POSITION PAPER

Fatigue Countermeasures in Aviation

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Pilot fatigue is a significant problem in modern aviation operations, largely because of the unpredictable work hours, long duty periods, circadian disruptions, and insufficient sleep that are commonplace in both civilian and military flight operations. The full impact of fatigue is often underappreciated, but many of its deleterious effects have long been known. Compared to people who are well-rested, people who are sleep deprived think and move more slowly, make more mistakes, and have memory difficulties. These negative effects may and do lead to aviation errors and accidents. In the 1930s, flight time limitations, suggested layover durations, and aircrew sleep recommendations were developed in an attempt to mitigate aircrew fatigue. Unfortunately, there have been few changes to aircrew scheduling provisions and flight time limitations since the time they were first introduced, despite evidence that updates are needed. Although the scientific understanding of fatigue, sleep, shift work, and circadian physiology has advanced significantly over the past several decades, current regulations and industry practices have in large part failed to adequately incorporate the new knowledge. Thus, the problem of pilot fatigue has steadily increased along with fatigue-related concerns over air safety. Accident statistics, reports from pilots themselves, and operational flight studies all show that fatigue is a growing concern within aviation operations. This position paper reviews the relevant scientific literature, summarizes applicable U.S. civilian and military flight regulations, evaluates various in-flight and pre-/postflight fatigue countermeasures, and describes emerging technologies for detecting and countering fatigue. Following the discussion of each major issue, position statements address ways to deal with fatigue in specific contexts with the goal of using current scientific knowledge to update policy and provide tools and techniques for improving air safety.

Keywords: alertness, sleep, hypnotics, stimulants, flight time regulations, duty time regulations, sustained operations.

FATIGUE COUNTERMEASURES IN AVIATION: OUTLINE OF CONTENTS

I. DESCRIPTION OF THE PROBLEM

Pilot fatigue is a significant problem in modern aviation operations, largely because of the unpredictable work hours, long duty periods, circadian disruptions,

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This Position Paper was adopted by the Aerospace Medical Association. It was prepared by a special subcommittee of the Aerospace Human Factors Committee chaired by Dr. David Neri and consisting of the authors. The paper is intended to review the relevant literature, describe fatigue-related issues and challenges, summarize applicable regulations, and present the Association's position with respect to fatigue countermeasures.

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and insufficient sleep that are commonplace in both civilian and military flight operations (147,186). The full impact of fatigue is often underappreciated, but many of its deleterious effects have long been known. Lindberg recognized the detrimental consequences of long duty hours (and long periods of wakefulness) on flight performance back in the 1920s and scientists began to appreciate the negative impact of rapid time zone transitions in the early 1930s (134). Compared to people who are well-rested, people who are sleep-deprived think and move more slowly, make more mistakes, and have memory difficulties. These negative effects may and do lead to aviation errors and accidents. In the long term, the irregular schedules worked by many aircrews during a career may lead, as they do for shift workers, to higher incidences of stomach problems (especially heartburn and indigestion), menstrual irregularities, colds, flu, weight gain, and cardiovascular problems.

In the 1930s, flight time limitations, suggested layover durations, and aircrew sleep recommendations were developed in an attempt to mitigate aircrew fatigue. Unfortunately, there have been few changes to aircrew scheduling provisions and flight time limitations since the time they were first introduced. To add further complexity, scheduling and flight time regulations vary among different countries.

Although scientific understanding of fatigue, sleep, shift work, and circadian physiology has advanced significantly over the past several decades, current regulations and industry practices have in large part failed to adequately incorporate the new knowledge (67). Thus, the problem of pilot fatigue has steadily increased along with fatigue-related concerns over air safety. Accident statistics, reports from pilots themselves, and operational flight studies all show that fatigue is a growing concern within aviation operations.

Long-haul pilots frequently attribute their fatigue to sleep deprivation and circadian disturbances associated with time zone transitions. Short-haul (domestic) pilots most frequently blame their fatigue on sleep deprivation and high workload (28). Both long- and short-haul pilots commonly associate their fatigue with night flights, jet lag, early wakeups, time pressure, multiple flight legs, and consecutive duty periods without sufficient recovery breaks. Corporate/executive pilots experience fatigue-related problems similar to those reported by their commercial counterparts. However, again, they most frequently cite scheduling issues (multi-segment flights, night flights, late arrivals, and early awakenings) as the most noteworthy contributors (179). Weather, turbulence, and sleep deprivation, in combination with consecutive and lengthy duty days, time zone transitions, and insufficient rest periods, are blamed as well. Despite the many differences between civilian and military aviation operations, surveys of military pilots generally support the findings obtained from the commercial sector. U.S. Army helicopter pilots and crews frequently blame inadequate sleep and/or insufficient sleep quality for impaired on-the-job alertness, and like their commercial counterparts, they indicate that fatigue in general is a significant problem (51). U.S. Air Force pilots report the same problems (130). Noteworthy fatigue factors include scheduling issues (frequently changing work/rest periods, operating at night, etc.) and uncomfortable sleep conditions (leading to sleep deprivation). U.S. Navy fighter pilots deployed in Operation Southern Watch in 1992 commonly complained that sleep restriction aboard aircraft carriers led to somatic complaints, alertness difficulties, and general performance degradations (18). U.S. Air Force F-15 pilots in Operation Desert Storm indicated that around-the-clock task demands, minimal rest periods, consecutive duty days, circadian disruptions, and sleep deprivation were commonplace (58), as did F-16 pilots (189,190). U.S. Air Force C-141 pilots in Operation Desert Storm likewise complained that insufficient sleep and lengthy flight times were primarily responsible for increased fatigue (147).

Duty times and aircrew fatigue will continue to be a challenge in both scheduled passenger airlines (major, national, commuter) and cargo operations, especially with the advent of ultra-long-range (ULR) aircraft (i.e., > 16-h block-to-block). Both Boeing and Airbus are currently manufacturing ULR aircraft. These aircraft have resulted in operations with longer duty periods than those encountered in current domestic and international flights. They will also increase the demands for crews to work nonstandard and nighttime duty schedules. Thus, an important question for ULR operations is whether the strains imposed by the extension of flight duty hours beyond the limits commonly flown will effectively be mitigated by the standard fatigue countermeasures, which in part have been responsible for the acceptable safety record of existing flight operations. Without proper management, ULR operations may exacerbate the fatigue levels that have already been shown to impair safety, alertness, and performance in existing flight operations (143).

Clearly, fatigue is not a one-dimensional phenomenon, but rather the product of several factors related to physiological sleep needs and internal biological rhythms. In spite of its complex nature, the operational causes of fatigue are strikingly consistent across diverse types of aviation operations. The consequences of aircrew fatigue are consistent as well.

From a physiological perspective, both simulator and in-flight studies have documented that fatigue impairs central nervous system functioning. Cabon and colleagues (37) demonstrated that long-haul pilots were particularly susceptible to vigilance lapses during low workload periods, and that such lapses could simultaneously appear in both crewmembers flying the aircraft at the same time (an obvious safety concern). In one of the crews evaluated, both the pilot and the copilot evidenced periods of increased slow-wave electroencephalography (EEG) activity (indicative of sleepiness) by the 4th and 5th hour of a lengthy flight. Wright and McGown (232) found that pilot microsleeps occurred most frequently during the cruise portion of long-haul operations (in the middle-to-late segments of the flight) and that microsleeps were more than nine times as likely during nighttime flights compared to daytime flights. Most of these lapses go unnoticed by the affected crewmembers. Samel and colleagues (187) essentially confirmed the EEG results from Cabon et al. (37) and Wright and McGown (232) by showing that, in general, spontaneous microsleeps increased with increasing flight duration. Also, nighttime flights were again found to be more problematic than daytime flights. Rosekind et al. (177) documented the presence of physiological micro-events (slow brain activity and eye movements) even during the period from top-of-descent to landing. In one group, 87% of the pilots experienced at least one microsleep greater than 5 s in duration, and on average, the pilots experienced six microsleeps during the last 90 min of the flight. In addition to microsleeps and lapses, many pilots admit to having fallen asleep in the cockpit. Of the 1424 flightcrew members responding to a NASA survey of fatigue factors in regional airline operations, 80% acknowledged having "nodded off" during a flight at some time (55). For corporate/executive airline operations, 71% of 1488 flightcrew survey respondents reported having nodded off during flight (175).

From a safety perspective, improperly managed fatigue poses a significant risk to crew, passengers, and aircraft. A National Transportation Safety Board (NTSB) study of major accidents in domestic air carriers from 1978 through 1990 in part concluded that "… Crews comprising captains and first officers whose time since awakening was above the median for their crew position made more errors overall, and significantly more procedural and tactical decision errors" (139, p. 75). Kirsch (103) estimated that fatigue may be involved in 4–7% of civil aviation mishaps, data from the U.S. Army Safety Center suggest fatigue is involved in 4% of Army accidents (48), and statistics from the Air Force Safety Center blame fatigue, at least in part, for 7.8% of U.S. Air Force Class A mishaps (124). Furthermore between 1974 and 1992, 25% of the Air Force's night tactical fighter Class A accidents were attributed to fatigue and from 1977 to 1990, 12.2% of the U.S. Navy's total Class A mishaps were thought to be the result of aircrew fatigue (166).*

Fatigue in aviation is a risk factor for occupational safety, performance effectiveness, and personal wellbeing. The multiple flight legs, long duty hours, limited time off, early report times, less-than-optimal sleeping conditions, rotating and nonstandard work shifts, and jet lag pose significant challenges for the basic biological capabilities of pilots and crews. Humans simply were not equipped (or did not evolve) to operate effectively on the pressured 24/7 schedules that often define today's flight operations, whether these consist of short-haul commercial flights, long-range transoceanic operations, or around-the-clock military missions. Because of this, well-planned, science-based, fatigue management strategies are crucial for managing sleep loss/sleep debt, sustained periods of wakefulness, and circadian factors that are primary contributors to fatigue-related flight mishaps (178). These strategies should begin with regulatory considerations, but should include in-flight countermeasures as well as both pre- and postflight interventions. The risks and benefits of each technique should be carefully considered and balanced.

In the following sections, this position paper will summarize relevant U.S. civilian and military flight regulations, evaluate various in-flight and pre-/postflight fatigue countermeasures, and describe emerging technologies for detecting and countering fatigue.† Following each major section, position statements and recommendations will be provided for addressing fatigue in that specific context.

II. CURRENT REGULATIONS, PRACTICES, AND AN ALTERNATIVE APPROACH

a. Crew Rest Guidelines

The Federal Aviation Administration (FAA) regulates crew rest for commercial aviation (1) in documents previously referred to as Federal Aviation Regulations (FARs) and renamed the Code of Federal Regulations (CFRs). Crew rest, as defined by the CFRs, is any time that a crewmember is free from all duties and responsibilities, including flying and administrative work. The FAA places strict limitations on minimum crew rest periods. The minimum mandatory rest period for both nonaugmented and augmented flightcrews is 10 h prior to a duty period. (An augmented flightcrew is composed of more than the minimum number required to operate the aircraft.) Nonaugmented crews are also required to have a minimum 10-h rest period after the duty period ends. It is important to note that this 10-h rest period includes local travel time to and from a place of rest (but not the time required to preposition a crew). Including travel time as part of the mandatory rest time between flights reduces the time that flightcrew have available for uninterrupted sleep periods. Therefore, flightcrews often fail to obtain 8 h of uninterrupted sleep. For example, if the crew were to land at the destination airport and the hotel where they planned to obtain their crew rest was a 1-h drive away, the travel between the airport and hotel (in both directions) would total 2 h and be

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* Although differences exist between civil and military operations, it is clear similar factors and conditions lead to fatigue in both civilian and military aviation environments and fatigue mitigation strategies for both contexts should be scientifically based. Understandably, however, different regulations and operational considerations have resulted in fatigue countermeasure approaches that differ in important ways. For example, a variety of pharmacological countermeasures have been approved for use in certain circumstances by U.S. military aviators but not by civilian aviators. The current prohibition regarding use of pharmacological countermeasures by civilian pilots can be attributed to safety concerns and issues of adequate policies for oversight. The military services have addressed these issues through targeted research, explicit policies on medical oversight, and recognition of the sometimes overriding importance of operational considerations (e.g., NAVMED P-6410). The use of pharmacological countermeasures to fatigue in civilian (but not military) pilots is addressed in this paper.

† U. S. civilian and military flight regulations were utilized due to space limitations and because of ready access compared to the corresponding sets of international regulations. While a full discussion in the context of the many international regulations is outside the scope of this paper, the proposed countermeasure approaches have broad applicability given their basis in human physiology.

considered part of their rest time. Therefore, they would have 8 h maximum in the hotel to obtain recovery sleep, eat, and attend to personal needs. It is highly unlikely the crew would have the opportunity to obtain a minimum 8- to 8.25-h sleep period, the average sleep need for an adult (222). However, for augmented crews, the rest period after duty is 12 h and is extended to 18 h for multiple time zone flights. While the extended time period is an improvement, it should be noted that none of the rest period guidelines account for the timing of sleep with respect to circadian phase, despite the fact sleep propensity varies significantly with time of day, making sleep obtained during the subjective daytime shorter, of poorer quality, and less restorative than nighttime sleep (6). Instead, rest period durations are constant and independent of time of day.

b. Flight and Duty Time Guidelines

In addition to specifying crew rest times, the FAA regulates crew flight and duty time for commercial aviation (1). Flight time duty limitations for the major airlines are covered in CFRs Part 121 and in Part 135 for commuter airlines (2,3).

Flight time is the time between "block-out" and "block-in". Flight time begins when the aircraft moves from its parked position and ends when the plane is parked at its destination. Although flight time and the workload endured throughout the flight are important, total duty time should be considered also when determining an individual's level of alertness. Flight time is a subset of duty time. Duty time is longer and includes the time period between when pilots report for a flight and when they are released after a flight. Therefore, it includes any administrative work required by the airline. Maximum allowable flight time and duty time differ for nonaugmented and augmented crews (flight time: 10 h vs. 12 h and duty time: 14 h vs. 16 h). However, the augmented crews are limited to 8 h on the flight deck and are provided rest facilities for in-flight rest opportunities. Although maximum duty time is 2 h longer for augmented crews than nonaugmented crews, maximum flight time additive over 1 wk, 1 mo, and 1 yr are the same. These limits are summarized in **Table I**.

An examination of crew duty and rest guidance for commercial versus military aviation operations reveals fewer similarities than differences. The primary similarity is the requirement for the attainment of 8 h of sleep, but this is far from a hard-and-fast rule. There are usually detailed guidelines for the manner in which shorter sleep durations will be handled in civil flight operations (e.g., by requiring a shorter subsequent duty period or a longer recovery period). In most cases, single-pilot operations are more restrictive than dual-pilot or augmented crew operations. Especially with regard to long-haul flights, careful consideration must be given to crew duty time, onboard rest scheduling, layover sleep opportunities (e.g., duration and recommended timing), and recovery sleep after returning to domicile.

TABLE I. CFRS FOR MINIMUM REST PERIODS AND MAXIMUM FLIGHT AND DUTY PERIODS FOR BOTH NONAUGMENTED AND AUGMENTED CREWS.

	Non-Augmented Crew (Single- or Two-Pilot Crew)	Augmented Crew
Minimum preduty rest period	10 h	10 h
Minimum postduty rest period	10 h	12 h 18 h for multiple time zones
Maximum flight time	10 h	12 h
Maximum duty time	14 h	16 h
Maximum duty time; 1 wk	30 h	30 h
Maximum duty time; 1 mo	100 h	100 h
Maximum duty time; 1 yr	1400 h	1400 h

c. Fatigue Risk Management System (FRMS): An Alternative Regulatory Approach

Each individual type of aviation operation offers its own complexity, whether it be working extended duty days, crossing multiple time zones, sleeping at adverse circadian times, or performing during a circadian nadir. These are just a few examples of the physiologically relevant factors that are unique to every schedule. They are also affected by specific organizational needs and airport operating requirements. The combination of these factors requires a new approach that addresses operations on an individual case basis and also allows for operational flexibility. One option for approaching this is by addressing both physiological and operational factors as part of a Fatigue Risk Management System (FRMS). A multicomponent FRMS program, with a scientific foundation, helps ensure that performance and safety levels are not compromised by offering an interactive way to safely schedule and conduct flight operations on a case-by-case basis. Fatigue risk management systems offer an alternative approach to traditional prescriptive duty and flight time limitations and rest time regulations currently enforced by the FAA.

An FRMS is an evidence-based system for the measurement, mitigation, and management of fatigue risk. It includes a combination of processes and procedures that are employed within an existing Safety Management System (195). It is a nonprescriptive way to monitor fatigue risk associated with aviation operations.

Multiple groups worldwide are recommending some minimum requirements for an effective FRMS. Two examples of recommendations are provided below.

> **The U.S.-based Flight Safety Foundation has suggested the following minimum activities as part of an effective FRMS (140):**
> - Develop a fatigue risk management policy;
> - Formalize education/awareness training programs;
> - Create a crew fatigue-reporting mechanism with associated feedback, procedures, and measures for monitoring fatigue levels;

- Develop procedures for reporting, investigating, and recording incidents in which fatigue was a factor;
- Implement processes and procedures for evaluating information on fatigue levels and fatigue-related incidents, implementing interventions, and evaluating their effects.

The Civil Aviation Safety Authority in Australia has defined impact areas that an FRMS must consider (13):

- Sleep opportunity provided by schedules;
- Sleep obtained by personnel to indicate fitness for duty;
- Hours of wakefulness;
- Circadian factors;
- Sleep disorders;
- Operational demographics.

Other organizations are already testing the effectiveness of these approaches. One of the more commonly known efforts is easyJet’s implementation of an FRMS as part of their Systems Integrated Risk Assessment (SIRA). Preliminary results have demonstrated its effectiveness at reducing fatigue (200). Within the U.S., the Flight Safety Foundation (FSF) has suggested that an FRMS approach be used for ultra-long-range operations (83). Their specific recommendations are described in more detail in Section d, below. FRMS programs are not only being explored in flightcrew operations but are being used by Transport Canada with Canadian aircraft maintenance engineers (26). The International Civil Aviation Organization (ICAO) is in the process of compiling a report with the recommended components of a FRMS. The FAA is also exploring ways to implement effective FRMS based programs in operations where fatigue has been identified as an inherent risk.

d. Ultra-Long-Range Flights: A Nontraditional Approach

Ultra-long-range (ULR) aircraft will extend the longest flight duty days from 14–16 h to 20+ h. Current CFRs do not address this 4- to 6-h increase in flight duration. Consequently, there are no crew rest, flight time, or duty time regulations *specific* to ULR operations.

In anticipation of the physiological challenges associated with proposed ULR flights, the Flight Safety Foundation, Airbus, and Boeing conducted four ULR Crew Alertness workshops that involved both scientific experts and aviation operational groups from throughout the world. These workshops were interactive, allowing for focused discussions of the operational and technological issues associated with maintaining maximal alertness levels during ULR operations (83). However, the workshops not only identified the issues, but, with the guidance of the Steering Committee, developed common methods and approaches to reduce errors, incidents, and accidents involving fatigue. The recommendations were largely based on an FRMS program and included three main components: 1) development of a fatigue risk management policy; 2) formation of a Fatigue Management Steering Committee; and 3) implementation of education and training programs. Other important recommendations from the workshop subgroup meetings included the following:

- Mandatory in-flight rest periods (not optional for flightcrew);
- Identification of departure windows that consider delays (not exceeding a specified duration) and approaches to handle such disruptions;
- Informing flightcrew 36 to 48 h prior to departure of scheduled on-board bunk sleep periods;
- Recurring validation of schedules using both objective and subjective measures to inform management of necessary schedule changes.

The FAA is currently using a case-by-case approach to approve ULR city pairs. They are approving these operations by issuing a nonstandard operations specification paragraph, (OpSpec A332) “Ultra Long Range (ULR) Flag Operations in Excess of 16 Hours Block-to-Block Time” to air carriers intending to conduct ultra-long-range operations. This paragraph contains requirements designed to “optimize opportunities for flightcrew members to obtain adequate rest to safely perform their operational duties during all phases of this ULR trip sequence.” OpSpec A332 has already been issued to one air carrier.

As detailed in OpSpec A332, carriers proposing a ULR city pair are requested to present a route-specific plan to the FAA. The FAA reviews the routes, from both a scientific and operational perspective, and carefully considers duty times, flight times, and rest periods to assess the opportunities available for rest and recovery periods in preparation for, during, and after scheduled ULR flights. The carrier is also requested to provide details of the on-board rest scheme, plans to assure preduty minimum rest periods and a method for addressing delays and cancellations. After a careful review process, the FAA determines the safety of the proposed city-pair plan and subsequently authorizes the carrier to fly the route. Since issuing the original OpSpec A332, the FAA also considers predicted crew performance levels using the SAFTE model (101), a scientifically based modeling approach, in its evaluation of the proposed ULR operation. It can be an iterative process and require multiple changes in the proposed plan before approval is given. Other requirements of OpSpec A332 include both subjective and objective data collection during the ULR route within 180 d of authorization for carriers to validate the effectiveness of the fatigue mitigation strategies included in OpSpec A332. The FAA requires that all ULR assigned crewmembers receive education and city-pair specific route guides that include suggested practices for maximizing total sleep times during ULR operations.

Position Statement on Crew Rest, Flight, and Duty Time Regulations

The prescriptive rule-making approach commonly used by regulatory agencies to regulate crew rest and flight and duty times is not derived from the foundational scientific research addressing the interaction of sleep and circadian processes and their effects on performance. The risks associated with nonscience-based regulatory approaches may have been unknown in the 1930s when flight and duty time limits were first addressed. At the time, research documenting the performance and alertness decrements associated with sleep loss and circadian disruption was limited and it seemed sufficient to ensure safety via agreements between flightcrew and management. However, with the demands of 24/7 aviation operations, it has become increasingly apparent that such prescriptive approaches do not address inherent sleep and circadian challenges nor do they provide operational flexibility.

The current FAA prescriptive regulations address duty time equally across all hours of the day (e.g., 8 h of nighttime flight duty is implicitly considered to be no more fatiguing than 8 h of daytime flight duty). However, a scientifically informed regulation would consider circadian placement or time of day when establishing work duty limits. It would also consider circadian variables when identifying the placement of opportunities for rest and sleep.

One example that clearly shows that regulatory limitations are arbitrarily chosen and are not informed by the scientific research is the regulation specifying maximum yearly flight times. The maximum flight time/year is 1400 h in the United States but is 900 h in Australia (12). If the establishment of yearly flight time limits considered human physiology and had a foundation in relevant sleep and circadian science, it would be expected that these limits would be similar among countries. However, this is not the case. Based on this 500 h difference, U.S.-based pilots are authorized to fly up to 64% more hours than Australia-based pilots.

Addressing fatigue as part of a scientifically based, comprehensive safety management system can help to minimize the risk associated with current and future aviation operations. An FRMS offers a way to more safely conduct flights beyond existing regulatory limits and should be considered an acceptable alternative to prescriptive flight and duty time and rest period regulations.

III. IN-FLIGHT COUNTERMEASURES AND STRATEGIES

In-flight countermeasures discussed in this section include the following: a) napping on the flight deck (cockpit napping); b) taking a break involving change in posture, mild physical activity, and increased social interaction (activity breaks); c) bunk sleep on long-haul and ULR flights; d) in-flight rostering approaches on long-haul and ULR flights; and e) increased exposure to available flight-deck lighting. While not all are either currently sanctioned or even frequently utilized, the list is intended to be inclusive and address the gamut of possible fatigue countermeasures for pilots operating in a restrictive environment acknowledging the need for safety and operational effectiveness at all times.

a. Cockpit Napping

In situations where some sleep is possible but the amount of sleep is limited, napping is the most effective nonpharmacological technique for restoring alertness. There is an abundance of evidence that a nap taken during long periods of otherwise continuous wakefulness is extremely beneficial (22,23,74,128,171,174,217,221). However, while naps can be used as a preventive countermeasure in preparation of an upcoming duty schedule or during layover periods (176; see section IV.b.ii), cockpit napping is not currently sanctioned by the FAA.

A direct examination of the effectiveness of a 40-min cockpit nap opportunity, resulting in an average 26-min nap, revealed significant improvements in subsequent pilot physiological alertness and psychomotor performance (177). Pilots in this study were assigned to either a rest group or a no-rest group. The rest group was allowed a planned, 40-min nap during a low workload portion of the flight. The no-rest group maintained their usual flight duties and were not allowed a nap period. Physiological data showed more alertness in the rest group during the last 90 min of flight than in the no-rest group. Reaction time and lapse data (failures to respond) from the Psychomotor Vigilance Test (PVT) indicated faster responses and fewer lapses in the rest group than in the no-rest group.

These naps virtually eliminated the inadvertent lapses in alertness immediately prior to landing present in the control group. Furthermore, in-seat cockpit naps have been authorized for use in a number of foreign air carriers (e.g., Air Canada, Air New Zealand, British Airways, Emirates, Finnair, Lufthansa, Swissair, Qantas; 92) without producing adverse effects. Survey results indicate U.S. commercial pilots are, in fact, already utilizing in-seat cockpit napping strategies. In the NASA regional airline operations survey, 56% of flightcrew respondents reported they had been on a flight during which arrangements had been made for one pilot to sleep in the seat during the segment (55). For flightcrew responding to the corporate/executive flight operations fatigue survey, the number was 39% (175). In an earlier long-haul study (87), flightcrew were observed napping 11% of the available time with an average duration of 46 min (range: 10–130 min). Finally, according to a National Sleep Foundation poll (141) in which respondents from the general public were asked to rate their level of agreement with the statement “An airline pilot who becomes drowsy while flying should be allowed to take a nap if another qualified pilot is awake and can take over during the nap,” the vast majority of respondents (86%) said that they completely or mostly agree with this statement, with more than one-half (57%) saying that they completely agree.

b. Activity Breaks

Short breaks can serve to increase alertness by reducing the monotony of a highly automated cockpit environment through conscious disengagement with the flying task and, possibly, by allowing mild physical activity, depending on the type of break and the behaviors allowed during the break. Although not as effective as some other countermeasures reviewed in this paper, there are anecdotal reports from pilots indicating that many take brief, out-of-the-seat breaks as a fatigue countermeasure.

Currently, the CFRs mandate a pilot remain seated through the flight, with few exceptions.[‡] Nevertheless, activity breaks that allow a pilot to change posture by getting up out of the cockpit seat and walking or otherwise physically moving while engaging in increased social interaction can increase alertness levels for brief periods. In a study directly addressing the effects of in-flight activity breaks, pilots flew a 6-h uneventful nighttime flight (~0200 to 0800) in a high-fidelity Boeing 747-400 flight simulator after having been awake 18 to 20 h (144). Pilots in the treatment group were provided a 7-min break every hour, at which time they exited the simulator and walked to a pilot briefing room where they could also engage in conversation with an experimenter. The control group received a single break midflight. The group that received hourly breaks showed significantly less physiological sleepiness up to 15 min after the 7-min break and significantly greater subjective alertness up to 25 min postbreak. However, performance on the psychomotor vigilance task (PVT), taken 15 min after the break, showed no significant differences. Nor were there significant differences in subjective alertness and sleepiness 40 min after the break. The beneficial subjective and physiological effects of the breaks were most pronounced around the low point in body temperature (i.e., circadian trough). Matsumoto and colleagues showed similar results but volunteers were provided a 15-min walking break at a leisurely speed (129). Subjects underwent the same sleep deprivation protocol two times: one with light exercise (i.e., walking breaks) and the other without exercise. Reductions in subjective sleepiness were seen up to 15 min after the walking breaks; however, there were no significant differences in performance measures. Sleepiness ratings were significantly greater when breaks were not taken.

The beneficial effects of breaks are in part due to postural changes that occur when a pilot temporarily hands off flight-related tasks. There are consistent results from laboratory-based sleep deprivation research examining the effects of posture. In one study, subjects who underwent 20 h of continuous wakefulness showed increased EEG arousal, decreased reaction times and increased attention when completing the PVT while standing, compared to when seated (49). In another total sleep deprivation laboratory protocol of 40 h, changes in body posture improved alertness levels during the circadian trough (64).

What about a break in which the pilot briefly disengages from the flying task (which may involve only monitoring instruments) during the cruise portion of the flight but does not leave the seat? Even if there is no associated increase in physical activity, several studies indicate an improvement in alertness and performance simply associated with a cognitive break from continuous tasks. A recently published study evaluated the effects of increasing the total break time received by individuals performing data entry, a task that can be monotonous and boring (86). Four 5-min supplemental breaks were added to the already scheduled two 15-min breaks in a workday. The data entry workers were studied for 4 wk in each of the break conditions (i.e., 30-min total and 50-min total). Results showed the additional 20 min of break time, incorporated into the workday, was associated with significantly faster data entry speeds (without a loss of productivity) and reductions in reports of physical discomfort.

Data have shown that breaks also can have positive effects when individuals are experiencing partial or total sleep loss. In two different total sleep deprivation protocols, ranging from 54 h to 64 h of continuous wakefulness, individuals who received five 20-min rest breaks showed improvements in performance, alertness, fatigue, and overall mood when compared to those who received no breaks (96). These beneficial effects also translate to actual aviation environments where rest breaks have been shown to help military pilots working sustained operations overcome increasing sleepiness and fatigue levels (7).

Whether engaging in a break involving activity or simply taking advantage of the opportunity to disengage from the current task, the available data suggest that the resulting increase in social interaction often accompanying a work break can play a role in maintaining alertness, especially during the early morning hours around the circadian nadir (64). However, despite substantial evidence that breaks are beneficial, it should be noted that the findings are not universally positive. For instance, in a study of industrial engineers, Tucker, Folkard, and Macdonald (208) found that, following a 15-min break after 2 h of continuous work, the risk of on-the-job mishaps increased approximately linearly across the next 2 h such that it doubled during the last 30-min period of the 2 h. Clearly, the decision whether or not to utilize rest breaks must take into account the context in which they are being considered, including the nature of the task itself.

c. Bunk Sleep

It was concluded during the ULR Crew Alertness workshops that ensuring adequate bunk sleep is one of the most important in-flight countermeasures that can be implemented to address sleep loss and circadian disruption during extended aviation operations (83). Obtaining sleep addresses the underlying physiology of sleep loss and is the only way to reverse cumulative sleep debt. Importantly, it is an operationally feasible

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[‡] Note that the Code of Federal Regulation 121.543 specifies that "… Except as provided in paragraph (b) of this section, each required flightcrew member on flight deck duty must remain at the assigned duty station with seat belt fastened while the aircraft is taking off or landing, and while it is enroute. (b) A required flightcrew member may leave the assigned duty station - (1) If the crewmember's absence is necessary for the performance of duties in connection with the operation of the aircraft; (2) If the crewmember's absence is in connection with physiological needs; or (3) If the crewmember is taking a rest period, and relief is provided…"

approach to address sleep loss associated with extended hours of wakefulness, crossing multiple time zones, and flying during nighttime hours.

In-flight bunk sleep periods can be challenging because they need to be scheduled in consideration of operational demands and be of a duration that allows all crewmembers to receive ample rest periods to ensure the safety of the flight. The body is programmed for two periods of sleepiness throughout the day with the maximum sleep propensity occurring during the early morning hours (in the latter half of the habitual sleep episode) and a second period of increased sleep propensity occurring in midafternoon (65,213). Therefore, crews can estimate the times during a flight at which there is an increased risk of inadvertent sleepiness, and these are the best times (from a circadian standpoint) to schedule in-flight bunk sleep opportunities. If flight demands permit, utilizing these periods of increased physiological sleep propensity will help to increase both the quantity and quality of bunk sleep, subsequently reducing physiological sleepiness across the flight (53,63,65). Unfortunately, bunk rest periods often unavoidably end up at less than optimal times because of a crewmember's job responsibilities. The signal or drive for wakefulness from the circadian clock increases throughout the waking day with a peak occurring several hours before habitual bedtime (111). Thus, trying to advance sleep initiation to a few hours before habitual bedtime will likely result in difficulty with sleep initiation and reduced sleep duration.

Research has shown that environmental factors in the bunk facilities can help to promote good sleep. A survey study conducted by NASA showed that the most common factors to interfere with bunk sleep are ambient temperature, noise in the galley, and background lighting (179). These are all environmental issues that can be addressed in the design of bunk facilities. Pilots also indicated that making the sleeping quarters more private and the use of comfortable bedding and blankets help to promote the quantity and quality of their sleep.

d. In-Flight Rostering

In-flight rostering, although not commonly discussed as a fatigue countermeasure, can be used to minimize fatigue. It refers to the scheduling of flightcrew to assigned positions on the flight deck, freeing other flightcrew to obtain in-flight rest or bunk sleep. In-flight rostering is directly related to the crew complement, or number of pilots assigned to the flight and is determined — in advance — during the scheduling process. Research has shown that performance begins to deteriorate after 18 to 20 h of continuous wakefulness with all aspects of cognitive functioning and mood being affected (24). Also, shift worker studies generally indicate that long duty hours increase the incidence of physical complaints, the use of unhealthy coping behaviors such as smoking and poor diet, domestic problems, and possibly musculoskeletal disorders. Furthermore, working shifts longer than 8 to 9 h is thought to increase the probability of having accidents or making errors (84,198). It has been shown specifically in aviation that when the "time since awakening" extends beyond the median for crew position, there is an increase in overall errors (139). Therefore, a sufficient number of crewmembers is necessary to provide multiple opportunities for rest.

Proper in-flight rostering can help to minimize extended wakefulness and minimize fatigue by ensuring that at least one crewmember is always rested. Importantly, it allows for scheduling of bunk sleep in a way that minimizes the hours of continuous wakefulness for the landing pilots and utilizes crewmembers who are well rested during other critical phases of flight. However, this approach only works if crew rostering is considered in the planning stages of the flight, the crew is educated about the rostering approach, and the crew adheres to the plan during the flight.

No studies have evaluated, in the context of extended aviation operations, the specific number of crewmembers needed to ensure adequate sleep opportunities to maintain performance and safety. Simply adding crewmembers without a sound evidence-based plan of how this will improve the situation is not a valid approach. Simply providing pilots more opportunity to sleep does not ensure they will sleep longer. One study showed that when flightcrews were given a 5-h bunk sleep opportunity they averaged approximately 3 h (97). Another study found that flightcrews who were provided with a 7-h sleep opportunity obtained only 3 h 25 min of bunk sleep (194).

e. Cockpit Lighting

Much is now known about the use of properly timed bright light to shift human circadian rhythms. The use of bright light as an aid to circadian adjustment pre- and postflight is discussed in Section IV.b.iii. However, while investigated to a lesser extent, light also appears to have an acute, immediate, alerting effect on mood and performance independent of its circadian phase-shifting properties. A recent review of the literature on the acute alerting effects of light (38) shows it to be a potentially useful countermeasure at night where conditions allow its use. Light's alerting effects are often believed to be tied to its suppression of melatonin, which is ordinarily released in the mid to late evening. Hence light has the potential to mitigate the usual alertness and performance decline seen in the nighttime hours, including on the flight deck. How much light is needed? Cajochen et al. (40) showed measurable increases in subjective alertness and reductions in slow eye movements with room light levels (100–200 lux). Short wavelength light appears to have the greatest alerting effect (122), with the spectrum of typical room light containing enough energy in the shorter wavelengths to be effective. There is also some evidence that the alerting effects of light are independent of the time of day, leading to the possibility of employing light during the daytime to improve alertness and performance in individuals impaired due to prior sleep deprivation (38).

Capitalizing on the immediate, direct alerting effects of light for fatigued flightcrew is particularly appealing because the flight-deck environment with its high automation level, limited opportunities for physical activity or social interaction, steady background noise, and low nighttime light levels creates a setting ripe for boredom, complacency, attentional lapses, sleepiness, and performance decrement. Adjusting the light level is one of a limited number of possible environmental manipulations. Provided increasing the flight-deck light level at night to at least 100 lux (room light level) does not interfere with flightcrew performance or visual requirements (e.g., dark adaptation level, or ability to see outside the cockpit), such light manipulation represents a potentially beneficial in-flight countermeasure. While additional research is needed to more fully characterize the acute effects of light on both daytime and nighttime alertness and performance, it should be noted that increasing the light level is almost certain to have an effect on circadian phase (38), though it may be slight depending on the timing.

Position Statement on the Use of In-Flight Countermeasures

All of the in-flight countermeasures described above clearly have a place in sustaining the alertness and performance of aviation personnel. However, the manner in which these strategies are employed should be based on the currently available scientific knowledge and should be implemented only after thoughtful consideration.

We recommend the authorized use of in-seat cockpit napping in commercial flight operations, under appropriate circumstances, with appropriate safeguards, and in accordance with clear guidelines to ensure operational safety. Cockpit napping should be viewed as a risk management tool. Naps have been shown to significantly improve alertness and performance in ground-based and in-flight studies, and naps can help sustain aircrew performance during situations in which unexpected delays require the postponement of the next consolidated sleep opportunity. In addition, naps can improve alertness during circadian low points, especially when schedule rotations or rapid time zone transitions require that work hours extend into the pilot's subjective nighttime. In-seat cockpit naps have been proven safe and effective. However, despite the beneficial effects of these naps, they should not be used as a replacement for in-flight bunk sleep during long-haul operations. Furthermore, in-seat cockpit napping should be utilized only when everyone on the flight deck concludes that this strategy is necessary to enhance the safety of flight operations. The duration of these naps should not exceed 40 min in order to avoid excessive postnap grogginess (sleep inertia). In a NASA study (177), a 40-min nap opportunity resulted in 26 min of actual sleep. The short duration of the nap probably minimized sleep inertia due to the fact that only 8% of the participants reached slow-wave sleep (which has been associated with sleep inertia). According to Dinges (65), after 18 h of continuous wakefulness, the latency to slow wave sleep is approximately 30 min. Therefore, during a nap opportunity of 40 min, it is unlikely most people will fall asleep fast enough to obtain more than 30 min of sleep, and during that 30 min of sleep, enter into slow wave. Other studies have also shown minimal sleep inertia effects with naps less than 30 min (30,204).

We recommend the use of in-flight activity breaks in commercial flight operations, under appropriate circumstances, with appropriate safeguards, and in accordance with clear guidelines to ensure operational safety. As with cockpit naps, such breaks should be viewed as a risk management tool. In a cockpit environment, which can be conducive to sleep, breaks associated with mild physical activity and increased social interaction or even just temporary disengagement from monotonous tasks, have been shown to temporarily boost alertness. When using breaks as a fatigue countermeasure, it is recommended that shorter breaks (i.e., 10 min) be used hourly or more frequently as opposed to longer breaks, which can be relatively infrequent.

The use of bunk sleep and in-flight rostering go hand-in-hand when used as a fatigue mitigation strategy. Scheduling practices should always take into account the research on both sleep and circadian process when scheduling critical phases of flight as well as in-flight sleep opportunities. Since the development of the rostering pattern should help minimize fatigue during operations, policies are necessary to allow for flexibility in these rostering approaches if a change, once the flight has begun, will contribute to the overall safety of operations. Additionally, future applied research is needed to determine the optimal timing for crewmembers to obtain rest in order to maintain maximum performance levels. Operational research evaluating the effects of varying crew augmentation options on the efficacy of onboard sleep can help address some of these issues. In light of the fact that in-flight work/rest planning can be a complex matter, it is our position that: 1) aircrews be educated with regard to the circadian and environmental factors that influence in-flight bunk rest quality; and 2) when possible, aircrews take advantage of validated work/rest scheduling tools to develop the most effective in-flight rest pattern given the available crewmembers.

Lastly, simply increasing the flight-deck light level, particularly at night, has the potential to temporarily boost alertness and performance. While several light parameters and the mechanism of action are still being investigated, the beneficial effects have been established in several laboratory studies. Any use of light must include an awareness of its potential effect on circadian phase.

IV. PRE-/POSTFLIGHT COUNTERMEASURES AND STRATEGIES

a. Hypnotics

Sleep is often difficult to obtain in operational contexts, even in situations where efforts have been made to ensure the existence of adequate sleep opportunities. There are a number of reasons for this, but generally speaking, the difficulties are due to one or more of the following: 1) the sleep environment is less than optimal (too noisy, hot, and/or uncomfortable); 2) the state of the individual is incompatible with the ability to sleep (too much excitement, apprehension, or anxiety); or 3) the sleep opportunity occurs at a time that is not biologically conducive to rapid sleep onset and/or sufficient sleep maintenance. This misalignment of the sleep/wake cycle and endogenous circadian rhythms could be the result of shift lag, jet lag, or attempting sleep at other than the habitual bedtime or at the second circadian dip in the afternoon. For such circumstances, the U.S. Air Force and Army have approved the limited use of temazepam, zolpidem, and zaleplon.§ These hypnotics can optimize the quality of crew rest in circumstances where sleep is possible, but difficult to obtain. The choice of which compound is best for each circumstance must take several factors into account, including time of day, half-life of the compound, length of the sleep period, and the probability of an earlier-than-expected awakening, which may increase the risk of sleep inertia effects.

Temazepam: Temazepam (Restoril®, Euhypnos®, Normison®, Remestox®, Norkotral®) (15–30 mg) has been recommended in military aviation populations in Great Britain since the 1980s (150–152). Given the pharmacodynamics of this substance, it may be the best choice for optimizing 8-h sleep periods that are out-of-phase with the body's circadian cycle because, under these circumstances, sleep is often easy to initiate, but difficult to maintain due to the circadian rise in alertness. Personnel who work at night generally find that they can easily fall asleep after the work shift since sleep pressure is high from their previous night (and often day) of continuous wakefulness. Also, in the early morning, the circadian drive for wakefulness is typically low, so the body's natural rhythms do not interfere with sleep onset. However, once daytime sleep has begun, night workers are frequently plagued by late morning or noontime awakenings that result from the increased prominence of circadian-based alerting cues. The net result is that the day sleep of night workers often is 2 or more hours shorter per day than their typical night sleep (5,205).

For these individuals, the longer half-life of temazepam is desirable because the problem usually is one of sleep *maintenance* and not sleep *initiation*. In addition to temazepam's known facilitation of nighttime sleep (133,138), this compound, particularly in the 30-mg dose, has been shown to objectively and subjectively improve daytime sleep as well (52,153,162). Temazepam's intermediate half-life of approximately 9 h provides a sufficiently lengthy hypnotic effect to mitigate the disruptive arousals that often lead to sleep deprivation in personnel suffering from shift lag or jet lag. The pharmacokinetic disposition of temazepam is affected by the time of administration; the absorption of the drug is faster and the half-life and distribution are shorter for daytime administration compared to nighttime administration (138). Furthermore, in studies involving simulated night operations, temazepam has been shown to improve nighttime performance by optimizing daytime sleep (162). A study using U.S. Army pilots who worked and flew at night in a simulated shift-work environment demonstrated that temazepam-induced improvements in daytime sleep led to better nighttime pilot performance (relative to placebo) as well as improvements in psychomotor vigilance and self-reported alertness (52).

Thus, temazepam appears to be a good choice for maximizing the restorative value of daytime sleep opportunities. However, caution should be exercised prior to using temazepam in certain operational settings since the compound does have a relatively long half-life. Although residual effects were not reported in a military study in which personnel were able to gain suitable sleep before reporting for duty (29), nor in some other situations in which 30–40 mg of temazepam were given prior to a full sleep opportunity (180,227), residual postdose drowsiness has been reported elsewhere. Paul, Gray, MacLellan, and Pigeau (158) observed that drowsiness was noticeable within 1.25 and 4.25 h of a midmorning 15-mg dose. They also noted that psychomotor performance was impaired between 2.25 and 4.25 h postdose (plasma levels were still elevated at 7 h postdose). These data suggest the possibility that temazepam's long half-life could exacerbate sleep inertia upon awakening; however, the potential for this drawback must be weighed against the potential for impairment from sleep truncation in the event that temazepam therapy is withheld. Along these lines, it should be noted that Roehrs, Burduvali, Bonahoom, Drake, and Roth (170) found that just 2 h of sleep loss produces the same level of sedative effect as the consumption of 0.54 g/kg of ethanol (the equivalent of 2 to 3 12-oz bottles of beer), whereas the effects of 4 h of sleep loss are similar to those of 1.0 g/kg of ethanol (5 to 6 12-oz beers). Other investigations have similarly shown that sleep restriction and sleep deprivation degrade performance as much as, or more than, alcohol intoxication.

The same qualities that make temazepam desirable for maintaining the daytime sleep of shift workers make it a good choice for temporarily augmenting the nighttime sleep of personnel who are deployed westward across as many as nine time zones (149,201). Upon arrival at their destination, these travelers are essentially facing the same sleep/wake problems as the night worker. Namely, they are able to fall asleep quickly since their local bedtime in the new time zone is much later than the one established by their circadian clock (from the origination time zone); however, they generally are unable to sleep throughout the night. The reason for this

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§ Note that at one time, the U.S. Air Force and Army both approved the use of triazolam (Halcion®), but that at present, only the U.S. Army continues to authorize the limited use of this medication for pre-deployment rest or sustained operations (although in actuality, it is rarely prescribed). Triazolam's purported association with adverse effects and its impact on memory have curtailed its use in many clinical settings. Therefore, a detailed discussion of triazolam will be omitted from the present paper in favor of concentrating on the more frequently used hypnotics (temazepam, zolpidem, and zaleplon).

is demonstrated by the following example: a 6-h westward time zone change places bed time at 2300 local time which is 0500 origination time; this is followed by a wakeup time of 0600 local which corresponds to a "body-clock time," still adjusted to the origination time, of 1200. Based on a readjustment rate of 1.5 d per time zone crossed (105), it could take up to a week for adjustment to the new time zone to occur. Until this adjustment is accomplished, temazepam can support adequate sleep maintenance despite conflicting circadian signals and the obvious benefit will be less performance-degrading sleep restriction. While the problem with daytime alertness due to circadian disruptions will not be alleviated, the daytime drowsiness associated with increased homeostatic sleep pressure (from sleep restriction) will be attenuated.

Thus, temazepam is a good choice when a prolonged hypnotic effect is desired as long as there is relative certainty that the hypnotic-induced sleep period will not be unexpectedly truncated. This compound is especially useful for promoting optimal sleep in personnel suffering from premature awakenings due to shift lag or jet lag since the hypnotic effect helps to overcome circadian factors that can disrupt sleep immediately following a time zone or schedule change. However, temazepam should not be used longer than is necessary to facilitate adjustment to the new schedule. Depending on the circumstances, temazepam therapy probably should be discontinued after 3 to 7 d either to prevent problems associated with tolerance or dependence (in the case of night workers) or because adjustment to the new time zone should be nearly complete (in the case of travelers or deployed personnel) (149). When discontinuing temazepam after several continuous days of therapy, it is recommended that the dosage be gradually reduced for 2 to 3 d prior to complete discontinuation in order to minimize the possibility of rebound insomnia (181,209).

Zolpidem: Zolpidem (Ambien®, Stilnox®, Myslee®) (5–10 mg) may be the optimal choice for sleep periods less than 8 h, and zolpidem would be a better choice than temazepam if there were a possibility that the hypnotic-induced sleep period is likely to be unexpectedly shortened. This compound is especially useful for promoting short- to moderate-length sleep durations (of 4 to 7 h) when these shorter sleep opportunities occur at times that are not naturally conducive to sleep. As noted above, daytime naps would fall into this category because, just like daytime sleep in general, daytime naps are typically difficult to maintain (61,111,205), especially in non-sleep-deprived individuals. Furthermore, unless the naps are placed early in the morning or shortly after noon, they can be extremely difficult to initiate without some type of pharmacological assistance (89). Zolpidem is a good choice for facilitating such naps because its relatively short half-life of 2.5 h provides short-term sleep promotion while minimizing the possibility of postnap hangovers. Thus, it is feasible to take advantage of a nap without significantly lengthening the postnap time needed to ensure that any drug effects have dissipated. However, as with temazepam, there should be a reasonable degree of certainty that there will not be an early interruption of the sleep period followed by an immediate demand for performance.

The efficacy of zolpidem as a nighttime sleep promoter has been clearly demonstrated in clinical trials (with up to 1 yr of administration) in normal, elderly, and psychiatric patient populations with insomnia (21). Rebound insomnia, tolerance (treatment over 6 to 12 mo), withdrawal symptoms, and drug interactions are absent, and the dependence/abuse potential is low (16). Overall, zolpidem is a clinically safe and useful hypnotic drug (156,188).

Zolpidem has been proven to possess utility in militarily relevant circumstances. An Army study (43) demonstrated that zolpidem-induced prophylactic naps enhanced the alertness and performance of sleep-deprived pilots (relative to placebo) during the final 20 h of a 38-h period of continuous wakefulness without producing significant hangover effects. Since these naps were placed at a time during which sleep is often difficult to obtain (111), the benefits in terms of sleep promotion and sleep quality were clear. Thus, zolpidem is an effective way to promote short naps, and, relative to placebo, is associated with improved subsequent alertness.

Zolpidem may also be helpful for promoting the sleep of personnel who have traveled eastward across 3 to 9 time zones (202). Unlike westward travelers who experience sleep *maintenance* difficulties, eastward-bound personnel suffer from sleep *initiation* problems. For example, a 6-h time zone change in the eastward direction creates difficulty with initiating sleep because a local bedtime of 2300 translates to a body clock time of only 1700, and it has been well established that such early sleep initiation is problematic (150,201,219). Thus, eastward travelers need something that will facilitate early sleep onset and suitable sleep maintenance until the normal circadian-driven sleep phase takes over; however, they do not need a compound with a long half life. This is because, in this example, any residual drug effect would only exacerbate the difficulty associated with awakening at a local time of 0700 that corresponds to an origination time (or body-clock time) of only 0100 in the morning. As stated above, sleep difficulties are only part of the jet-lag syndrome, but alleviating sleep restriction or sleep disruption will help to attenuate the alertness and performance problems associated with jet lag.

Thus, zolpidem is a good compound for facilitating naps of moderate durations (4 to 7 h), even when these naps occur under less-than-optimal circumstance and/or at the "wrong" circadian time. Zolpidem is also appropriate for treating sleep-onset difficulties in eastward travelers. However, as is the case with any hypnotic, this medication normally should be used only when necessary, i.e., prior to circadian adjustment to a new work or sleep schedule. More chronic zolpidem administration may be essential for promoting naps that occur under uncomfortable conditions or naps that are "out of phase" since, by definition, these generally are difficult to initiate and maintain, but zolpidem probably should not be used for more than 7 d to counter insomnia from jet lag.

After this time, most of the adjustment to the new time zone should be accomplished (201,219).

Zaleplon: Zaleplon (Sonata®, Starnoc®) (5–10 mg) may be the best choice for initiating very short naps (1 to 2 h) during a period of otherwise sustained wakefulness or for initiating early sleep onsets in personnel who are trying to ensure sufficient sleep prior to a very early start time the next morning. With regard to facilitating early report times, zaleplon is an option to zolpidem, but both compounds are important for the same reason. As noted earlier, it is extremely difficult for most people to initiate sleep 1 to 4 h prior to their typical bedtimes unless they are severely fatigued (6,90,111). Since these individuals are unable to fall asleep early, the total length of their sleep period is truncated by the early rise time even if, once they finally go to sleep, they sleep relatively well. Personnel who are required to report to duty in the predawn hours can easily suffer 2 to 3 h of sleep deprivation because of physiologically based sleep initiation difficulties. This is why short-haul pilots attribute a substantial percentage of their fatigue-related problems to early report for duty times (28). Sleep truncation of this amount has been shown to significantly impair both alertness and performance (17,162,214). Similar to zolpidem (which has a 2.5-h half-life), zaleplon can overcome this sleep initiation problem, and its ultra-short 1-h half life is less likely to pose hazards in terms of residual drug effects that can exacerbate the drowsiness associated with the predawn awakening dictated by the early start time.

Clinical trials of the hypnotic efficacy of zaleplon have shown improvement in sleep initiation, particularly with the 20-mg dose (54,80,85). In people diagnosed with primary insomnia, the latency to sleep onset decreased significantly compared to placebo (54). After zaleplon exerts its initial effects, the drug is subsequently (and quickly) eliminated in time for more natural physiological mechanisms to take over and maintain the remainder of the sleep period. There is evidence that there are no hangover problems as early as 6 to 7 h later (54). The rapid initiation of sleep at an earlier-than-normal time permits a full sleep period despite the requirement for an early awakening, and thus bolsters subsequent performance. Paul et al. (157) found that 10 mg zaleplon impaired psychomotor performance for up to 2.25 h after ingestion. The same dose increased drowsiness from 2 to 5 h after dosing (158), with plasma drug levels equal to placebo by 5 h postdose. These authors recommend zaleplon for times when an individual may have to awaken no earlier than 3 h after drug ingestion.

Thus, zaleplon (10 mg) is a good hypnotic for promoting short naps (2 to 4 h) which would otherwise be difficult to initiate and maintain, as well as for hastening the early-to-bed sleep onset of personnel who are faced with an acute demand to report for duty in the early morning (i.e., at 0400 to 0500). In addition, as was the case with zolpidem, zaleplon can be considered useful for the treatment of sleep-onset insomnia in eastward travelers who are experiencing mild cases of jet lag. For instance, those who have transitioned eastward only 3 to 4 time zones can use this short-acting drug to initiate and maintain what the body believes to be an early sleep period. As with any hypnotic, the course of treatment should be kept as short as reasonably possible to minimize drug tolerance and drug dependence (149). **Table II** summarizes some of the characteristics of each of the hypnotics discussed.

Newer hypnotics: Some of the newer hypnotics available help with sleep maintenance without the extended long half-life of temazepam. For example, the *extended-release zolpidem (Ambien CR®)* improves sleep maintenance beyond that of *zolpidem* (93). In addition, *eszopiclone* (*Lunesta®*) has a half-life of 5 to 6 h with minimal residual drug effects after as little as 10 h post dose (114). *Ramelteon (Rozerem®)* is a novel hypnotic in that it targets the melatonin receptors in the brain in order to regulate the body's sleep-wake cycle (119). Research indicates that this drug is efficacious for sleep onset, but not for sleep maintenance (119).

New sleep-promoting compounds are being produced by the pharmaceutical industry each year. One hypnotic slated to come on the market in the near future is indiplon. This drug is similar in structure to zaleplon and has a half-life of approximately 1.5 h; it is also being formulated with a modified release as well which will extend its half-life to aid in sleep maintenance (79). There are new compounds which are rapidly absorbed and

TABLE II. LIST OF HYPNOTICS AND THEIR USES.

Generic name	Brand Name	Dosage	Average Half-life	Recommended Use	Cautions
Temazepam	Restoril® Euhypnos® Normison® Remestox® Norkotral®	15–30 mg	9 h	Sleep maintenance; daytime sleep; prolonging sleep to avoid early morning awakenings from jet lag/shift lag	Need an 8-h sleep period; not recommended if on-call
Zolpidem	Ambien® Stilnox® Myslee®	5–10 mg	2.5 h	Sleep initiation; intermediate-length naps; assisting early sleep onset due to early bedtimes from shift or time zone change	Need to have at least 4-6 h of sleep; not recommended if on-call
Zaleplon	Sonata® Starnoc®	5–10 mg	1 h	Sleep initiation; short naps; assisting early sleep onset due to early bedtimes from shift or time zone change	Not recommended if on-call

have a short half-life, and some have the ability to increase both slow-wave sleep and slow-wave activity, which improves sleep efficiency. These compounds may improve sleep efficiency to the point that effective wakefulness can be sustained on fewer than the 8 h of daily sleep that is now required. Perhaps short power naps of 3 to 4 h could become equally effective, but research remains to substantiate this possibility.

Current civilian aviation policy allows limited use of zolpidem only. The FAA allows its use no more than twice a week, and states that it cannot be used for circadian adjustment. In addition, there is a 24-h grounding policy for any pilot who uses zolpidem. While melatonin is not a prescription hypnotic medication in the United States, it is a controlled substance in many other countries. The use of melatonin to promote sleep is discussed in a later section on nonpharmacological substances.

Sleep promoting compounds can be useful in operational contexts where there are problems with sleep initiation or sleep maintenance. However, it should be noted that, like all medications, there are both benefits and risks associated with the use of these compounds. These should be considered by the prescribing physician and the individual pilot before the decision to utilize hypnotic therapy is finalized. A hypnotic of any type probably should not be used if the crewmember is likely to be called back to duty earlier than anticipated because this would put them at risk of performing flight duties before the medication has been fully metabolized. Although temazepam, zolpidem, and zaleplon are widely recognized as being both safe and effective, personnel should be cautioned about potential side effects and instructed to bring these to the attention of their physician should they occur. Potential problems may include morning hangover, which may cause detrimental effects on performance, dizziness, and amnesia that may be associated with awakenings that are forced before the drug has been eliminated, and various idiosyncratic effects (14,131,149,181). If any difficulties occur, it may be necessary to discontinue the specific compound or to abandon hypnotic therapy altogether. However, it is likely that significant side effects can be reduced or eliminated by using the correct compound or by modifying dosages or dose intervals (150). For these reasons, military personnel are required to receive a test dose of the hypnotic of interest under medical supervision before using the medication during operational situations. Even after the test dose yields favorable results and it is clear that operationally important side effects are absent, hypnotics should be used with particular caution when the aim is to aid in advancing or delaying circadian rhythms in response to time zone shifts (149,201,219). Reviews by Waterhouse and associates (219), Nicholson (149), and Stone and Turner (201) offer detailed information on this rather complex issue.

While the use of sleep aids is authorized in both civilian and military aviation, the restrictions in the civilian community are such that pilots do not receive the intended benefits of their use. The policy that hypnotics not be used for circadian disruption is overly restrictive since it is precisely for this reason that hypnotics would be useful for pilots crossing multiple time zones or flying early morning flights. The policy adopted by the military community allows the use of hypnotics with specified grounding times, allowing pilots to obtain restful sleep prior to a difficult schedule, but such that hypnotic use does not interfere with flight times. It would be useful for the civilian community to evaluate the hypnotic policy implemented by the military to allow safe use of hypnotics by civilian pilots. Education concerning the appropriate use of hypnotics, along with relevant grounding periods, would allow pilots to obtain sleep which may not otherwise occur. Also, by allowing a choice of hypnotics rather than allowing only one, a variety of hypnotics with varying length of action will allow the appropriate drug for the specific time of use.

Position Statement on the Use of Hypnotics

For the present time, it is our position that zolpidem be authorized for civilian commercial pilots a maximum of 4 times per week in situations where natural sleep is difficult or impossible due to circadian or other reasons provided that: 1) the pilot has checked for any unusual reactions to the medication during an off-duty period; 2) the dose does not exceed 10 mg in any given 24-h period; and 3) there is a minimal interval of 12 h between the ingestion of the medication and the return to duty. This recommendation is based on research which shows that: 1) zolpidem's half-life of 2.5 h (extended release half-life is 2.8 h) allows it to be fully metabolized in 10 h (11.2 h for extended release); and 2) research has shown that repeated use of zolpidem in clinical settings continuously improves sleep quality without causing rebound insomnia or exerting a negative impact on next day alertness (107). Zolpidem should not be taken to promote any type of in-flight sleep. It should be noted that facilitating quality sleep with the use of a well-tested, safe pharmacological compound is far better than having pilots return to duty when sleep deprived or having them return to duty following a sleep episode that has been induced with alcohol. Studies have shown that despite the "8-h bottle-to-throttle" rule, impairments due to even moderate alcohol consumption may persist throughout the night to the morning after (234).

b. Improving Sleep and Alertness

This section describes improving pre- and postflight sleep and alertness without the use of medications or pharmacological countermeasures. Such countermeasures are discussed in the context of military aviation (see Section VI.) where they are currently permitted under specified circumstances and with specified controls.

i. Healthy Sleep Practices: Whenever possible, getting a sufficient quantity of high quality sleep on a daily basis must be the number one focus in fighting fatigue. How much is sufficient? Generally speaking, people require about 8 h of sleep per day in order to sustain optimum alertness (222). Although some people can function well on less, they are small in number. Two strategies can help determine individual sleep need.

The first strategy is to extend the nightly sleep period an extra hour over the course of the next 7 d, and after the 7th d, self-reflect on whether the additional sleep has been beneficial in terms of cognitive performance, mood, and alertness. The second, and more reliable, strategy is to keep a sleep diary during the next vacation when it is possible to sleep ad lib for several days. After recording the time of natural sleep onset and natural awakening (without the aid of an alarm clock) for 5 to 7 d (excluding the first 2 vacation days), obtain the average sleep time and make this amount of sleep each night the goal upon returning to work.

Obtaining the required *quantity* of sleep on a day-to-day basis obviously is important, but obtaining high *quality* sleep is beneficial as well. Sleep fragmentation is known to degrade memory, reaction time, vigilance, and mood (25). Specific strategies can help optimize each sleep opportunity, and these are presented below.

Strategies for Optimizing Sleep Opportunities:
- When possible, wake up and go to bed at the same time every day to avoid circadian disruptions.
- Use the sleeping quarters only for sleep and not for work.
- If possible, establish a consistent and comforting bedtime routine (e.g., reading, taking a hot shower, and then going to bed).
- Perform aerobic exercise every day, but not within 2 h of going to bed.
- Make sure the sleeping quarters are quiet, totally dark, and comfortable. For this to work, day workers should be housed separately from night workers.
- Keep the sleep environment cool (~26° C if you are covered).
- Move the alarm clock out of sight so you can't be a clock watcher.
- Avoid caffeine in drinks and other forms during the afternoons/evenings.
- Don't use alcohol as a sleep aid (it may make you sleepy, but you won't sleep well).
- Avoid cigarettes or other sources of nicotine right before bedtime.
- Don't lie in bed awake if you don't fall asleep within 30 min– instead, leave the bedroom and do something relaxing and quiet until you are sleepy.

ii. Napping: In employing a napping strategy pre/postflight, an important factor is *nap timing* or placement. A nap taken during the day before an all-night work shift (a prophylactic nap), with no sleep loss prior to the shift, will result in improved performance over the night compared to performance without the nap (23,191). Although naps taken later in the sleep-deprivation period also are beneficial, these naps probably should be longer than prophylactic naps in order to derive the same performance benefit. Schweitzer et al. (191) demonstrated that when subjects received a 2- to 3-h nap before a night work shift (with concurrent sleep loss) they performed better than when receiving no nap. Bonnet (23) showed that a nap before a 52-h continuous performance period was beneficial in keeping performance and alertness from decreasing for up to 24 h compared to the no-nap condition, but by the second night of sleep loss, the benefit of the naps could not be reliably measured.

Another important factor is *nap length*. A relationship between nap length and performance was reported by Bonnet (23) based on a study in which subjects were allowed either a 2-, 4-, or 8-h nap before 52 h of continuous operations. The results indicated a dose-response relationship between the length of the nap and performance during the first 24 h of sleep deprivation. Bonnet concluded that the nap before an all-night shift should be as long as possible to produce maximum performance benefits and that prophylactic naps were better than naps designed to replace sleep that was already lost due to the requirement for continuous wakefulness. This conclusion was supported in a study by Brooks and Lack (30), who tested afternoon naps of 5, 10, 20, and 30 min following nighttime sleep of 5 h. The longer 20- and 30-min naps showed improvement in overall cognitive performance for as long as 155 min compared to the 10-min nap which showed cognitive performance effects for only 95 min. This finding is consistent with a recent meta-analysis on the efficacy of naps as a fatigue countermeasure (75). This meta-analysis of 12 studies consisting of a total of 178 tests not only concluded that naps led to performance benefits equal to, and sometimes greater than, baseline performance levels, but also that the length of performance benefit was directly proportional to the length of the nap (e.g., a 15-min nap led to 2 h of benefit while a 4-h nap led to 10 h of benefit). However, it was also noted that, regardless of nap length, the performance benefit decreased as postnap interval increased (i.e., the benefits of a 4-h nap were greater shortly after awakening than after 10 h, though performance at the later time still met or exceeded baseline performance).

A final consideration is the *placement of the nap with regard to the phase of the body clock* (circadian phase). Nap timing should take into account the impact of circadian phase on sleep propensity, structure, and quality across the day as well as the effects on performance both immediately after awakening and later in the work period. Sleep tendency is highest during the daily trough in core body temperature (in the predawn and early morning hours) and lowest when core body temperature peaks (in the early evening hours) (65). Thus, there may be significant problems initiating and/or maintaining a nap during an adverse circadian phase when core temperature is near its peak, as during the "forbidden zone for sleep" a couple of hours prior to habitual bedtime (111). Naps placed during the circadian troughs are the easiest to maintain and they show beneficial effects on later performance. Gillberg (89) showed that a 1-h nap placed at 0430 (in the circadian trough) was more beneficial to next-day performance than one placed at 2100. However, while naps during the circadian trough may be more effective for performance sustainment, they also are the more difficult naps from which to awaken. Generally, studies have shown that postnap sleepiness, termed "sleep inertia," is higher and performance is lower immediately upon awakening from a nap taken during the circadian trough as compared to naps taken during the circadian peak (71). For this reason, some authors suggest that naps in the circadian trough should be avoided, and naps should be taken before a person's sleep loss extends beyond 36 h. However, it should be possible to take advantage of the improved quality of naps in the circadian trough while avoiding the negative sleep-inertia effects if napping personnel can be awakened about 1 h prior to their work shifts. This will allow time to overcome most of the effects of sleep inertia.

iii. Circadian Adjustment: The circadian clock cannot adapt immediately to a change in the duty/rest cycle or changes in environmental cues, such as those experienced with transmeridien travel (106). When crossing time zones, the circadian clock is out of sync with the local environment. Adjustment is usually faster after traveling in the westward than the eastward direction (27,185). Adjustment depends on direction of travel, the number of time zones crossed, the rhythm being measured and an individual's exposure to time cues (e.g., light/dark cycle). Adjustment does not appear to be linear and those who are evening types ("owls") tend to adjust to the new time zone more quickly relative to morning types ("larks").

Aircrew fatigue resulting from circadian disruption is subject to partial alleviation with hypnotics; however, in cases where the crewmember will remain in the new time zone on a consistent duty schedule for several consecutive days, it may be better to restore the body's natural sleep/wake rhythm through other circadian reentrainment techniques. Adjusting to new time zones or work schedules is largely a matter of controlling exposure to sunlight, placing meals and activities at appropriate times, and making every effort to optimize sleep during available sleep periods (11,33,196,220). Although operational requirements often make it difficult, aircrew should pay close attention to their behaviors following schedule changes. Several of the recommendations that are typically made to help industrial shiftworkers are also useful in aviation settings.

Recommendations for Rotating to Different Shift Schedules:

- When remaining within the same time zone but rotating to night duty, avoid morning sunlight by wearing dark glasses and by staying indoors as much as possible prior to sleeping.
- For daytime sleep, make sure the sleep environment is dark and cool.
- For daytime sleep, use eye masks and earplugs (or a masking noise like a box fan) to minimize light and noise interference.
- For daytime sleep, make sure to implement the good sleep habits discussed previously.
- When on duty at night, try to take a short nap before reporting for duty.
- After waking from daytime sleep, get at least 2 h of sunlight (or artificial bright light) in the late afternoon or early evening if possible.

When traveling to a new time, crews will face circadian disruptions similar to those encountered by people rotating from day shift to night shift within the same time zone. Upon arrival in the new time zone (assuming that this will be the new duty location for several days, weeks, or months and that crewmembers will be flying/working in the daytime rather than at night), the following recommendations are available to aid in adjusting to new time zones.

Recommendations for Time Zone Adjustments:

- Quickly adjust meal, activity, and sleep times to the new time zone schedule[¶].
- Maximize sunlight exposure during the first part of the day.
- Minimize sunlight exposure during the afternoons.
- Avoid heavy meals at night because stomach discomfort will disrupt sleep.
- Follow good sleep habit recommendations to optimize nighttime sleep.
- Try self-administered relaxation techniques to promote nighttime sleep.
- If possible, prior to bed time, take a hot bath. Cooling off afterwards may mimic the circadian-related temperature reduction that normally occurs during sleep.
- During the first few days of circadian adjustment, use sleep medications (if authorized) to promote sleep at night, and use caffeine to augment alertness during the day.

Properly timed bright light is an alternative strategy for resynchronizing circadian rhythms after schedule changes (62,88,185). Several researchers have published recommendations about the use of light to promote circadian adjustment, but they have pointed out difficulties associated with the correct timing of administration of light therapy as well (77,117,168). Consensus reports summarizing issues related to the use of bright light as a treatment for jet lag and shift lag also have been published (27,78).

Unfortunately, the difficulties associated with appropriate timing of artificial bright light therapy often leave experts to recommend a reliance on other approaches. In addition, it is often difficult to establish any type of bright light facility on the ground much less on board aircraft. Finally, an approximate understanding of one's circadian status is a prerequisite for phase changes with supplementary melatonin. Self-administration techniques such as natural sunlight exposure, appropriately timed naps, and proper exposure to zeitgebers (time cues) may facilitate circadian adjustment to new duty or time zone schedules (154,167,201,219).

iv. Exercise: Exercise has been shown to be an effective fatigue countermeasure in both the laboratory and aviation environments. Those who exercise regularly actually show improved sleep quantity and quality (199). However, if engaged in too close to bedtime, exercise can have negative effects on sleep, making it more disrupted (137). Exercise increases physiological arousal and can help promote alertness in the short-term. However, it is important to consider the level of exercise and the timing when determining its effectiveness as a countermeasure. Research has suggested that only heavy exercise ($70\% VO_{2max}$) results in changes in objective vigilance performance, and the effects last no longer than 30 min (98). These heavy exercise periods were brief (10 min) because if too long (~1 h), they would actually increase fatigue and sleepiness levels. When exercise levels were in the light to moderate range, subjects seemed to be more alert and less sleepy for up to a 15-min postexercise period. However, more recent research has shown that

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[¶] If persons who have been working nights in the U.S. will be working days in Europe, it might not be necessary to readjust the body clock since it already will be on the proper schedule.

the subjective effects of moderate exercise bouts can last up to 30 min (113). Subjects who engaged in 10 min of moderate exercise every 2 h throughout a 40-h sleep deprivation protocol showed less subjective sleepiness up to 30 min after exercising. Similar to other research, no differences were seen in objective performance.

While exercise can be used as a fatigue countermeasure to improve alertness levels in the short term, it can also induce phase shifts in the melatonin circadian rhythm and the circadian clock (35,78). Data collected by Shiota and colleagues on airline crewmembers flying a 4-d flight pattern between Tokyo and Los Angeles (8-h time difference) showed that moderate to heavy exercise (both in origin and destination cities) helped the pilots adapt to the local time zone (193). This conclusion was based on subjective sleep/wake diaries, subjective sleepiness levels, and urine excretion of 17-hydroxycorticosteroids; however, due to data being collected during operations, there was no way to conclude that it was the exercise alone that helped resynchronize the individuals to the new environment. Since then, controlled studies have evaluated the ability of exercise to shift circadian rhythms (99). Barger and colleagues have evaluated exercise and its effect on circadian rhythms in a controlled environment in which light was held at a constant dim level (15). The data showed that over a 15-d trial, exercise of appropriately timed duration and amount (three 45-min nightly periods), altered the volunteers' melatonin profiles. Thus, the outcomes suggest that exercise can be helpful in facilitating a delay of the sleep/wake cycle which is experienced during westbound travel.

v. Nutrition: While eating a meal immediately before the sleep period is not recommended, it is important to maintain good nutrition. If personnel eat immediately before sleep, they should favor grains, breads, pastas, vegetables, and/or fruits. At the same time, personnel should avoid large meals, high-fat meals, high-acid meals, sweets, and significant hunger.

Normal variations in nutrition have few, if any, major effects on sleep structure (123,146). However, dietary supplementation and unusual variations in diet may have mild effects. For example, high carbohydrate (CHO) supplementation prior to bedtime has been associated with reduced amounts of wakefulness and stage 1 sleep, decreased stage 4 sleep, and increased rapid eye movement (REM) sleep (164). The somnolent effects of high CHO meals may depend in part on gender, age, and time of day of consumption (197). A CHO lunch has been shown to increase the length of a siesta (236). Recently, it was observed that a 90% CHO meal with a high glycemic index (GI) shortened sleep latency by about 50% compared to a low glycemic index meal, and about 40% when fed 4 h prior to sleep onset compared to 1 h before (4). Conversely, drowsiness may be offset immediately after high- and low-GI CHO intake, but low-GI CHO intake may delay the onset of drowsiness (110). A comparison of low-fat, high-CHO meals to high-fat, low-CHO meals indicated that higher cholecystokinin (CCK) concentrations after high-fat, low-CHO meals were associated with greater feelings of sleepiness and fatigue (224).

The essential amino acid, tryptophan, is a precursor of the monoamine neurotransmitter serotonin. Serotonin is involved in the regulation of sleeping and waking (163). The presleep ingestion of an amino-acid mixture lacking tryptophan, compared to the ingestion of a mixture containing all essential amino acids, caused a decrease in stage 4 sleep latency and an increase in stage 4 sleep during the first 3 h of sleep (135). Depletion has also been observed to decrease stage 2 sleep, to increase wake time after sleep onset and rapid eye movement density, and to shorten the first and second REM period intervals (218). Midmorning tryptophan depletion delays REM sleep latency during the following night's sleep (10).

Thus, it appears that the purposeful manipulation of dietary CHO by aircrew to help induce and sustain their sleep periods may be ill-advised due to the unpredictability of effects. However, tryptophan depletion should probably be avoided. Obviously, those prone to gastric reflux disorders should avoid large or high-fat meals before bedtime.

The failure to eat may trigger sleep disruption and fatigue. Low blood glucose may elevate plasma glucagon, with concomitant elevations of heart rate, and blood pressure. This is not conducive to restful sleep. Of course, hypoglycemia can lead to poor cognitive performance. Studies of the effects of intermittent fasting during Ramadan have revealed increased nocturnal sleep latency, decreased daytime sleep latencies, and decreased total sleep time. These effects may be dependent upon the late dinners ingested during Ramadan (172,173).

Position Statement on Improving Sleep and Alertness

A number of alertness-enhancing strategies are available that do not rely on medications of any type. Whenever possible, these should be applied during off-duty periods to maximize the safety of flight operations. Promoting quality preduty sleep is essential for ensuring optimal flight performance. Since healthy sleep practices ensure that crews will be able to make the most of available sleep opportunities, all aircrew members should be provided with educational materials that outline natural sleep-promoting behaviors. In addition, they should be educated regarding the importance of naps for bridging the gap between consolidated sleep episodes. Naps should be as long as possible and whenever feasible they should occur at the circadian times most conducive to natural sleep (i.e., early afternoon or early predawn hours according to the body clock). The principles outlined for good sleep hygiene should be followed to promote optimal nap quality and duration. Upon awakening from a nap lasting more than 40 min (i.e., where sleep inertia upon awakening is likely), there should be a wake-up period of at least 30 min prior to the performance of any safety-sensitive tasks.

With regard to circadian adjustment techniques, it is our position that crewmembers who have moved to a new time zone or work schedule and who expect to remain in the new location or on the new schedule for several days should employ natural adjustment techniques such as controlling the timing of light exposure, meals, and other activities. The detailed recommendations presented earlier in this paper should be followed to the extent possible.

Since aerobic exercise has been shown to improve the quality of a subsequent sleep period, it is our position that crewmembers engage in at least 30 min of aerobic exercise every 24 h. However, since exercise increases body temperature, most sleep experts say the best time to exercise is usually late afternoon. The exercise period should not be placed within 2 h immediately preceding bed time in order to allow the body to cool (76,199,235).

Although evidence is weak that nutrition exerts a practically significant effect on sleep and alertness, we recommend that aircrews emphasize balanced meals at regular intervals to promote and maintain general health, and that they avoid consuming meals (particularly large meals) immediately prior to bedtime. It is possible that the ingestion of high-carbohydrate foods approximately 4 h prior to bedtime may promote sleep, but in general attempting to control sleep and alertness by manipulating dietary constituents is not advised.

c. Non-FDA-Regulated Substances

Alternative, non-FDA-regulated medicines and substances are sometimes used to counter fatigue through assisting with sleep or promoting alertness. Melatonin is probably the most used substance of the nonregulated ones available. Its efficacy as a hypnotic continues to be debated (211,237). Generally, as a sleep aid, it has not consistently been shown to be clinically efficacious for insomnia when taken during the biological night (32). However, there is evidence that melatonin has a soporific effect when taken outside the normal sleep period, particularly when taken to phase-advance the sleep period (8).

Melatonin administration may help to overcome shift lag in operations involving rapid schedule changes and jet lag in circumstances requiring rapid time zone transitions. There is a substantial amount of research which indicates that appropriate administration of this hormone can improve circadian adjustment to new time schedules (9,32,206). There also is evidence that melatonin possesses weak hypnotic or “soporific” properties that may facilitate out-of-phase sleep (118,231). Typically, exogenous melatonin should be administered at approximately the *desired bed time* since melatonin naturally peaks after sleep onset. Melatonin is especially useful for facilitation of daytime sleep (early circadian sleep) but less efficacious for facilitation of normally timed nocturnal sleep unless one produces little or no melatonin. In normal individuals who are not stressed with circadian desynchrony [i.e., individuals who can safely be assumed to have a dim light melatonin onset (DLMO) in the range of ~2000 to 2200], melatonin should be ingested in the late afternoon (approximately 1700) to achieve a circadian phase advance, or in the morning (approximately 0800) to achieve a circadian phase delay (34). For individuals who are suffering from circadian desynchrony, ingestion of melatonin or phototherapy should be used with proper guidance in order to avoid a circadian shift in the undesired direction. Since melatonin is not considered a drug, it is widely available for use with few restrictions, at least in the U.S. Unfortunately, most potential users of melatonin possess little knowledge about circadian rhythms and/or endogenous melatonin secretion, and this could lead to compromised alertness and decreased performance associated with improper use.

Other substances to promote sleep are also available, but most of them have not been studied thoroughly and their effectiveness has not been established. However, of these substances, valerian and kava have the most research on efficacy. A systematic review of valerian concluded that, while some studies have found some evidence that valerian has significant effects on sleep, it is does not have the clinical efficacy needed to treat insomnia (203). However, evidence suggests that valerian is a safe herb which can be helpful with mild insomnia when taken continuously. Good clinical studies are needed to establish both its efficacy for severe insomnia and its safety profile (95,136,230). Kava has been shown to help with sleep latency and sleep quality in people with insomnia, but more studies are needed to establish its efficacy and safety as well (136).

For promoting alertness, caffeine can be considered a valuable non-FDA-regulated pharmacological fatigue countermeasure. Numerous studies have shown that caffeine increases vigilance and improves performance in sleep-deprived individuals, especially those who normally do not consume high doses (142). Caffeine (generally in the form of coffee, tea, or soft drinks) is already used as an alertness-enhancing substance in a variety of civilian and military flight operations, and it has proven safe and effective. For a very complete review of the applicability of caffeine in operations, see the Institute of Medicine report, especially pp. 79–82 (56). Caffeine is used best for the short-term elevation of cortical arousal; regular use may lead to tolerance and various undesirable side effects, including elevated blood pressure, stomach problems, and insomnia. Caffeine is widely available and affects the nervous system within 15 to 20 min. The effects of caffeine last for about 4 to 5 h and may include a more rapid heartbeat and sharply increased alertness/decreased sleepiness; the effects may last up to 10 h in especially sensitive individuals. There are individual differences in the effects of caffeine on sleep. For some personnel, even small amounts can cause problems sleeping. For others, caffeine has no apparent detrimental effect on sleep. Chronic overuse may also cause dehydration, nervousness, and irritability. Tolerance to cortical arousal occurs with the repeated consumption of caffeine at more than about 200 to 300 mg per day. Personnel should consume caffeine sparingly, and save the arousal effect until they really need it. This is called “tactical caffeine use.” The U.S. Army-developed caffeine gum, *Stay Alert*, is now in Army supply channels (NSN #8925-01-530-1219). It provides an excellent delivery mechanism for caffeine when the latter is needed during prolonged operations. The caffeine content of commonly used substances is listed in **Table III**. More specific guidance regarding caffeine use is provided in Section VI.c.i.

The amino acid tyrosine, a precursor of the neurotransmitter norepinephrine, might be effective in countering the stress-related performance decrement and mood deterioration associated with sleep deprivation (155). In a direct test of its effectiveness on cognitive performance during one night of total sleep loss, 150 $\mathrm{mg} \cdot \mathrm{kg}^{-1}$ of tyrosine, administered in a split dose, resulted in an amelioration of the performance decline seen on a psychomotor task and a reduction in lapse probability on a vigilance task compared to placebo (145). The results lasted approximately 3 h. While there are relatively few data, it appears that tyrosine is a relatively benign substance that may prove useful under high stress conditions, including those associated with sleep loss.

Position Statement on Non-FDA-Regulated Substances

While nonregulated substances are easy to purchase in many places in the U.S., they should still be consumed with the same caution as any prescription substance. In some individuals, many of the herbal remedies can lead to sleepiness levels which will impair performance. In addition, since these substances are not under federal control, the manufacturing quality is left to the individual companies. For example, one study found the stated amount of melatonin and the actual amount of melatonin varied considerably between lots as well as within bottles for several brands of melatonin sold over the counter (165). Research continues in determining the safety, dosage, formulation, and time of administration of melatonin since this substance shows the most promise in helping sleep and circadian disorders. However, there is still debate about its use and long-term safety, and for this reason we do not recommend the use of melatonin to readjust circadian rhythms or to promote sleep. Other substances such as valerian and kava also should not be relied upon to manipulate either sleep or performance. Caffeine, on the other hand, is an effective alertness-enhancing compound, and it is our position that it should continue to be used as an aviation fatigue countermeasure. Crewmembers should adhere to the following: 1) avoid ingesting more than 1000 mg of caffeine in any 24-h period; 2) make an effort to use caffeine judiciously (i.e., only when it is truly needed to reduce the impact of fatigue); and 3) avoid ingesting caffeine within 4 h of bedtime. However, the effects of caffeine on sleep are dependent on factors such as usual caffeine consumption and age (199). Here are some situations where using caffeine makes sense: 1) leading in to the predawn hours; 2) midafternoon when the alertness dip is greater because of inadequate nocturnal sleep; and 3) prior to driving after night duty, but not within 4 h of going to sleep.

TABLE III. CAFFEINE CONTENT OF COMMON DRINKS AND OVER-THE-COUNTER MEDICINES.

Substance	Average Caffeine Content
1 cup Maxwell House®	100 mg
1 Starbucks® Short	250 mg
1 Starbucks® Tall	375 mg
1 Starbucks® Grande	550 mg
1 Coke®	50 mg
1 Mountain Dew®	55 mg
1 cup tea	50 mg
2 Anacin®	65 mg
2 Excedrin Xtra. Strength	130 mg
1 Max. Strength NoDoz®	200 mg

V. NEW TECHNOLOGIES

The need for real-time fatigue detection technologies and predictive modeling algorithms that focus on minimizing fatigue-related errors, incidents, and accidents during flight has been realized for several years. This is largely due to fatigue's continued persistence as an occupational hazard and the related cognitive deficits that inhibit the ability of an operator to identify decreases in alertness (31). Therefore, many efforts have focused on developing unobtrusive technologies that aim to detect fatigue in pilots prior to its onset so that an operationally valid and effective countermeasure can be implemented. Advances in fatigue technologies and algorithm development have made this goal achievable. However, before being transitioned to operational environments, these technologies and algorithms must be shown to meet a number of engineering, scientific, practical, and legal/ethical standards and criteria (69). Efforts to demonstrate validity have been conducted through a variety of venues including controlled laboratory settings, simulation research protocols, operational evaluations, and workshops involving subject matter experts from the field (68,70,72,100,125,212).

a. On-Line, Real-Time Assessment

On-line operator status technologies are the most common of the fatigue monitoring devices because of their ability to provide meaningful measures of alertness levels and performance ability in real time (69). They aim to monitor some aspect of the individual's physiology or behavior that is sensitive to increasing fatigue and sleepiness levels. Available and developing on-line, operator status detection technologies monitor either the physiological behavior of the individual (EEG, eye gaze, facial feature recognition) or their physical characteristics (muscle tone, head position, percent eye closure, wrist inactivity). They offer great potential for pilots who are challenged with maintaining alertness and performance during long, uneventful flights (36).

Research over the past 40 yr has established the EEG as a highly predictive and reliable neural index of cognition along with event-related brain potentials (ERPs) (82). It has been accepted as the '"gold standard" for the detection of impaired alertness. These EEG signals and analyses are now being incorporated into a real-time technological countermeasure device for fatigue detection (109). For example, the B-alert® (20) has been validated as an alertness indicator for driver fatigue (115) and has also demonstrated sensitivity to individual fatigue vulnerability (116). The B-alert® system can also be implemented in combination with ERPs to capture a more detailed image of information processing in the brain (20). Other researchers (e.g., 120) are also developing EEG-based drowsiness estimation systems based on computed correlations between changes in EEG power spectrum and fluctuations in driving performance. From this information, individualized linear regression models for each subject applied to principal components of EEG spectra can be constructed for further real-time monitoring.

Although the detection of fatigue based on the EEG changes that occur simultaneously in the delta, theta, alpha, and beta bands has been accepted as a valid measure of fatigue, obtaining brain wave activity in the operational environment is often times not feasible. Research has shown that the eye and visual system, under central nervous system control, can also provide information about an individual's alertness level and cognitive state (39,121,112,207). Deteriorations in many ocular measures occur with fatigue and extended waking periods, with the most sensitive being those that change just prior to the sleep onset period, such as eye blinks, long duration eye closures, eye movements, and pupillary response. Various devices have been designed to monitor these ocular changes, but each device differs somewhat in terms of exactly what is measured, how it is measured, and how the data are processed. In addition, there are differences in the precise nature of the fatigue-monitoring algorithms and in the hardware technology used to obtain the ocular measures. Some are unobtrusive and require simple video while others can require the user to place a sensor near the eye or require the person to wear specially equipped eyeglasses. A number of promising ocular devices are in the validation phase for real-time, noninvasive detection of operator fatigue. These include devices that assess the percentage of eye closure, such as the Co-Pilot (Attention Technologies, PA), Optalert (Sleep Diagnostics, Australia), and Eye-Com (Eye-Com Corp., Reno, NV). Selection of the PERCLOS metric (a measure of the proportion of time subjects had slow eye closures; 228,229) for these devices is based on research demonstrating its high correlation with psychomotor vigilance behavior (70).

Facial feature recognition technology is also currently being validated as a fatigue detection device (73, 94; Dinges DF. Personal communication; 2008). The simultaneous extraction of changes in multiple locations on the face such as around the eyes, nose, and mouth provide a great deal of information regarding individual alertness levels. Moreover, Ji, Zhu, and Lan (102) have incorporated other critical factors such as PERCLOS and circadian variations into facial feature recognition technology for the development of a real-time, nonintrusive monitor device for fatigue.

Additional fatigue detection devices that compared successfully to the EEG technique and/or the PERCLOS technique include a wrist-worn alertness device that triggers an alarm sound when wrist inactivity occurs for a preset amount of time (e.g., 5 min; 233) and a device that assesses head position "XYZ" data analyzed over various time periods to signify micronods or microsleeps (104).

All fatigue detection devices, independent of the variable being measured, have both positive and negative aspects. Their usefulness as real-time technologies is dependent on the requirements and conditions of the operational environment and some may not even be practical for use in highly restrictive environments such as the flight deck. For example, based on a study that showed an automated PERCLOS device was effective in improving alertness and performance in truck drivers (125), a similar study was conducted in a B747-400 flight simulator (127). The goal of the study was to establish the feasibility, potential usefulness, and applicability of the automated PERCLOS monitor for drowsiness detection and mitigation of fatigue on the flight deck. The automated PERCLOS system with feedback did *not* significantly counteract decrements in performance, physiological sleepiness, or mood on the flight deck, which was very different from the results found in the truck-driving environment. This was largely due to the PERCLOS system having a limited field of view that could not capture pilots' eyes at all times during the flight due to operational requirements of constant visual scanning and head movements. These results clearly demonstrate that, although an automated, real-time technology may be valid in one operational environment, it does not always transition to another operational environment without the emergence of implementation obstacles.

b. Off-Line Fatigue Prediction Algorithms

Off-line fatigue prediction algorithms are being developed to provide an estimate of an individuals' alertness level or performance effectiveness during a work period to be performed in the future. These measures (e.g., alertness levels, performance estimates) of physiological state are measured relative to a standard such as the individual's baseline and/or a group norm (91). For example, ocular-based, readiness-to-perform, or fitness-for-duty devices often measure various aspects of the visual system of the individual prior to a duty period to determine if they can maintain optimal performance throughout the work period (60). Such a device as the FIT device (161) has already been shown to detect changes attributable to sleep loss (182–184).

Over the years, there have also been recent developments of biomathematical models of alertness for the prediction of alertness and performance levels (125). They can be very useful in the prediction of performance or effectiveness levels when comparing different operational schedules. Although models can differ in their specific algorithm, they all aim to model the interaction of sleep and circadian processes and effects on the sleep/wake cycle and waking neurobehavioral performance. The operational usefulness of these models lies directly in them being incorporated into scheduling tools. Such tools can be used to develop work schedules that maximize safety by: 1) predicting times when performance is optimal; 2) identifying timeframes in which recovery sleep will be most restorative; and 3) determining what impact proposed work/rest schedules will have on overall neurobehavioral functioning (126).

Models of alertness and performance vary in their specific algorithms and differ in the number and type of input variables, output variables, and goals and capabilities. It is also important to consider the operational environment for their intended use. Of the seven models evaluated at a modeling workshop sponsored by the U.S. Department of Defense, U.S. Department of Transportation, and NASA, only two of them specifically relied on aviation data for development or stated their relevance to aviation operations (126). At the time of the workshop in 2002, the System for Aircrew Fatigue Evaluation (SAFE) model was specifically developed for aviation operations. It had been adjusted using data collected on long-haul flights and required aviation-specific variables for its input (19). Another model, the Sleep, Activity and Fatigue Task Effectiveness (SAFTE) model was developed for military and industrial settings and included a translation function for pilots. The SAFTE model is the foundation of the Fatigue Avoidance Scheduling Tool (FAST), which was designed to help optimize the operational management of aviation ground- and flightcrews (101). While all of the biomathematical modeling software showed promise in the prediction of performance, there is room to improve their validity and reliability based on refinements with real world data, and they should not be transitioned to operational environments until their scientific validity can be demonstrated (66).

Position Statement on New Technologies

Fatigue detection technologies (fitness for duty and real-time assessment devices) and scheduling tools that incorporate biomathematical models of alertness should not be solely relied upon for the determination of safe or ‘fatigue-free’ flights. They are tools that can be effectively incorporated as part of an overall safety management approach and should not be used in place of regulatory limitations. Selection of the ‘best tool’ should be dependent on its *demonstrated validity for mitigating fatigue risk during aviation operations*.

At present, none of the real-time fatigue detection technologies have been sufficiently proven in an aviation environment (with the possible exception of the wrist-worn alertness device that triggers an alarm sound when wrist inactivity occurs for a preset amount of time) to warrant widespread implementation. However, some crew scheduling approaches based on validated fatigue-prediction models have already been proven, to a limited extent, feasible and worthwhile. The SAFTE model for instance, is currently being used in a number of aviation settings to evaluate the fatiguing impact of different schedules and to help design better alternatives.

Refinement of both the new fatigue monitoring technologies and scientifically based scheduling software must continue, and once they are validated for specific types of operations, they should be incorporated as part of an overall safety management approach supplementing regulatory duty limitations. Fatigue detection technologies and biomathematical models can also be used in combination. The online, realtime measurements (e. g., actigraphy, performance measures) could be used as input data to the scheduling tools, thus increasing their predictive value, being reflective of what is occurring during actual operations. Research is also needed to identify embedded (flying) performance metrics that are sensitive to fatigue over time, allowing for model refinement and continuous assessment of the safety of operations.

A final consideration in the development of new technologies is to combine biomathematical models of alertness with scheduling tools that do not have a foundation in sleep and circadian research (e.g., tools that incorporate labor contract rules, government regulations, available staff, vacation time, currency training, etc.). Combining the two would result in scheduling regimes that consider both the physiological limitations of humans and operational constraints, resulting in both compliant and safe operations.

VI. MILITARY AVIATION

a. Relevant Regulations and Policies

A review of the fatigue management (crew rest) policies implemented by the U.S. Army, the U.S. Air Force, and the U.S. Navy shows far less complexity than is found in the civil aviation regulations. Complete guidance may be found in Army Regulation 385-95 (10 Jan 2000), Air Force Instruction 11-202 v3 (05 Apr 2006), and OPNAV Instruction 3710.7T (01 Mar 04).

b. Crew Rest and Duty Limitations

The primary requirement for crew rest and duty limitations is somewhat similar to that specified in the civil aviation regulations; specifically, that 8 h of continuous rest be obtained prior to the duty period. The U.S. Air Force instruction requires a 12-h nonduty crew rest period in which 8 h of uninterrupted sleep must be obtained in the 12 h prior to duty. If this 8-h sleep period is interrupted, another 8 h must be added. The U.S. Navy instruction requires that 8 h of continuous rest be obtained within the 24-h period, and that any continuous wakefulness period should not exceed 18 h. If the 18-h requirement is not met, a minimum of 15 h of continuous off-duty time must follow. The U.S. Army at one time had one of the most detailed crew rest and duty limitation guides of the three U.S. services. However, the Army guidance now more generally states that commanders are responsible for endurance management by ensuring that fatigue is controlled or eliminated as a risk factor in all operations by providing for sufficient sleep time in each 24-h period as well as for circadian adjustment of the individual body clocks of personnel changing time zones or work cycles. Army commanders are directed to consult the Leaders Guide to Crew Endurance Management (57) for complete details.

Air Force Instruction 11-202, Vol. 3, offers some of the most detailed current guidance. It advises commanders and mission planners to consider fatigue-related factors for upcoming flight missions including the fatiguing impact of adverse weather, temperature extremes, night operations, and mission delays, as well as the fatigue from sleep loss and continuous work. Additional guidance, paraphrased from Air Force Instruction 11-202 (waivers may be requested for specific circumstances) and the U.S. Navy guidance paraphrased from Chief of Naval Operations Instruction 3710.7T, are listed below:

U.S. Air Force Guidance for Scheduling Flight Missions to Avoid Fatigue in Aircrew:

- Provisions should be made for augmenting flightcrews when possible to permit in-flight rest periods.
- Cockpit naps (taken by one crewmember at a time) of up to 45 min in duration are authorized during noncritical flight phases, and multiple naps are permitted when feasible.
- Crew bunks or other suitable rest facilities should be provided on board aircraft when possible.
- Adequate crew rest is required prior to flight duty periods. Normally, this means 12 h off duty every 24 h. There should be a minimum of 10 h of restful time that includes an opportunity for at least 8 h of uninterrupted sleep during the 12 h preceding the flight duty period.
- Shorter off-duty periods of 10 h may be used as an exception in continuous operations, but this exception should be minimized, and after several days of shorter off-duty periods, commanders should provide sufficient rest to counter cumulative fatigue.
- Maximum flying time should be limited to 56 h per 7 d, 125 h per 30 d, and 330 h per 90 consecutive days.
- If nonflight duties significantly extend the overall duty period (by 2 h or more), consideration should be given to reducing the number of allowed flight hours.
- Generally speaking, the maximum flight duty period for any given day should fall within the range of 12 to16 h in situations where crew augmentation is not possible.
- When augmented crews are an option, duty days normally can extend to 16 to 24 h (in the case of the B-2 Bomber, some missions extend to 44 h).
- Factors affecting maximum flight duty period include: single vs. multiseat aircraft, level of automation, availability of onboard rest facilities, and type of flight mission.
- Alertness management strategies such as techniques to promote preduty sleep, extended crew rest periods, controlled cockpit rest, bright light exposure, activity breaks, pharmacological sleep and alertness aids, and fatigue management education should be implemented as appropriate.

U.S. Navy Guidance for Scheduling Flight Missions to Avoid Fatigue in Aircrew:

- Schedule ground time between flight operations to allow flightcrew to eat and obtain at least 8 h of uninterrupted sleep.
- Flightcrew should not be scheduled for continuous alert or flight duty in excess of 18 h. If mission requirements exceed 18 h, then 15 h of continuous off-duty time should be provided.
- Following a time zone change of at least 3 h, flightcrew requires close observation by the flight surgeon since performance will be compromised during the adjustment period.
- For single-piloted aircraft: Daily flight time should not exceed 3 flights or 6.5 h total flight time for flight personnel. The weekly maximum flight time should not normally exceed 30 h, 65 h per 30 d, 165 h per 90 d, and 595 h per 365 d.
- For multipiloted aircraft: Individual daily flight time should not exceed 12 h for flight personnel. The weekly maximum flight time for ejection seat aircraft should not normally exceed 50 h, 80 h per 30 d (100 and 120 for nonpressurized and pressurized aircraft, respectively), 200 h per 90 d (265 and 320 for nonpressurized and pressurized aircraft, respectively), and 720 h per 365 d (960 and 1120 for nonpressurized and pressurized aircraft, respectively). These limitations assume an average requirement of 4 h of ground time for briefing and debriefing.
- If operational tempo requires the flight time limitations to be exceeded, the commanding officer, with the flight surgeon's advice, will closely monitor and specifically clear flight personnel, commenting particularly in regard to stress level and adequacy of rest and nutrition.
- Particular notice should be made of flights involving contour, nap of the Earth, chemical defense gear, night and night vision devices, and adverse environmental factors (i.e., dust, cloud cover, precipitation) since these flights are more stressful and demanding than daytime VFR conditions.

c. Stimulants/Wake Promoters

As noted above, alertness-enhancing medications are one option for sustaining the wakefulness of flightcrews during extended missions in which adequate crew rest is not possible. Needless to say, these compounds should not be considered a replacement for adequate crew rest planning and they should never be considered a substitute for restorative sleep. However, in sustained aviation operations, the occasional use of the alertness-enhancing medications such as dextroamphetamine (authorized by all three U.S. services) and modafinil (authorized for use in the U.S. Air Force) can often significantly enhance the safety and effectiveness of sleep-deprived personnel.

Modafinil (Provigil®, Vigil®, Alertec® and others): The prescription drug modafinil (100 to 200 mg) exerts a wide array of positive effects on alertness and performance. Lagarde and Batejat (108) found that 200-mg doses every 8 h reduced episodes of microsleeps and maintained more normal (i.e., rested) mental states and performance levels than placebo for 44 h of continuous wakefulness (but not the full 60 h of sleep deprivation). Wesensten et al. (226) found 200 to 400 mg doses of modafinil effectively countered performance and alertness decrements in volunteers kept awake for over 48 h. Caldwell and colleagues (47) found that 200 mg of modafinil every 4 h maintained the simulator flight performance of pilots at near-well-rested levels despite 40 h of continuous wakefulness, but that there were complaints of nausea and vertigo (likely due to the high dosage used). A more recent study with U.S. Air Force F-117 pilots indicated that three 100-mg doses of modafinil (administered every 5 h) sustained flight performance within 27% of baseline levels during the latter part of a 37-h period of continuous wakefulness. Performance under the no-treatment condition was degraded by over 82% (46). Similar beneficial effects were seen on measures of alertness and cognitive performance. Furthermore, the lower dose produced these positive effects without causing the side effects noted in the earlier study (47). Due to these and other positive results, modafinil is gaining popularity as a way to enhance the alertness of sleepy personnel, largely because it is considered safer and less addictive than compounds such as the amphetamines. Modafinil also produces less cardiovascular stimulation than amphetamine, and despite its half-life of approximately 12 to 15 h (159,169), the drug's impact on sleep architecture is minimal. However, it should be kept in mind that modafinil has not been as thoroughly tested as dextroamphetamine in real-world operational environments and some data suggests that modafinil is less effective than amphetamine (132). Nevertheless, approval has been received for the use of modafinil in certain long-range U.S. Air Force combat aviation missions, and it is likely that modafinil soon will be approved for use in the U.S. Army and the U.S. Navy.

Amphetamine (Dexedrine®, Dextrostat®): Dextroamphetamine (5 to 10 mg) has been authorized for use by all three U.S. services for certain types of lengthy (i.e., 12 or more hours) flight missions. In comparison to caffeine, dextroamphetamine appears to offer a more consistent and prolonged alerting effect (223). In comparison to modafinil, studies suggest that amphetamine is either more efficacious (132) or, at least in the case of 40-h sleep-deprivation periods, equivalent (41,160,225). In terms of the efficacy of amphetamine as a fatigue countermeasure, Newhouse et al. (148) studied d-amphetamine (5, 10, or 20 mg) in people deprived of sleep for over 48 h and found that 20 mg d-amphetamine (administered after 41 h of continuous wakefulness) produced marked improvements in addition/subtraction (lasting for over 10 h), a gradual improvement in logical reasoning (significant between 5.5 and 7.5 h postdose), a long-lasting improvement in the speed of responding during the choice reaction-time task (10 h), and an increase in alertness for 7 h. It was noted that the drug did not impair judgment. The 10-mg dose exerted fewer and shorter-lasting effects, whereas the 5-mg dose was ineffective. Two flight simulation studies involving U.S. Army pilots indicated that repeated 10-mg doses of dextroamphetamine (given at midnight, 0400, and 0800) maintained flight performance and alertness nearly at well-rested levels throughout 40 h of continuous wakefulness (44,45). Benefits were especially noticeable between 0300 and 1100, when fatigue-related problems were most severe. In a later study, 10 pilots completed a series of 1-h sorties in a specially instrumented UH-60 helicopter during 40 h of sleep deprivation. The results revealed that 10-mg doses of dextroamphetamine sustained performance nearly as well under actual in-flight conditions as in the laboratory (42). A follow-on simulator investigation extended these findings by showing that with additional amphetamine dosing, pilot performance and alertness could be sustained for over 58 continuous hours of wakefulness (2 nights of sleep loss) (50). Reports from the field indicate dextroamphetamine has been used successfully in a number of combat situations such as Vietnam (58), the 1986 Air Force strike on Libya (192), and Operation Desert Shield/Storm (59). Emonson and Vanderbeek (81) found that U.S. Air Force pilots who were administered dextroamphetamine during Operation Desert Shield/Storm were better able to maintain acceptable performance during continuous and sustained missions, and that the medication contributed to both safety and effectiveness. To date, no major side effects or other problems have been reported from the medical use of dextroamphetamine in military settings. In light of these and other findings, dextroamphetamine doses of 10 to 20 mg (not to exceed 60 mg per day) are recommended for situations in which heavily fatigued military pilots simply must complete the mission despite dangerous levels of sleep deprivation. Guidance from the U.S. Air Force is shown below.

U.S. Air Force Combat Aviation Operations Guidance for Use of Stimulants:

- Prior to the operational use of dextroamphetamine or modafinil, an informed consent agreement must be obtained to ensure that crews are fully aware of both the positive and the potential negative effects of these compounds.
- The decision to authorize the use of alertness-enhancing compounds should be made by the Wing Commander in conjunction with the Senior Flight Surgeon.
- All distribution of alertness-enhancing medications must be closely monitored and documented.
- Ground testing (during nonflight periods) is required prior to operational use.
- The currently authorized dose of dextroamphetamine is 5 to 10 mg, and although the dosing interval is not explicitly stated, a 4-h interval is often recommended. No more than 60 mg should be administered in any 24-h period, and often, no more than 30 mg are administered.
- The currently authorized dose of modafinil is 200 mg every 8 h, not to exceed 400 mg in any 24-h period; however, recent F-117 research has indicated that 100-mg doses also are efficacious (and this lower dose is authorized as well).
- The use of alertness-enhancing compounds normally can be authorized in fighter missions longer than 8 h or bomber missions longer than 12 h (although exceptions can be made).
- Caffeine generally is not considered to be a suitable alternative for modafinil or dextroamphetamine; however, caffeine in the form of foods or beverages may be consumed without restriction. Caffeine in the form of tablets or capsules can only be used after flight surgeon approval.

The U.S. Army and U.S. Navy guidance is mostly consistent with U.S. Air Force guidance with the most notable exception being that modafinil is not currently authorized in the Army or Navy. The U.S. Army guidance for use of dextroamphetamine endorses the administration of 5- to 10-mg doses and specifies that no more than 30 mg may be used in any 24-h period. It is also stated that the medication not be used to sustain wakefulness longer than 64 continuous hours. The U.S. Navy guidance suggests that dextroamphetamine be administered in 5-mg doses which may be repeated every 2 to 3 h; however, total dosage should not exceed 30 mg in any 24-h period. An upper level for the duration of any period of continuous wakefulness is not specified, but it is clear that extended periods without sleep should be avoided.

Position Statement on the Use of Stimulants to Sustain Flight Performance

Alertness-enhancing compounds of some description are already authorized for use in all U.S. military services during periods of unavoidable sleep deprivation. Thus far, the U.S. Air Force is the only service that has authorized the use of both modafinil and dextroamphetamine, whereas only dextroamphetamine is currently authorized by the U.S. Army and U.S. Navy. Based on Air Force experience, it is recommended that modafinil use be sanctioned by all three U.S. services under guidance consistent with that currently followed by the Air Force. Relatively uncontrolled caffeine use is also an option in all three U.S. services, and the use of caffeine, while not recommended as a primary pharmacological fatigue countermeasure, should continue to be sanctioned by the U.S. services. Aircrew should avoid habituation to caffeine and take advantage of the cortical stimulant properties of caffeine when it is needed to help ensure safe operations. More specifically, when aircrews are not suffering from the effects of fatigue, they should limit their total daily caffeine consumption from all sources to 200 to 250 mg per day. Additional doses of caffeine should be used during situations in which fatigue elevates the risk of a mishap. These situations may include low-workload, long-duration transits over land or water during the predawn hours; approach and landing during the predawn hours; and approach and landing at the end of an extraordinarily long crew duty day. In any given 24-h period, the total amount of caffeine consumed should not exceed 1000 mg. Aircrew should be aware of the 4-6-h half-life of circulating caffeine and preplan its use such that postduty day sleep is disturbed minimally by caffeine use.

With the exception of caffeine and various nutritional supplements, no alertness-enhancing medications are currently authorized for use in any type of civil aviation operation. Due to the fact that civil operations generally are more predictable than military operations, and due to the fact that prolonged periods of sleep deprivation are not the norm in civil operations (whereas such periods are often unavoidable in the military sector), it would seem prudent to withhold widespread authorization of prescription alertness enhancers in the civilian aviation sector. Also, there is the matter that intense military operations are generally time limited, exposing military pilots to only relatively brief periods in which intense sleep deprivation necessitates the administration of appropriate counter-fatigue medications, whereas civil operations continue day in and day out for the duration of a pilot's career, potentially exposing moderately fatigued pilots to years of chronic medication use if such medications were authorized. This difference between military and civil aviation scenarios likewise seems to argue against the widespread authorization of alertness-enhancing drugs in civil operations. However, it would be worthwhile to consider the temporary authorization of counter-fatigue medications in civil emergency flight operations such as when airlifting disaster relief supplies, rapidly evacuating medical casualties following some catastrophic event, etc.

d. Sleep-Inducing Agents

When individuals are given the opportunity to sleep, but are unable to do so due to various circumstances (i.e., wrong circadian time, poor sleep conditions), sleep aids represent a viable countermeasure. The characteristics of various hypnotics were discussed earlier. However, each branch of the military has its own policy concerning the use of hypnotics. **Table IV** indicates the U.S. military's policies on hypnotic use. As with the stimulant policy, a ground test is necessary prior to use during operations. The U.S. Navy guidance explicitly forbids the administration of more than one dose of a hypnotic per 24-h period, with no more than 2 d of consecutive use of temazepam. There is also guidance for planning and briefing in the grounding restriction (210). As with other medications, the use of hypnotics is voluntary.

Position Statement on the Military Use of Sleep-Inducing Agents

Sleep-promoting compounds are useful for mitigating the sleep loss associated with circadian disruptions, poor sleeping conditions, and poor sleep timing often associated with combat or other high-tempo military operations. They should continue to be authorized in circumstances where: 1) their use is justified by the presence of one or more of the previously noted factors; 2) there is appropriate medical supervision; 3) there is evidence that the crewmember has completed a pre-mission

TABLE IV. U.S. MILITARY POLICIES FOR HYPNOTIC USE.

Medication	Dose	Half-life	Grounding
U.S. Army Rest Agent Policy			
Temazepam (Restoril®)	15 or 30 mg	8.0–12.0 h	24 h
Triazolam (Halcion®)	0.125 or 0.25 mg	2.0–4.0 h	9 h
Zolpidem (Ambien®)	5 or 10 mg	2.0–2.5 h	8 h
Zaleplon (Sonata®)	5 or 10 mg	1.0 h	8 h
U.S. Air Force No-Go Pill Policy			
Temazepam (Restoril®)	15 or 30 mg	8.0–12.0 h	12 h
Triazolam (Halcion®)	Not authorized	na	na
Zolpidem (Ambien®)	10 mg	2.0–2.5 h	6 h
Zaleplon (Sonata®)	10 mg	1.0 h	4 h
U.S. Navy Sleep Initiator Policy			
Temazepam (Restoril®)	15 mg	8.0–12.0 h	7 h
Triazolam (Halcion®)	Not authorized	na	na
Zolpidem (Ambien®)	5 or 10 mg	2.0–2.5 h	6 h
Zaleplon (Sonata®)	Not authorized	Na	na

ground-test to check for idiosyncratic reactions; and 4) the mission is such that there is little or no chance that the aircrew member will be subject to an unexpected truncation of the sleep period. Obviously, personnel who are "on-call" and may need to fly a mission at a moment's notice should not utilize sleep medications of any type due to the possibility that the medication would not have time to be adequately metabolized prior to returning to duty. Education concerning use and effects, ground testing, and grounding times are important for successful and safe use of sleep substances.

e. Nonpharmacological Countermeasures and Strategies

Of the U.S. military services, the Air Force guidance on nonpharmacological counter-fatigue strategies is the most specific. For instance, controlled cockpit rest is explained in detail below:

Cockpit Rest Guidelines:

- Controlled cockpit rest may be implemented when the basic aircrew includes a second qualified pilot.
- Cockpit rest must be restricted to noncritical phases of flight between cruise and 1 h prior to planned descent.
- Resting crewmember must be immediately awakened if a situation develops that may affect flight safety.
- Cockpit rest shall only be taken by one crewmember at a time.
- All cockpit crewmembers including the resting member must remain at their stations.
- A rest period shall be limited to a maximum of 45 min.
- More than one rest period per crewmember is permitted if the opportunity exists.
- Controlled cockpit rest is not authorized with any aircraft system malfunctions that increase cockpit workload.
- Cockpit rest should not be used as a substitute for any required crew rest.

Of course, the U.S. Air Force as well as the U.S. Army and the U.S. Navy brief personnel on the correct use of a variety of alertness-management strategies such as the promotion of preduty sleep, implementation of extended crew rest periods when possible, bright light exposure when feasible, in-flight activity/rest breaks, and general fatigue management. All can be used in combination when appropriate.

VII. CONCLUSIONS AND RECOMMENDATIONS

Given the state of the art in fatigue countermeasures, our summary recommendations, most of which apply to both civil and military aviation except where noted, are as follows:

Education—about the dangers of fatigue, the causes of sleepiness, and the importance of sleep and proper sleep habits—is one of the keys to addressing fatigue in operational contexts. All aviation personnel including supervisors, schedulers, and crewmembers should be educated regarding the effects of fatigue, the factors responsible for fatigue, and the available scientifically proven fatigue countermeasures. Ultimately, the individual pilot, schedulers, and management must be convinced that sleep and circadian rhythms are important and that quality day-to-day sleep is the best possible protection against on-the-job fatigue. Recent studies have made it clear that as little as 1 to 2 h of sleep restriction almost immediately degrades vigilance and performance in subsequent duty periods (17,214). Thus, educational programs should communicate the central points conveyed in this position paper:

1) fatigue is a physiological problem that cannot be overcome by motivation, training, or willpower;
2) people cannot reliably self-judge their own level of fatigue-related impairment;
3) there are wide individual differences in fatigue susceptibility that must be taken into account but which presently cannot be reliably predicted;
4) there is no one-size-fits-all "magic bullet" (other than adequate sleep) that can counter fatigue for every person in every situation; but
5) there are valid counter-fatigue strategies that will enhance safety and productivity, but only when they are correctly applied.

Concurrent with the educational effort, a large-scale program should be undertaken to implement a nonprescriptive fatigue risk management system (FRMS) that determines optimum flight schedules from both a physiological and operational standpoint on a case-by-case basis since prescriptive hours-of-service limitations cannot account for human circadian rhythms or sleep propensity. With regard to in-flight counter-fatigue strategies, we concur with the present primary reliance on in-flight bunk rest in long-haul operations, but suggest that computerized scheduling tools be used to optimize crew rostering and bunk rest timing. We likewise believe that short in-flight breaks are beneficial, and we recommend that any regulations governing the use of these breaks be liberalized (i.e., that alertness-promoting breaks be permitted as a clearly acceptable reason for pilots to deviate from the requirement to remain in their seats with seatbelts fastened at all times). Given the scientific evidence that cockpit napping is safe and highly effective, as well as clear indications that the general public appreciates the value of cockpit napping, we take exception to the current prohibition on in-seat cockpit napping in civil aviation, and instead recommend that in-seat cockpit naps up to 45 min in duration be permitted in U.S. commercial flight operations as long as the naps are not used as a replacement for other sleep opportunities (i.e., bunk sleep or pre/post duty sleep). This procedure is in agreement with current U.S. Air Force policy.

To promote on-duty alertness in the absence of sufficient contiguous hours of preduty sleep, the importance of napping should be emphasized as a primary strategy. Off-duty naps should be as long as possible and whenever feasible they should occur at the circadian times most conducive to natural sleep (i.e., early afternoon or early predawn hours according to the body clock). The principles outlined for good sleep hygiene should be followed to promote optimal nap quality and duration. Upon awakening from a nap, there should be a wake-up period of at least 30 min prior to the performance of any safety sensitive tasks. When naps are insufficient, personnel should consider the ingestion of caffeine (up to 1000 mg per day) as an alertness-enhancing strategy, and they should make an effort to use caffeine judiciously (i.e., only when it is truly needed to reduce the impact of fatigue).

With regard to the use of pharmacological compounds in civil flight operations, it is our position that on the one hand, prescription alertness-enhancing compounds not be authorized on a routine basis since they are not justified by a cost/benefit analysis for flight operations that are relatively predictable, and there is insufficient medical oversight to ensure appropriate use. Also, it should be noted that when civil as opposed to military flights are cancelled or modified due to crew fatigue, there is virtually no "downside" from a safety perspective. A possible exception to the prohibition against alertness-enhancing compounds in civil operations could be to temporarily authorize these medications for pilots flying disaster relief or intense, but time-limited emergency medical flights when untreated fatigue would necessitate the cancellation or delay of these flights and thus jeopardize the safety of others. On the other hand, the prescription sleep-promoting compound zolpidem should be authorized for use by civilian commercial pilots in situations where quality natural sleep is difficult or impossible to obtain due to circadian or other reasons provided that: 1) the pilot has previously checked for any unusual reactions to the medication; 2) the dose does not exceed 10 mg in any given 24-h period; 3) the medication is used no more than 4 times in any 7-d period; and 4) there is an interval of 12 h between the ingestion of the medication and the return to duty. The benefits of restful sleep induced by a medication with short duration of action and excellent safety profile (as established by military aviation experience) are far preferable to the adverse effects of sleep deprivation when medication is withheld or the adverse effects of alcohol-induced sleep. Zolpidem should not be taken to promote in-flight bunk sleep or cockpit naps. To minimize complete reliance on medication for the improvement of quality preduty or postduty sleep, it is our contention that crewmembers should be educated about proper sleep hygiene, the benefits of aerobic exercise for promoting quality sleep, and natural strategies designed to promote circadian readjustment (assuming crewmembers will remain in a new time zone for 5 or more days). In the United States, the use of non-FDA regulated substances such as valerian, kava, and melatonin is not recommended because the quality of the compounds cannot be assured and there is insufficient scientific evidence of safety and/or effectiveness. In other jurisdictions, melatonin is available in pharmaceutical grade. In laboratory environments, pharmaceutical-grade melatonin has been effective in circadian entrainment or facilitation of daytime sleep (8,9,118,119,196,231).

Fatigue detection technologies (fitness for duty and real-time assessment devices) and scheduling tools that incorporate biomathematical models of alertness can be incorporated as part of an overall safety management approach but should not be used in place of regulatory limitations. Prior to using any of these technologies, the scientific literature should be consulted to establish the validity of the specific technique.

With regard to the use of prescription pharmacological alertness-enhancing compounds in military aviation operations, it is our contention that the compound dextroamphetamine remains an authorized option and that modafinil, which is already authorized by the U.S. Air Force, be authorized by the other services as well. Military flight operations are intense and unpredictable, and fatigued pilots often have little choice (in consideration of all the relevant mission factors) except to complete a scheduled mission. Failure to do so could jeopardize the safety or survivability of other military personnel or civilians. The benefits of appropriate stimulant use have been shown by scientific study to far outweigh the negative effects of sleep deprivation. Furthermore, proper medical oversight is typically available in the military aviation context.

Concerning the use of prescription pharmacological sleep-inducing compounds in military flight operations, we believe the existing authorized use of temazepam, zolpidem, and zaleplon should be continued. Since adequate routine medical oversight is available in the military aviation context, a physician can choose the correct medication based on the specific situation and monitor for proper usage and the occurrence of unexpected side effects. Furthermore, it is certainly the case that the effects of restful sleep induced by one of the above medications are far superior to the effects of alcohol-induced sleep or to the adverse effects of sleep deprivation.

In developing fatigue countermeasures of every sort, individual differences must be better addressed. There are differences in how people respond to sleep loss, sleep disruption, and time zone transitions. Research is focusing on identifying individual differences in sleep regulatory mechanisms, circadian rhythmicity, recovery sleep, and responses to fatigue countermeasures (215, 216). Examining the impact of various individual factors (circadian phase, sleep need, etc.) on susceptibility to decrements and the efficacy of countermeasures will facilitate optimal fatigue management in the aviation environment. Such data are being used for the development of biomathematical models of fatigue to predict performance and alertness levels at an individual level (215). Due to a range of differences in how individuals respond to the operational challenges associated with long-haul and ULR flight operations, modeling work is also aiming to predict relative group performance for an overall trip pattern. Many issues associated with flight operations remain unanswered and can only be answered by collecting data during carefully scientifically designed research.

In sum, while fatigue represents a significant risk in aviation when left unaddressed, there are currently numerous countermeasures and strategies that can be employed to increase safety. Furthermore, new technologies and countermeasures are being developed that hold great promise for the future. It is our hope that the countermeasures and strategies described in this paper, when employed appropriately, will serve to reduce the risk of aviation accidents and incidents attributable to the insidious effects of fatigue.

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REFERENCES

1. Aeronautics and Space General operating and flight rules. 14 C.F.R. § 91.1057, 91.1059, 91.1061 (2007a).
2. Aeronautics and Space General operating and flight rules. 14 C.F.R. § 121 (2007b).
3. Aeronautics and Space General operating and flight rules. 14 C.F.R. § 135 (2007c).
4. Afaghi A, O'Connor H, Chow CM. High-glycemic-index carbohydrate meals shorten sleep onset. Am J Clin Nutr 2007; 85:426–30.
5. Ahasan R, Lewko J, Campbell D, Salmoni A. Adaptation to night shifts and synchronisation processes of night workers. J Physiol Anthropol Appl Human Sci 2001; 20:215–26.
6. Akerstedt T. Shift work and disturbed sleep/wakefulness. Occup Med (Lond) 2003; 53:89–94.
7. Angus RG, Pigeau RA, Heslegrave RJ. Sustained-operations studies: from the field to the laboratory. In: Stampi C, ed. Why we nap. Boston: Birkhauser; 1992:217–41.
8. Arendt J. Melatonin characteristics, concerns, and prospects. J Biol Rhythms 2005; 20:291–303.
9. Arendt JT, Skene DJ. Melatonin as a chronobiotic. Sleep Med Rev 2005; 9:25–39.
10. Arnulf I, Quintin P, Alvarez JC, Vigil L, Touitou Y, Lèbre AS, et al. Mid-morning tryptophan depletion delays REM sleep onset in healthy subjects. Neuropsychopharmacology 2002; 27:843–51.
11. Atkinson G, Edwards B, Reilly T, Waterhouse J. Exercise as a synchronizer of human circadian rhythms: an update and discussion of the methodological problems. Eur J Appl Physiol 2007; 99:331–41.
12. Australian Government Civil Aviation Safety Authority. Civil Aviation Orders. Flight time limitations –pilots Part 48, Section 48.1, Issue 9 –December 8, 2004, Amdt. No. 29. http://www.casa.gov.au/download/orders/cao48/4801.pdf.
13. Australian Government Civil Aviation Safety Authority. Rules watch. Flight Safety Australia 2008; 60:50–1.
14. Balter MB, Uhlenhuth EH. New epidemiologic findings about insomnia and its treatment. J Clin Psychiatry 1992; 53(Suppl. 12):34–9.
15. Barger LK. Wright KP, Jr, Hughes RJ, Czeisler CA. Daily exercise facilitates phase delays of circadian melatonin rhythm in very dim light. Am J Physiol Regul Integr Comp Physiol 2004; 286:R1077–84 Epub 2004 Mar 18.
16. Bartholini G. Growing aspects of hypnotic drugs. In: Sauvanet JP, Langer SZ, Morselli PL, eds. Imidazopyridines in sleep disorders. New York: Raven Press; 1988:1–9.
17. Belenky G, Wesensten NJ, Thorne DR, Thomas ML, Sing HC, Redmond DP, et al. Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose-response study. J Sleep Res 2003; 12:1–12.
18. Belland KM, Bissell C. A subjective study of fatigue during navy flight operations over southern Iraq: Operation Southern Watch. Aviat Space Environ Med 1994; 65:557–61.
19. Belyavin A, Spencer MB. Modeling performance and alertness: the QinetiQ approach. Aviat Space Environ Med 2004; 75(3, Suppl.):A93–A103.
20. Berka C, Levendowski DJ, Cvetinovic MM, Petrovic MM, Davis G, Lumicao MN, et al. Real-time analysis of EEG indexes of alertness, cognition, and memory acquired with a wireless EEG headset. Int J Hum Comput Interact 2004; 17:151–70.
21. Blois R, Gaillard J, Attali P, Coqueline J. Effect of zolpidem on sleep in healthy subjects: a placebo controlled trial with polysomnographic recordings. Clin Ther 1993; 15:797–809.
22. Bonnet MH. Dealing with shift work: physical fitness, temperature, and napping. Work Stress 1990; 4:261–74.
23. Bonnet MH. The effect of varying prophylactic naps on performance, alertness and mood throughout a 52-hour continuous operation. Sleep 1991; 14:307–15.
24. Bonnet MH. Acute sleep deprivation. In: Kryger MA, Roth T, Dement WC, eds. Principles and practice of sleep medicine. Philadelphia: Elsevier Saunders; 2005:51–66.
25. Bonnet MH, Arand DL. Clinical effects of sleep fragmentation versus sleep deprivation. Sleep Med Rev 2003; 7:293–310.
26. Booth-Bourdeau J, Marcil I, Laurence M, McCulloch K, Dawson D. Development of fatigue risk management systems for the Canadian aviation industry. Proceedings of the 2005 International Conference on Fatigue Management in Transportation Operations; 2005 September 11-15; Seattle. WA: Transport Canada; 2005.
27. Boulos Z, Campbell SS, Lewy AJ, Terman M, Dijk D, Eastman CI. Light treatment for sleep disorders: consensus report. VI. Jet lag. J Biol Rhythms 1995; 10:167–76.
28. Bourgeois-Bougrine S, Carbon P, Gounelle C, Mollard R, Coblentz A. Perceived fatigue for short- and long-haul flights: a survey of 739 airline pilots. Aviat Space Environ Med 2003; 74:1072–7.
29. Bricknell MCM. Sleep manipulation prior to airborne exercises. J R Army Med Corps 1991; 137:22–6.
30. Brooks A, Lack L. A brief afternoon nap following nocturnal sleep restriction: which nap duration is most recuperative? Sleep 2006; 29:831–40.
31. Brown ID. Prospectus for technological countermeasures against driver fatigue. Accid Anal Prev 1997; 29:525–31.
32. Brzezinski A, Vangel MG, Wurtman RJ, Norrie G, Zhdanova I, Ben-Shushan A, et al. Effects of exogenous melatonin on sleep: a meta-analysis. Sleep Med Rev 2005; 9:41–50.
33. Burgess HJ, Sharkey KM, Eastman CI. Bright light, dark and melatonin can promote circadian adaptation in night shift workers. Sleep Med Rev 2002; 6:407–20.
34. Burgess HJ, Revell VL, Eastman CI. A three pulse phase response curve to three milligrams of melatonin in humans. J Physiol 2008; 586:639–47.
35. Buxton OM, Lee CW, L'Hermite-Baleriaux M, Turek FW, Van Cauter E. Exercise elicits phase shifts and acute alterations of melatonin that vary with circadian phase. Am J Physiol Regul Integr Comp Physiol 2003; 284:R714–24.
36. Cabon P, Bourgeois-Bougrine S, Mollard R, Coblentz A, Speyer JJ. Electronic pilot-activity monitor: a countermeasure against fatigue on long-haul flights. Aviat Space Environ Med 2003; 74(6 Pt 1):679–82.
37. Cabon P, Coblentz A, Mollard R, Fouillot JP. Human vigilance in railway and long-haul flight operation. Ergonomics 1993; 36:1019–33.
38. Cajochen C. Alerting effects of light. Sleep Med Rev 2007; 11: 453–64.
39. Cajochen C, Khalsa SB, Wyatt JK, Czeisler CA, Dijk DJ. EEG and ocular correlates of circadian melatonin phase and human performance decrements during sleep loss. Am J Physiol 1999; 277:R640–9.
40. Cajochen C, Zeitzer JM, Czeisler CA, Dijk DJ. Dose response relationship for light intensity and ocular and electroencephalographic correlates of human alertness. Behav Brain Res 2000; 115:75–83.
41. Caldwell JA. Efficacy of stimulants for fatigue management: the effects of Provigil and Dexedrine on sleep-deprived aviators. Transportation Research Part F: Traffic Psychology and Behaviour 2001; 4 (1):19–37.
42. Caldwell JA, Caldwell JL. An in-flight investigation of the efficacy of dextroamphetamine for sustaining helicopter pilot performance. Aviat Space Environ Med 1997; 68:1073–80.
43. Caldwell JA, Caldwell JL. Comparison of the effects of zolpidem-induced prophylactic naps to placebo naps and forced rest periods in prolonged work schedules. Sleep 1998; 21:79–90.

44. Caldwell JA, Caldwell JL, Crowley JS. Sustaining female helicopter pilot performance with Dexedrine during sustained operations. Int J Aviat Psychol 1997; 7:15–36.
45. Caldwell JA, Caldwell JL, Crowley JS, Jones HD. Sustaining helicopter pilot performance with Dexedrine during periods of sleep deprivation. Aviat Space Environ Med 1995; 66: 930–7.
46. Caldwell JA, Caldwell JL, Smith JK, Alvarado L, Heintz T, Mylar JT, et al. The efficacy of modafinil for sustaining alertness and simulator flight performance in F-117 pilots during 37 hours of continuous wakefulness. Brooks City-Base, TX: U.S. Air Force Research Laboratory; 2004 Jan. Report No. AFRL-HE-BR-TR-2004-0003.
47. Caldwell JA, Caldwell JL, Smythe NK, Hall KK. A double-blind, placebo-controlled investigation of the efficacy of modafinil for sustaining alertness and performance of aviators: a helicopter simulator study. Psychopharmacology (Berl) 2000; 150:272–82.
48. Caldwell JA, Gilreath SR. A survey of aircrew fatigue in a sample of Army aviation personnel. Aviat Space Environ Med 2002; 73:472–80.
49. Caldwell JA, Prazinko B, Caldwell JL. Body posture affects electroencephalographic activity and psychomotor vigilance task performance in sleep-deprived subjects. Clin Neurophysiol 2003; 114:23–31.
50. Caldwell JA, Smythe NK, LeDuc PA, Caldwell JL. Efficacy of dextroamphetamine for the maintenance of aviator performance during 64 hours of sustained wakefulness. Aviat Space Environ Med 2000; 71:7–18.
51. Caldwell JL, Gilreath SR. Work and sleep hours of U.S. Army aviation personnel working reverse cycle. Mil Med 2001; 166:159–66.
52. Caldwell JL, Prazinko BF, Rowe T, Norman D, Hall KK, Caldwell JA. Improving daytime sleep with temazepam as a countermeasure for shift lag. Aviat Space Environ Med 2003; 74:153–63.
53. Carskadon MA. Ontogeny of human sleepiness as measured by sleep latency. In: Dinges DF, Broughton RJ, eds. Sleep and alertness: chronobiological, behavioral, and medical aspects of napping New York: Raven Press; 1989:53–69.
54. Chagan L, Cicero LA. Zaleplon: A possible advance in the treatment of insomnia. P&T 1999; 24:590–9.
55. Co EL. Gregory KB, Johnson JM, & Rosekind MR. Crew factors in flight operations XI: A survey of fatigue factors in regional airline operations. Moffett Field, CA: NASA Ames Research Center; 1999. Report No: NASA/TM –1999–208799.
56. Committee on Military Nutrition Research. Caffeine for the sustainment of mental task performance: Formulations for military operations. Washington, DC: National Academy Press 2001.
57. Comperatore CA, Caldwell JA, Caldwell JL. Leader's guide to crew endurance. Instructional brochure on crew work/rest scheduling, circadian rhythms, fatigue, and fatigue countermeasures. Fort Rucker, AL: U.S. Army Aeromedical Research Laboratory and the U.S. Army Safety Center, 1997.
58. Cornum KG, Cornum R, Storm W. Use of psychostimulants in extended flight operations: a Desert Shield experience. In: Advisory Group for Aerospace Research and Development Conference Proceedings No. 579, Neurological Limitations of Aircraft Operations: Human Performance Implications. Neuilly-sur-Seine, France: NATO Advisory Group for Aerospace Research and Development; 1996:371–4.
59. Cornum R, Caldwell JA, Cornum KG. Stimulant use in extended flight operations. Airpower J 1997; 11(1):53–8.
60. Cosenzo KA, Fatkin LT, Patton DJ. Ready or not: enhancing operational effectiveness through use of readiness measures. Aviat Space Environ Med 2007; 75(5, Suppl.):B96–106.
61. Costa G. The problem: shiftwork. Chronobiol Int 1997; 14:89–98.
62. Daan S, Lewy AJ. Scheduled exposure to daylight: a potential strategy to reduce "jet lag" following transmeridian flight. Psychopharmacol Bull 1984; 20:566–8.
63. Dijk DJ, Franken P. Interaction of sleep homeostasis and circadian rhythmicity: dependent or independent systems? In: Kryger MA, Roth T, Dement WC, eds. Principles and practice of sleep medicine. Philadelphia: Elsevier Saunders; 2005: 418–434.
64. Dijkman M, Sachs N, Levine E, Mallis M, Carlin MM, Gillen KA, et al. Effects of reduced stimulation on neurobehavioral alertness depend on circadian phase during human sleep deprivation. Sleep Res 1997; 26:265.
65. Dinges DF. Differential effects of prior wakefulness and circadian phase on nap sleep. Electroencephalogr Clin Neurophysiol 1986; 64:224–7.
66. Dinges DF. Critical research issues in development of biomathematical models of fatigue and performance. Aviat Space Environ Med 2004; 75(3, Suppl)A181–91.
67. Dinges DF, Graeber RC, Rosekind MR, Samel A, Wegmann HM. Principles and guidelines for duty and rest scheduling in commercial aviation. Moffett Field, CA: NASA Ames Research Center; 1996. Report No: 110404.
68. Dinges DF, Maislin G, Brewster RM, Krueger GP, Carroll RJ. Pilot test of fatigue management technologies. Washington, DC: Transportation Research Board of the National Academies, Journal of the Transportation Research Board; 2005 Report No. 1922.
69. Dinges DF, Mallis MM. Managing fatigue by drowsiness detection: can technological promises be realized? In: Hartley L, eds. Managing fatigue in transportation. Kidlington, Oxford, UK: Elsevier Science Ltd; 1998: 209–29.
70. Dinges DF, Mallis MM, Maislin G, Powell JW. Final report: evaluation of techniques for ocular measurement as an index of fatigue and as the basis for alertness management. Washington, DC: National Highway Traffic Safety Administration; 1998 Report No: DOT HS 808 762.
71. Dinges DF, Orne MT, Orne EC. Assessing performance upon abrupt awakening from naps during quasi-continuous operations. Behav Res Methods Inst Comput 1985; 17:37–45.
72. Dinges DF, Price NJ, Maislin G, Powell JW, Ecker AJ, Mallis MM. Szuba, et al. Prospective laboratory re-validation of ocular-based drowsiness detection technologies and countermeasures. In: Wierwille WW, Hanowski RJ, Olson RL, Dinges DF, Price NJ, Maislin G, et al. NHTSA Drowsy Driver Detection And Interface Project: Subtask A; 2002; Report No: DTNH 22-00-D-07007.
73. Dinges DF, Rider RL, Dorrian J, McGlinchey EL, Rogers NL, Cizman Z, et al. Optical computer recognition of facial expressions associated with stress induced by performance demands. Aviat Space Environ Med 2005; 76(6, Suppl)B172–82.
74. Dinges DF, Whitehouse WG, Orne EC, Orne MT. The benefits of a nap during prolonged work and wakefulness. Work Stress 1988; 2:139–53.
75. Driskell JE, Mullen B. The efficacy of naps as a fatigue countermeasure: a meta-analytic integration. Hum Factors 2005; 47:360–77.
76. Driver HS, Taylor SR. Sleep and exercise. Sleep Med Rev 2000; 4:387–402.
77. Duffy JF, Wright KP. Entrainment of the human circadian system by light. J Biol Rhythms 2005; 20:326–38.
78. Eastman CI, Boulos Z, Terman M, Campbell SS, Dijk D, Lewy AJ. Light treatment for sleep disorders: consensus report. VI. shift work. J Biol Rhythms 1995; 10:157–64.
79. Ebert B, Wafford KA, Deacon S. Treating insomnia: current and investigational pharmacological approaches. Pharmacol Ther 2006; 112:612–29.
80. Elie R, Ruther E, Farr I, Emilien G, Salinas E. Sleep latency is shortened during 4 weeks of treatment with zaleplon, a novel nonbenzodiazepine hypnotic. J Clin Psychiatry 1999; 60: 536–44.
81. Emonson DL, Vanderbeek RD. The use of amphetamine in U.S. Air Force tactical operations during Desert Shield and Storm. Aviat Space Environ Med 1995; 66:260–3.
82. Fabiani M, Gratton G, Coles MG Event-related brain potentials In: Caciooppo JT, Tassinary LG, Berntson GG, eds. Handbook of psychophysiology. Cambridge, England: Cambridge University Press; 2000:53–84.
83. Flight Safety Foundation. Lessons from the dawn of ultra-long-range flight. Flight Saf Dig 2005; Aug-Sept:1–60.
84. Folkard S, Tucker P. Shift work, safety and productivity. Occup Med 2003; 53:95–101.
85. Fry J, Scharf M, Mangano R, Fujimori M. Zaleplon improves sleep without producing rebound effects in outpatients with insomnia. Int Clin Psychopharmacol 2000; 15:141–52.

86. Galinsky T, Swanson N, Sauter S, Dunkin R, Hurrell J, Schleifer L. Supplementary breaks and stretching exercises for data entry operators: a follow-up field study. Am J Ind Med 2007; 50:519–27.
87. Gander PH, Graeber RC, Connell LJ, Gregory KB. Crew factors in flight operations VIII: factors influencing sleep timing and subjective sleep quality in commercial long-haul flight crews. Moffett Field, CA: NASA; 1991. Technical Memorandum 103852.
88. Gander PH, Myhre G, Graeber RC, Anderson HT, Lauber JK. Adjustment of sleep and the circadian temperature rhythm after flights across nine time zones. Aviat Space Environ Med 1989; 60:733–43.
89. Gillberg M. The effects of two alternative timings of a one-hour nap on early morning performance. Biol Psychol 1984; 19:45–54.
90. Gillberg M. Sleepiness and its relation to the length, content, and continuity of sleep. J Sleep Res 1995; 4(Suppl. 2):37–40.
91. Gilliland K, Schlegel RE. Readiness to perform: a critical analysis of the concept and current practices. Oklahoma City, OK: Office of Aviation Medicine, Federal Aviation Administration. NTIS No. AD 1993; A269:379.
92. Goldsmith C. More carriers sanction their pilots' cockpit snoozes. The Wall Street Journal 1998 Jan 21, B1.
93. Greenblatt DJ, Zammit G, Harmatz J, Legangneux E. Zolpidem modified-release demonstrates sustained and greater pharmacodynamic effects from 3 to 6 hours postdose as compared with standard zolpidem in healthy adult subjects. [Abstract] Sleep 2005; 28(Suppl.):A245.
94. Gu H, Ji Q. An automated face reader for fatigue detection. Proceedings of the Sixth IEEE International Conference on Automatic Face and Gesture Recognition; 2004. Los Alamitos, CA: IEEE; 2004:111–6.
95. Hadley S, Petry JJ. Valerian. Am Fam Physician 2003; 67:1755–8.
96. Heslegrave RJ, Angus RG. The effects of task duration and work-session location on performance degradation induced by sleep loss and sustained cognitive work. Behav Res Methods Inst Comput 1985; 17:592–603.
97. Ho P, Landsberger S, Signal L, Singh J, Stone B. The Singapore experience: task force studies scientific data to assess flights. Flight Safety Digest 2005; 24(8–9):20–40.
98. Horne JA, Foster SC. Can exercise overcome sleepiness? [Abstract] Sleep Research 1995; 24A:437.
99. Horowitz TS, Tanigawa T. Circadian-based new technologies for night workers. Ind Health 2002; 40:223–36.
100. Hursh SR, Raslear TG, Kaye SA, Fanzone JF Jr. Validation and calibration of a fatigue assessment tool for railroad work schedules, summary report. Washington, DC: Department of Transportation; 2006; DOT/FRA/ORD-06/21, October 31, 2006.
101. Hursh SR, Redmond DP, Johnson ML, Thorne DR, Belenky TJ, Storm WF, et al. Fatigue models for applied research in warfighting. Aviat Space Environ Med 2004; 75(3, Suppl.): A44-A53.
102. Ji Q, Zhu Z, Lan P. Real-time nonintrusive monitoring and prediction of driver fatigue Vehicular Technology. IEEE Transactions 2004; 53:1052–68.
103. Kirsch AD. Report on the statistical methods employed by the U.S. Federal Aviation Administration in its cost/benefit analysis of the proposed flight crewmember duty period limitations, flight time limitations and rest requirements. Washington, DC; United States Federal Aviation Administration; 1996. Docket No: 28081.
104. Kithil PW, Jones RD, MacCuish J. Development of driver alertness detection system using overhead capacitive sensor array. 2006; Retrieved from http://internet.cybermesa.com/~roger_jones/drowsy.htm.
105. Klein KE, Bruner H, Holtmann H, Rehme H, Stolze J, Steinhoff WD, et al. Circadian rhythm of pilots' efficiency and effects of multiple time zone travel. Aerosp Med 1970; 41:125–32.
106. Klein KE, Wegmann HM. Significance of circadian rhythms in aerospace operations. AGARDograph No. 247, 1980. Neuilly-sur-Seine, France.
107. Krystal AD, Erman M, Zammit GK, Soubrane C, Roth T; ZOLONG Study Group. Long-term efficacy and safety of zolpidem extended-release 12.5 mg, administered 3 to 7 nights per week for 24 weeks, in patients with chronic primary insomnia: a 6-month, randomized, double-blind, placebo-controlled, parallel-group, multicenter study. Sleep 2008; 31:79–90.
108. Lagarde D, Batejat D. Disrupted sleep-wake rhythm and performance: Advantages of modafinil. Mil Psychol 1995; 7:165–91.
109. Lal SKL, Craig A. Reproducibility of the spectral components of the electroencephalogram during driver fatigue. Int J Psychophysiol 2005; 55:137–43.
110. Landström U, Knutsson A, Lennernäs M, Söderberg L. Laboratory studies of the effects of carbohydrate consumption on wakefulness. Nutr Health 2000; 13:213–25.
111. Lavie P. Ultrashort sleep-waking schedule. III. "Gates" and "forbidden zones" for sleep. Electroencephalogr Clin Neurophysiol 1986; 63:414–25.
112. Lavine RA, Sibert JL, Gokturk M, Dickens B. Eye-tracking measures and human performance in a vigilance task. Aviat Space Environ Med 2002; 73:367–72.
113. LeDuc PA, Caldwell JA, Ruyak PS. The effects of exercise versus napping on alertness and mood in sleep-deprived aviators. Fort Rucker, AL: U.S. Aeromedical Research Laboratory; 2000; Technical Report 2000–12.
114. Leese P, Maier G, Vaickus L, Akylbekova E. Esopiclone: pharmacokinetic and pharmacodynamic effects of a novel sedative hypnotic after daytime administration in healthy subjects.[Abstract] Sleep 2002; 25(Suppl.):A45.
115. Levendowski DJ, Berka C, Olmstead RE, Jarvik M. Correlations between EEG indices of alertness measures of performance and self-reported states while operating a driving simulator. [Abstract]. 29th Annual Meeting, Society for Neuroscience; 1999 October 25; Miami Beach, FL. Washington, DC Soceity for Neuroscience; 1999; Vol. 25.
116. Levendowski DJ, Olmstead RE, Konstantinovic ZR, Berka C, Westbrook PR. Detection of electroencephalographic indices of drowsiness in real time using a multi-level discriminant function analysis. Sleep 2000; 23(Abstract Suppl. 2):A243–4
117. Lewy AJ, Bauer VK, Ahmed S, Thomas KH, Cutler NL, Singer CM, et al. The human phase response curve (PRC) to melatonin is about 12 hours out of phase with the PRC to light. Chronobiol Int 1998; 15:71–83.
118. Lewy AJ, Emens J, Jackman A, Yuhas K. Circadian uses of melatonin in humans. Chronobiol Int 2006; 23:403–12.
119. Lieberman JA. Update on the safety considerations in the management of insomnia with hypnotics: Incorporating modified-release formulations into primary care. Prim Care Companion J Clin Psychiatry 2007; 9:25–31.
120. Lin C, Wu R, Jung T, Liang S, Huang T. Estimating driving performance based on EEG spectrum analysis. EURASIP J Appl Signal Processing 2005; 19:3165–74.
121. Lobb ML, Stern JA. Pattern of eyelid motion predictive of decision errors during drowsiness: oculomotor indices of altered states. Int J Neurosci 1986; 30:17-22.
122. Lockley SW, Evans EE, Scheer FA, Brainard GC, Czeisler CA, Aeschbach D. Short-wavelength sensitivity for the direct effects of light on alertness, vigilance, and the waking electroencephalogram in humans. Sleep 2006; 29:161–8.
123. Lucero K, Hicks RA. Relationship between habitual sleep duration and diet. Percept Mot Skills 1990; 71(3 Pt 2):1377–8.
124. Luna T. Fatigue in context: USAF mishap experience. [Abstract] Aviat Space Environ Med 2003; 74:388.
125. Mallis M, Maislin G, Konowal N, Byrne V, Bierman D, Davis R, et al. Biobehavioral responses to drowsy driving alarms and alerting stimuli. Washington, DC: U.S. Department of Transportation; 1998; Final Report: 1–127.
126. Mallis MM, Mejdal S, Nguyen TT, Dinges DF. Summary of the key features of seven biomathematical models of human fatigue and performance. Aviat Space Environ Med 2004; 75:A4–14.
127. Mallis MM, Neri DF, Colletti LM, Oyung RL, Reduta DD, Van Dongen H, et al. Feasibility of an automated drowsiness monitoring device on the flightdeck. Sleep 2004; 27(Abstract Suppl.):A167-8.
128. Matsumoto K, Harada M. The effect of night-time naps on recovery from fatigue following night work. Ergonomics 1994; 37:899–907.
129. Matsumoto Y, Mishima K, Satoh K, Shimizu T, Hishikawa Y. Physical activity increases the dissociation between subjective

sleepiness and objective performance levels during extended wakefulness in human. Neurosci Lett 2002; 326:133–6.

130. Melfi ML, Miller JC. Causes and effects of fatigue in experienced military aircrew and the countermeasures needed to improve flight safety. Brooks City-Base, TX: Air Force Research Laboratory; 2006 Jan. Report No AFRL-HE-BR-TR-2006-0071.

131. Menkes DB. Hypnosedatives and anxiolytics. In: Dukes MNG, Aronson JK, eds. Meyler's side effects of drugs, 14th ed. Amsterdam: Elsevier Science; 2000: 121–38.

132. Mitler MM, Aldrich MS. Stimulants: efficacy and adverse effects. In: Kryger MH, Roth T, Dement WC, eds. Principles and practice of sleep medicine. 3rd ed. Philadelphia: W.B. Saunders Co; 2000: 429–40.

133. Mitler MM, Carskadon MA, Phillips RL, Sterling WR, Zarcone VP, Jr., Spiegels R, et al. Hypnotic efficacy of temazepam: a long-term sleep laboratory evaluation. Br J Clin Pharmacol 1979; 8:63S–8S.

134. Mohler SR. Clinical problems in aviation medicine: fatigue in aviation activities. Aerosp Med 1966; 37:722–32.

135. Moja EA, Antinoro E, Cesa-Bianchi M, Gessa GL. Increase in stage 4 sleep after ingestion of a tryptophan-free diet in humans. Pharmacol Res Commun 1984; 16:909–14.

136. Monti JM. Primary and secondary insomnia: prevalence, causes and current therapeutics. Curr Med Chem Cent Nerv Syst Agents 2004; 4:119–37.

137. Morin AK. Strategies for treating chronic insomnia. Am J Manag Care 2006; 12:S230–46.

138. Muller FO, Dyk MV, Hundt HKL, Joubert AL, Luus HG, Groenewound G, et al. Pharmacokinetics of temazepam after day-time and night-time oral administration. Eur J Clin Pharmacol 1987; 33:211–4.

139. National Transportation Safety Board. A review of flightcrew-involved, major accidents of U.S. air carriers, 1978 through 1990. Washington, DC: National Transportation Safety Board; 1994. Report No: NTSB Safety Study No. SS-94-01.

140. National Transportation Safety Board's Most Wanted Aviation Safety Improvements: Hearing before the Subcommittee on Aviation of the Committee on Transportation and Infrastructure, 110th Cong., 1st Sess., 35–37 (2007) (testimony of William R. Voss).

141. National Sleep Foundation. 2002 Sleep in America poll. Washington: National Sleep Foundation 2002.

142. Nehlig A. Are we dependent upon coffee and caffeine? a review on human and animal data. Neurosci Biobehav Rev 1999; 23:563–76.

143. Neri DF. Scientific and operational issues associated with ultra long range flight [Abstract]. Aviat Space Environ Med 2005; 76:247

144. Neri DF, Oyung RL, Colletti LM, Mallis MM, Tam PY, Dinges DF. Controlled breaks as a fatigue countermeasure on the flight deck. Aviat Space Environ Med 2002; 73:654–64.

145. Neri DF, Wiegmann D, Stanny RR, Shappell SA, McCardie A, McKay DL. The effects of tyrosine on cognitive performance during extended wakefulness. Aviat Space Environ Med 1995; 66:313–9.

146. Neumann M, Jacobs KW. Relationship between dietary components and aspects of sleep. Percept Mot Skills 1992; 75(3 Pt 1):873–4.

147. Neville KJ, Bisson RU, French J, Boll PA, Storm WF. Subjective fatigue of C-141 aircrews during Operation Desert Storm. Hum Factors 1994; 36:339–49.

148. Newhouse PA, Penetar DM, Fertig JB, Thorne DR, Sing HC, Thomas ML, et al. Stimulant drug effects on performance and behavior after prolonged sleep deprivation: a comparison of amphetamine, nicotine, and deprenyl. Mil Psychol 1992; 4: 207–33.

149. Nicholson AN. Hypnotics and occupational medicine. J Occup Med 1990; 32:335–41.

150. Nicholson AN, Pascoe PA, Spencer MB, Stone BM, Roehrs TA, Roth T. Sleep after transmeridian flights. Lancet 1986; 2: 1205–8.

151. Nicholson AN, Roth T, Stone BM. Hypnotics and aircrew. Aviat Space Environ Med 1985; 56:299–303.

152. Nicholson AN, Stone BM. Sleep and wakefulness handbook for flight medical officers. Neuilly-sur-Seine, France: Advisory Group for Aerospace Research and Development; 1982.

153. Nicholson AN, Stone BM, Pascoe PA. Efficacy of some benzodiazepines for day-time sleep. Br J Clin Pharmacol 1980; 10:459–63.

154. Oren DA, Reich W, Rosenthal NE, Wehr TA. How to beat jet lag: a practical guide for air travelers. New York: Henry Holt; 1993.

155. Owasoyo JO, Neri DF, Lamberth JG. Tyrosine and its potential use as a countermeasure to performance decrement in military sustained operations. Aviat Space Environ Med 1992; 63:364–9.

156. Palminteri R, Narbonne G. Safety profile of zolpidem. In: Sauvanet JP, Langer SZ, Morselli PL, eds. Imidazopyridines in sleep disorders. New York: Raven Press; 1988:351–60.

157. Paul MA, Gray G, Kenny G, Pigeau R. Impact of melatonin, zaleplon, zopiclone, and temazepam on psychomotor performance. Aviat Space Environ Med 2003; 74:1263–70.

158. Paul MA, Gray G, MacLellan M, Pigeau RA. Sleep-inducing pharmaceuticals: a comparison of melatonin, zaleplon, zopiclone, and temazepam. Aviat Space Environ Med 2004; 75:512–9.

159. Physician's Desk Reference. Modafinil. In: Physician's Desk Reference. Montvale, NJ: Thomson PDR; 2003:1193-6.

160. Pigeau R, Naitoh P, Buguet A, McCann C, Baranski J, Taylor M, et al. Modafinil, d-amphetamine and placebo during 64 hours of sustained mental work. effects on mood, fatigue, cognitive performance and body temperature. J Sleep Res 1995; 4:212–28.

161. PMI, Inc. FIT Workplace Safety Screener: theory and validation. Rockville, MD: PMI, Inc 1999.

162. Porcu S, Bellatreccia A, Ferrara M, Casagrande M. Performance, ability to stay awake, and tendency to fall asleep during the night after a diurnal sleep with temazepam or placebo. Sleep 1997; 20:535–41.

163. Portas CM, Bjorvatn B, Ursin R. Serotonin and the sleep/wake cycle: special emphasis on microdialysis studies. Prog Neurobiol 2000; 60:13–35.

164. Porter JM, Horne JA. Bed-time food supplements and sleep: effects of different carbohydrate levels. Electroencephalogr Clin Neurophysiol 1981; 51:426–33.

165. Prazinko BF, Sam JA, Caldwell JL, Townsend AT. Dose uniformity of over-the-counter melatonin as determined by high-pressure liquid chromatography. Fort Rucker, AL: U. S. Army Aeromedical Research Laboratory; 2000; USAARL Technical Report 2000–23.

166. Ramsey CS, McGlohn SE. Zolpidem as a fatigue countermeasure. Aviat Space Environ Med 1997; 68:926–31.

167. Reid KJ, Burgess HJ. Circadian rhythm sleep disorders. Prim Care 2005; 32:449–73.

168. Revell VL, Eastman CI. How to trick Mother Nature into letting you fly around or stay up all night. J Biol Rhythms 2005; 20:353–65.

169. Robertson P, Hillriegel ET. Clinical pharmacokinetic profile of modafinil. Clin Pharmacokinet 2003; 42:123–37.

170. Roehrs T, Burduvali E, Bonahoom A, Drake C, Roth T. Ethanol and sleep loss: a "dose" comparison of impairing effects. Sleep 2003; 26:981–5.

171. Rogers AS, Spencer MB, Stone BM, Nicholson AN. The influence of a 1 h nap on performance overnight. Ergonomics 1989; 32:1193–205.

172. Roky R, Chapatot F, Benchekroun MT, Benaji B, Hakkou F, Elkhalifi H, et al. Daytime sleepiness during Ramadan intermittent fasting: polysomnographic and quantitative waking EEG study. J Sleep Res 2003; 12:95–101.

173. Roky R, Chapatot F, Hakkou F, Benchekroun MT, Benaji B, Buguet A. Sleep during Ramadan intermittent fasting. J Sleep Res 2001; 10:319–27.

174. Rosa RR. Napping at home and alertness on the job in rotating shift workers. Sleep 1993; 16:727–35.

175. Rosekind MR, Co EL, Gregory KB, Miller DL. Crew factors in flight operations XIII: a survey of fatigue factors in corporate/executive aviation operations. Moffett Field, CA: NASA Ames Research Center; 2000. Report No.: NASA/TM–2000–209610.

176. Rosekind MR, Gander PH, Connell LJ, Co EL. Crew factors in flight operations X: alertness management in flight operations education module. Moffett Field, California:

National Aeronautics and Space Administration; 2001; NASA Technical Memorandum No. 2001-211385.

177. Rosekind MR, Graeber RC, Dinges DF, Connell LJ, Rountree MS, Spinweber CL, et al. Crew factors in flight operations IX: effects of planned cockpit rest on crew performance and alertness in long-haul operations. Moffett Field, CA: NASA Ames Research Center; 1994; Report No: DOT/FAA/92/24.
178. Rosekind MR, Gregory KB, Miller DL, Co EI, Lebacqz JV, Brenner M. Crew fatigue factors in the Guantanamo Bay aviation accident. [Abstract] Sleep Res 1996; 25:571.
179. Rosekind MR, Miller DL, Gregory KB, Dinges DF. Crew factors in flight operations XII: a survey of sleep quantity and quality in on-board crew rest facilities. Moffett Field, CA: NASA; 2000; Report No: NASA/TM-2000-20961.
180. Roth T, Piccione P, Salis P, Kramer M, Kaffeman M. Effects of temazepam, flurazepam and quinalbarbitone on sleep: psychomotor and cognitive function. Br J Clin Pharmacol 1979; 8:47S–54S.
181. Roth T, Roehrs T. A review of the safety profiles of benzodiazepine hypnotics. J Clin Psychiatry 1991; 52(9, Suppl)38–47.
182. Rowland L, Thomas M, Thorne D, Sing H, Davis HQ, Redmond D, et al. Oculomotor changes during 64 hours of sleep. [Abstract] Sleep Res 1997; 26:626.
183. Russo M, Thomas M, Sing H, Thorne D, Balkin T, Wesensten N, et al. Saccadic velocity and pupil constriction latency changes in partial sleep deprivation, and correlations with simulated motor vehicle crashes. Sleep 1999;22(Suppl. 1):S297–8.
184. Russo M, Thomas M, Thorne D, Sing H, Redmond D, Rowland L, et al. Oculomotor impairment during chronic partial sleep deprivation. Elsevier Science Ireland, Ltd. for the International Federation of Clinical Neurophysiology, 2003; 114:723–736.
185. Sack RL, Auckley D, Auger RR, Carskadon MA, Wright KP, Jr., Vitiello MV, et al. Circadian rhythm sleep disorders: part I, basic principles, shift work and jet lag disorders. An American Academy of Sleep Medicine review. Sleep 2007; 30:1460–83.
186. Samel A, Wegmann HM, Vejvoda M. Jet lag and sleepiness in aircrew. J Sleep Res 1995; 4(S2):30–6.
187. Samel A, Wegmann HM, Vejvoda M. Aircrew fatigue in long-haul operations. Accid Anal Prev 1997; 29:439–52.
188. Sanger DJ, Perrault G, Morel E, Joly D, Zivkovic B. The behavioral profile of zolpidem, a novel hypnotic drug of imidazopyridine structure. Physiol Behav 1987; 41:235–40.
189. Schultz D, Miller JC. Fatigue and use of go/no-go pills in extraordinarily long combat sorties [Commentary]. Aviat Space Environ Med 2004; 75:370–1.
190. Schultz D, Miller JC. Fatigue and use of go/no go pills in F-16 pilots subjected to extraordinarily long combat sorties Brooks City-Base, TX: Air Force Research Laboratory; 2004 Apr.; Technical report: AFRL-HE-BR-TR-2004-0014.
191. Schweitzer PK, Muehlback MJ, Walsh JK. Countermeasures for night work performance deficits: the effect of napping or caffeine on continuous performance at night. Work Stress 1992; 6:355–65.
192. Senechal PK. Flight surgeon support of combat operations at RAF Upper Heyford. Aviat Space Environ Med 1988; 59:776–7.
193. Shiota M, Sudou M, Ohshima M. Using outdoor exercise to decrease jet lag in airline crewmembers. Aviat Space Environ Med 1996; 67:1155–60.
194. Signal L, Gander P, van den Berg M. Sleep during ultra-long range flights: a study of sleep on board the 777-200 ER during rest opportunities of 7 hours. Report Published for the Boeing Commercial Airplane Group Sleep/Wake Research Centre, Massey University. Wellington, New Zealand: 2003.
195. Signal L, Ratieta D, Gander P. Fatigue management in the New Zealand aviation industry. Australian Transport Safety Bureau Research and Analysis Report April, 2006.
196. Skene DJ, Arnedt J. Human circadian rhythms: physiological and therapeutic relevance of light and melatonin. Ann Clin Biochem 2006; 43:344–53.
197. Spring B, Maller O, Wurtman J, Digman L, Cozolino L. Effects of protein and carbohydrate meals on mood and performance: interactions with sex and age. J Psychiatr Res 1982-1983; 17:155–67.
198. Spurgeon A. Working time: its impact on safety and health. International Labour Office Report. Geneva: International Labour Organization, 2003.
199. Stepanski EJ, Wyatt JK. Use of sleep hygiene in the treatment of insomnia. Sleep Med Rev 2003; 7:215–25.
200. Stewart S, Holmes A, Jackson P, Abboud R. An integrated system for managing fatigue risk within a low cost carrier. Enhancing Safety Worldwide: Proceedings of the 59th annual IASS; 2006 Oct 23-25; Paris, France. Alexandria, VA: Flight Safety Foundation; 2006.
201. Stone BM, Turner C. Promoting sleep in shiftworkers and intercontinental travelers. Chronobiol Int 1997; 14:133–43.
202. Suhner A, Schlagenhauf P, Hofer I, Johnson R, Tschopp A, Steffen R. Effectiveness and tolerability of melatonin and zolpidem for the alleviation of jet lag. Aviat Space Environ Med 2001; 72:638–46.
203. Taibi DM, Landis CA, Petry H, Vitiello MV. A systematic review of valerian as a sleep aid: safe but not effective. Sleep Med Rev 2007; 11:209–30.
204. Tietzel AJ, Lack LC. The short-term benefits of brief and long naps following nocturnal sleep restriction. Sleep 2001; 24:293–300.
205. Tilley AJ, Wilkinson RT, Warren PSG, Watson B, Drud M. The sleep and performance of shift workers. Hum Factors 1982; 24:629–41.
206. Touitou Y, Bogdan A. Promoting adjustment of the sleep-wake cycle by chronobiotics. Physiol Behav 2007; 90:294–300.
207. Tsai YF, Viirre E, Strychacz C, Chase B, Jung TP. Task performance and eye activity: predicting behavior relating to cognitive workload. Aviat Space Environ Med 2007; 78(5, Suppl) B176–85.
208. Tucker P, Folkard S, Macdonald I. Rest breaks and accident risk. Lancet 2003; 361(9358):680.
209. U.S. National Library of Medicine and the National Institutes of Health. Drug information: Temazepam. In: Medline Plus; 2004. www.nlm.nih.gov/**medlineplus**/
210. Navy US. Performance maintenance during continuous flight operations—a guide for flight surgeons. Fallon, NV: Naval Strike and Air Warfare Center; 2000.
211. Van den Heuvel CJ, Ferguson SA, Macchi MM, Dawson D. Melatonin as a hypnotic: con. Sleep Med Rev 2005; 9:71–80.
212. Van Dongen HPA. Comparison of mathematical model predictions to experimental data of fatigue and performance. Aviat Space Environ Med 2004; 75(3, Suppl)A122–4.
213. Van Dongen HP, Dinges DF. Sleep, circadian rhythms, and psychomotor vigilance. Clin Sports Med 2005; 24:237–49 (vii-viii.).
214. Van Dongen HPA, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: Dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep 2003; 26:117–26.
215. Van Dongen HP, Mott CG, Huang JK, Mollicone DJ, McKenzie FD, Dinges DF. Optimization of biomathematical model predictions for cognitive performance impairment in individuals: accounting for unknown traits and uncertain states in homeostatic and circadian processes. Sleep 2007; 30:1129–43.
216. Van Dongen HP, Vitellaro KM, Dinges DF. Individual differences in adult human sleep and wakefulness: Leitmotif for a research agenda. Sleep 2005; 28:479–96.
217. Vgontzas AN, Pejovic S, Zoumakis E, Lin HM, Bixler EO, Basta M, et al. Daytime napping after a night of sleep loss decreases sleepiness, improves performance, and causes beneficial changes in cortisol and interleukin-6 secretion. Am J Physiol Endocrinol Metab 2007; 292:E253–61.
218. Voderholzer U, Hornyak M, Thiel B, Huwig-Poppe C, Kiemen A, König A, et al. Impact of experimentally induced serotonin deficiency by tryptophan depletion on sleep EEG in healthy subjects. Neuropsychopharmacology 1998; 18:112–24.
219. Waterhouse J, Reilly T, Atkinson G. Jet-lag. Lancet 1997; 350:1611–6.
220. Waterhouse J, Reilly T, Atkinson G, Edwards B. Jet lag: trends and coping strategies. Lancet 2007; 369:1117–29.
221. Webb WB. The proximal effects of two and four hour naps within extended performance without sleep. Psychophysiology 1987; 24:426–9.

222. Wehr TA, Moul DE, Barbato G, Giesen HA, Seidel JA, Barker C, et al. Conservation of photoperiod-responsive mechanisms in humans. Am J Physiol 1993; 265:R846–57.
223. Weiss B, Laties VG. Enhancement of human performance by caffeine and the amphetamines. Pharmacol Rev 1962; 14: 1–36.
224. Wells AS, Read NW, Uvnas-Moberg K, Alster P. Influences of fat and carbohydrate on postprandial sleepiness, mood, and hormones. Physiol Behav 1997; 61:679–86.
225. Wesensten N, Balkin T, Thorne D, Killgore R, Reichardt RM, Belenky G. Caffeine, dextroamphetamine modafinil during 85 hours of sleep deprivation. I. Performance and alertness effects. Aviat Space Environ Med 2004; 75(4, Suppl):B108.
226. Wesensten NJ, Belenky G, Kautz MA, Thorne D, Reichardt RM, Balkin T. Maintaining alertness and performance during sleep deprivation: modafinil versus caffeine. Psychopharmacology (Berl) 2002; 159:238–47.
227. Wesnes K, Warburton DM. A comparison of temazepam and flurazepam in terms of sleep quality and residual changes in performance. Neuropsychobiology 1984; 11:255–9.
228. Wierwille WW, Ellsworth LA. Evaluation of driver drowsiness by trained raters. Accid Anal Prev 1994; 26:571
229. Wierwille WW, Wreggit SS, Kim CL, Ellsworth LA, Fairbanks RJ. Research on vehicle-based driver status/performance monitoring: development, validation, and refinement of algorithms for detection of driver drowsiness. Washington, DC: National Highway Traffic Safety Administration; 1994; Report No: DOT HS 808 247.
230. Wing YK. Herbal treatment of insomnia. Hong Kong Med J 2001; 7:392–402.
231. Wirz-Justice A, Armstrong SM. Melatonin. nature's soporific? J Sleep Res 1996; 5:137–41.
232. Wright N, McGown A. Vigilance on the civil flight deck: incidence of sleepiness and sleep during long-haul flights and associated changes in physiological parameters. Ergonomics 2001; 44:82–106.
233. Wright N, Powell D, McGown A, Broadbent E, Loft P. Avoiding involuntary sleep during civil air operations: Validation of a wrist-worn alertness device. Aviat Space Environ Med 2005; 76:847–56.
234. Yesavage JA, Leirer VO. Hangover effects on aircraft pilots 14 h after alcohol ingestion: a preliminary report. Am J Psychiatry 1986; 143:1546–50.
235. Youngstedt SD, O'Connor PJ, Dishman RK. Effects of acute exercise on sleep: a quantitative synthesis. Sleep 1997; 20:203–14.
236. Zammit GK, Kolevzon A, Fauci M, Shindledecker R, Ackerman S. Postprandial sleep in healthy men. Sleep 1995; 18:229–31.
237. Zhdanova IV. Melatonin as a hypnotic: pro. Sleep Med Rev 2005; 9:51–65.