a variety of individual characteristics, including circadian chronotype, amplitude and stability, and gender. Knowledge of these factors may enable prediction of individual adaptability to altered work/rest schedules during space missions.

Aside from sleep medications, countermeasures have primarily focused on preventing sleep disruption due to altered work/rest schedules and circadian dysrhythmia. Work is proceeding to develop more effective countermeasures using scheduled naps, optimizing exercise regimens and lighting exposures in terms of duration, intensity, and continuous or intermittent exposure. In addition to the evaluation of countermeasures, experiments are necessary to discriminate between the microgravity and multi-stressor hypotheses and these experiments should include multiple dependent measures (55). The effects of external stressors, such as sleep loss, on mental performance are not uniform but may be described by specific profiles of performance deficits across different indicator variables (90). Therefore, it is important to design experiments to evaluate the potential effects of sleep loss on performance and well-being which incorporate a variety of physiological and performance measures that provide diagnosticity (i.e., the capability of tests, measures, and sophisticated data analytical procedures to reveal the underlying causes of the decrements; 90).

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