

Sleep in Space Flight Breath Easy—Sleep Less?

Completion of the International Space Station is the most recent tangible evidence that the age of prolonged human exploration and habitation in space is dawning. There are, however, significant biomedical challenges to maintaining a human presence in space, and as more scientific research is conducted to mitigate the health risks posed by space flight, it is likely this work will provide insights into biomedical problems encountered on Earth. An excellent example of the latter outcome is the investigation by Elliott and colleagues in this issue of the *American Journal of Respiratory and Critical Care Medicine* (pp. 478–485) (1). They recorded respiration and sleep physiology in healthy astronauts during two National Aeronautics and Space Administration (NASA) space shuttle flights and compared these recordings to those made when subjects were Earth-bound before and after flight. They found that microgravity was associated with marked reductions in sleep-disordered breathing, in time spent snoring, in arousals during sleep, in respiratory rate during presleep waking, and in heart rate during both presleep waking and slow wave sleep. The results highlight not only the relative importance of gravity in ventilatory mechanics during sleep, but also reveal that within physically fit subjects there is a covariation between upper airway resistance, snoring, and the likelihood of respiratory-related arousals during sleep. It suggests Earth's gravity has a key role both in upper airway resistance and obstruction, and in the relationship of these factors to arousals during sleep.

The results of Elliott and colleagues (1) are novel, because other recent studies of human sleep physiology in space did not record respiratory variables (2, 3). These latter studies did, however, find altered and reduced sleep in space flight that in part motivated the hypothesis that sleep-disordered breathing might be the basis for the reports of sleep disturbances in microgravity. However the data of Elliott and coworkers (1) virtually rule out sleep-disordered breathing as a factor in space flight sleep alterations. In fact their results suggest that microgravity actually improves sleep by virtually eliminating arousals induced by upper airway resistance during sleep. Sleep improvement in microgravity is an unexpected finding in light of other evidence that sleep in space flight is disturbed relative to sleep on Earth.

Both the ability to sleep and the quality of sleep appear to be reduced in space flight, making hypnotic use in space relatively common—45% of all medications taken by 219 astronauts on 79 shuttle missions were hypnotics for sleep disturbances, and they were used throughout the mission (4). Although current hypnotics are relatively safe and effective for sleep initiation, they cannot solve the more ubiquitous problem of reduced sleep duration in space flight. Despite NASA's recommendation that astronauts sleep 8 h each day while in space, reports over the past 15 yr have found that during space flight daily

sleep durations average approximately 6 h (2, 3, 5, 6). The sleep results from Elliott and colleagues will be published elsewhere, but there are indications in their report that the sleep durations they recorded in space are in the range of 6.1 to 6.4 h/d (1), consistent with previous reports.

The cause or causes of reduced sleep duration in space flight remain occult. Candidates include circadian rhythm disturbance, environmental disruptions, motion sickness, excitement and stress, and mission work demands. It is likely these factors transiently affect sleep in space flight to varying degrees, but another possibility must also be considered. The marked reduction in sleep-disordered breathing engendered by microgravity may make sleep more consolidated, more efficient, and therefore afford a more rapid recovery of waking functions relative to the time invested in sleep. In other words, sleep duration may shorten in space flight because upper airway resistance is not fragmenting sleep and arousing the brain at the levels it normally does in Earth's gravity. Consolidation of sleep is essential for the homeostatic restoration of waking alertness and stable waking neurobehavioral functions (7). Fragmentation of sleep by frequent arousals, as occurs in moderate to severe sleep-disordered breathing, is typically associated with daytime sleepiness, elevated sleep propensity, and neurobehavioral deficits (8). Is it possible that even modest, nonpathological levels of arousal from sleep in healthy, physically fit subjects, can affect the recovery dynamics of sleep?

If subclinical levels of sleep-disordered breathing are reduced to near zero, as appears to be the case in microgravity, the physiological processes of sleep that result in waking restoration might occur more quickly and reduce the need for longer sleep duration. There is evidence that waking psychomotor vigilance capability—which is highly sensitive to sleep quantity—shows a saturating exponential function relative to sleep duration, such that the first few hours of sleep yield a much greater recovery of waking performance capability than subsequent hours of sleep (9). Perhaps reduction of arousals associated with respiratory events during sleep from an average of 5/h to 2/h, as Elliott and colleagues observed (1), can increase the recovery exponent as a function of sleep duration to the point where sleep time can shorten by 1–2 h while still providing full recovery. If so, astronauts chronically sleeping in microgravity for durations that average 6 h/d, should not experience the cumulative sleepiness and waking neurobehavioral impairments that have been recorded in Earth-based experiments on chronic sleep restriction (10–12). Although the astronauts appeared to be in need of sleep upon returning to Earth (1), the basis for their postflight fatigue is not known and may include the effects of returning to 1 g as well as any acute or cumulative sleep loss in space.

Clearly, to understand the implications of the findings of Elliott and colleagues (1) for health and safety during prolonged human habitation in space, the relationship between chronically reduced sleep in space flight and astronauts' waking neurobehavioral functions must be established. If we are to understand the implications of their findings for sleep on Earth, the mechanisms by which increased upper airway resistance affects sleep homeostasis must also be discovered.

DAVID F. DINGES, PH.D.
 University of Pennsylvania
 School of Medicine
 Philadelphia, Pennsylvania

References

1. Elliott AR, Shea SA, Dijk D-J, Wyatt JK, Riel E, Neri DF, Czeisler CA, West JB, Prisk GK. Microgravity reduces sleep-disordered breathing in humans. *Am J Respir Crit Care Med* 2001;164:478–485.
2. Gundel A, Polyakov VV, Zully J. The alteration of human sleep and circadian rhythms during space flight. *J Sleep Res* 1997;6:1–8.
3. Monk TH, Buysse DJ, Billy BD, Kennedy KS, Willrich LM. Sleep and circadian rhythms in four orbiting astronauts. *J Biol Rhythms* 1998;13:188–201.
4. Pucha LJ, Berens KL, Marshburn TH, Ortega HJ, Billica RD. Pharmaceutical use by U.S. astronauts on space shuttle missions. *Aviat Space Environ Med* 1999;70:705–708.
5. Santy PA, Kapanka H, Davis JR, Stewart DF. Analysis of sleep on shuttle missions. *Aviat Space Environ Med* 1988;59:1094–1097.
6. Garshnek V. Soviet space flight: the human element. *Aviat Space Environ Med* 1989;60:695.
7. Bonnet M. Sleep deprivation. In: Kryger M, Roth T, Dement WC, editors. Principles and practice of sleep medicine, 3rd ed. Philadelphia: W. B. Saunders; 2000. p. 53–71.
8. Bennett L, Langford B, Stradling J, Davies R. Sleep fragmentation indices and predictors of daytime sleepiness and nCPAP response in obstructive sleep apnea. *Am J Respir Crit Care Med* 1998;158:778–786.
9. Jewett M, Dijk D-J, Kronauer R, Dinges DF. Dose-response relationship between sleep duration and human psychomotor vigilance and subjective alertness. *Sleep* 1999;22:171–179.
10. Carskadon MA, Dement WC. Cumulative effects of sleep restriction on daytime sleepiness. *Psychophysiology* 1989;18:107–113.
11. Dinges DF, Pack F, Williams K, Gillen KA, Powell JW, Ott GE, Aptowicz C, Pack AI. Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 hours per night. *Sleep* 1997;20:267–277.
12. Balkin T, Thorne D, Sing H, Thomas M, Redmond D, Wesensten N, Williams J, Hall S. Effects of sleep schedules on commercial motor vehicle driver performance. FMCSA Report No. DOT-C-00-133, U.S. Department of Transportation; 2000.

Prevention of Ventilator-associated Pneumonia by Oral Decontamination Just Another SDD Study?

Ventilator-associated pneumonia (VAP) is a leading morbid outcome among critically ill patients with a reported incidence of 1.5 to 3% per day of mechanical ventilation. Although not universally documented, it has been associated with 20 to 30% increased risk of mortality and likely prolongs the length of ICU stay (1). Considerable efforts have been invested to develop and evaluate methods for reducing the incidence of VAP (2).

Upper digestive tract colonization by potentially pathogenic microorganisms of either endogenous or exogenous origin assumes a major role in the pathogenesis of subsequent VAP. The concept of selective decontamination of the digestive tract (SDD) is to prevent infection by modulating the carriage of these microorganisms from the oropharynx, stomach, and gut, but the relative role of each of these colonization sites has not yet been determined. Traditionally, SDD consists of nonabsorbable antibiotics applied topically to the oropharynx and/or through a nasogastric tube. In most instances, treatment with parenteral antibiotics is added in the first days after ICU admission to prevent early infections.

Ever since the observation by Stoutenbeeck and colleagues (3) in 1984 of an important reduction in the incidence of VAP in a nonrandomized comparison with a historical control group, dozens of randomized controlled trials have followed. Unfortunately, lack of standard protocols, trials in heterogeneous populations, or with insufficient numbers of patients made it difficult to derive meaningful conclusions from individual studies. During the nineties, several meta-analyses confirmed a significant reduction in infection, but the estimated impact on mortality was less evident and generated considerable controversy on the cost-effectiveness of therapy (4, 5). Recently, D'Amico and colleagues (6) conducted a refined meta-analysis in which 33 trials combining 5,727 patients were included. The effect of prophylaxis was evaluated for two distinct SDD categories: a regimen combining topical and parenteral antibiotics, or topical antibiotics only. A strong protective effect was observed for the combined regimen, both regarding the incidence of VAP and overall mortality. A clear though less extreme protection was found for topical antibiotics only, but without any impact on mortality.

The protective effect of SDD is primarily attributed to the parenteral component, which partially explains why its routine use has never become a standard of care in ICU patients (7, 8). SDD has become unpopular mainly because of concerns regarding short- and long-term emergence of antibiotic resistance, increasing costs, and enhanced mortality when inappropriate empirical antibiotic treatment of VAP is used (7, 9). These topics remain unresolved by currently available data and expert opinions reflect the same reservations (www.cdc.gov/epo/mmwr/preview/mmwrhtml/00045365.htm) (8).

In this issue of the Journal (pp. 382–388), Bergmans and colleagues (10) report a study designed to address a focused hypothesis regarding the role of SDD in preventing VAP, i.e., that colonization of the oropharynx only, and not of the stomach or gut, is responsible for subsequent infection. Consistent with their hypothesis, topical application of antibiotic paste (gentamicin, colistin, vancomycin) to the oral cavity of mechanically ventilated patients modulated oropharyngeal carriage of potentially pathogenic microorganisms, did not interfere with gastrointestinal colonization, and significantly reduced the incidence of late-onset VAP.

Does this work bring new insights into the controversial issue of SDD?

First, in contrast to previous SDD studies, the demonstration of a reduction in the orotracheal colonization without impact on the endogenous flora of the stomach and gut is significant. This provides a fresh look at the pathogenesis of VAP and the rigorous methodology of the study clearly points to the pivotal role of oropharyngeal colonization in the development of subsequent VAP.

Second, the study suggests that SDD may reduce the use of antibiotics with potential impact on additional costs, increased risk of adverse events and, most importantly, increased risk of emergence of antibiotic resistance—a priority target of health-care management (11). Unfortunately, these investigators measured overall antibiotic use without specification, and the impact on the reduction of utilization, directly derived from prevention of VAP, could not be demonstrated.