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14. ABSTRACT This article provides a review which addresses the problem of fatigue attributable to sleep loss in modern society and the scientifically proven strategies useful for reducing fatigue-related risks. Fatigue has become pervasive because many people work non-standard schedules, and/or they consistently fail to obtain sufficient sleep. Sleep restriction, sleep deprivation, and circadian desynchronization produce a variety of decrements in cognitive performance as well as an array of occupational and health risks. A number of real-world mishaps have resulted from performance failures associated with operator sleepiness. In some cases, fatigue/sleepiness is unavoidable, at least temporarily, due to job-related or other factors, but in other cases, fatigue/sleepiness results from poor personal choices. Furthermore, some individuals are more vulnerable to the effects of sleep loss than others. Fortunately, fatigue-related risks can be mitigated with scientifically-valid alertness-management strategies. Proper work/rest scheduling and good sleep hygiene are of primary importance. If sleep time is available but sleep is difficult to obtain, sleep-inducing medications and behavioral circadian-adjustment strategies are key. In fatiguing situations such as when sleep opportunities are temporarily inadequate, limiting time on tasks, strategic napping, and the potential use of alertness-enhancing compounds must be considered. To optimize any alertness-management program, everyone must first be educated about the nature of the problem and the manner in which accepted remedies should be implemented. In the near future, objective fatigue-detection technologies may contribute substantially to the alleviation of fatigue-related risks in real-world operations.					
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CLINICAL REVIEW

Alertness management strategies for operational contexts

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Summary This review addresses the problem of fatigue (on-the-job-sleepiness) attributable to sleep loss in modern society and the scientifically proven strategies useful for reducing fatigue-related risks. Fatigue has become pervasive because many people work non-standard schedules, and/or they consistently fail to obtain sufficient sleep. Sleep restriction, sleep deprivation, and circadian desynchronization produce a variety of decrements in cognitive performance as well as an array of occupational and health risks. A number of real-world mishaps have resulted from performance failures associated with operator sleepiness. In some cases, fatigue/sleepiness is unavoidable, at least temporarily, due to job-related or other factors, but in other cases, fatigue/sleepiness results from poor personal choices. Furthermore, some individuals are more vulnerable to the effects of sleep loss than others. Fortunately, fatigue-related risks can be mitigated with scientifically valid alertness-management strategies. Proper work/rest scheduling and good sleep hygiene are of primary importance. If sleep time is available but sleep is difficult to obtain, sleep-inducing medications and behavioral circadian-adjustment strategies are key. In fatiguing situations such as when sleep opportunities are temporarily inadequate, limiting time on tasks, strategic napping, and the potential use of alertness-enhancing compounds must be considered. To optimize any alertness-management program, everyone must first be educated about the nature of the problem and the manner in which accepted remedies should be implemented. In the near future, objective fatigue-detection technologies may contribute substantially to the alleviation of fatigue-related risks in real-world operations.

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Introduction

Fatigue, which for present purposes will be considered synonymous with on-the-job or daytime sleepiness, is a growing problem in modern society. Unfortunately, the insufficient sleep and circadian disruptions that have become all too common in today's fast-paced world are increasingly taking their toll both in the workplace and in everyday life. Although sleep experts have found that most adults need 8 h of sleep per night,¹ the average American adult is sleeping only 6.8 h per night,² and as much as 20% of the population appears to be acquiring only 6.5 h of sleep per night.³ Furthermore, there is a downward trend in the number of people who report acquiring a full 8 h of nightly sleep—38% in 2001, 30% in 2002, and 26% in 2005.² Dinges et al.⁴ attribute this chronic lack of sufficient sleep to factors such as medical conditions, sleep disorders, work demands, and social and domestic responsibilities. People suffering from acute or chronic pain have been shown to experience shortened and disrupted sleep⁵; sleep disorders are known to produce deficits in sleep quality and quantity⁶; and shift workers, who have long been known to experience greater sleep difficulties than their day-worker counterparts,⁷ tend to suffer numerous adverse alertness and health consequences due to the conflict between their work hours and their biological clocks.⁸ As for sleep loss associated with social or domestic responsibilities, despite the fact that such sleep deprivation is often considered "voluntary", it nevertheless exerts a negative impact on daytime functioning.⁹

Effects of sleep deprivation

In general terms, chronically reduced sleep exerts cumulative adverse effects on waking performance which include vigilance decrements, increased lapses of attention, cognitive slowing, short-term memory failures, deficits in frontal lobe functions, and rapid and involuntary sleep onsets.^{10–17} Dinges et al.¹⁸ showed that sleep restricted to 4–6 h per day, creates a "sleep debt" which seriously impairs waking performance within a week. Other experiments indicate that 5 h or less sleep per night decreases cognitive performance, reduces sleep latency values, increases subjective sleepiness, increases behavioral, mood, and physical complaints, and produces polysomnographic indications of elevated sleep pressure.^{19–31} It is clear that losing even small amounts of sleep each night will seriously degrade alertness, performance, and vigilance.^{32,33}

Studies comparing the effects of increased blood alcohol concentrations (BAC) to the effects of sleep loss illustrate the seriousness of insufficient sleep on alertness and performance. Four investigations have shown that sustained wakefulness of 20–24 h produces decrements equal to those observed with BAC levels of between 0.08% and 0.10% on tests of psychomotor performance, grammatical reasoning, vigilance, and simulated driving performance.^{34–37} Another study indicates that approximately 24 h of sustained wakefulness creates performance impairments equal to those associated with 0.05% BAC on tasks of continuous attention, memory and learning.³⁸ The combined effects of fatigue and alcohol are more detrimental than the effects of either alcohol or fatigue alone.³⁴ In light of such findings, it is peculiar that driving while intoxicated has become a societal taboo when at the same time, driving while severely fatigued is considered an admirable mark of high motivation and machismo.

Effects of circadian disruption

The human biological system operates on an internal clock in which different functions run on different cycle lengths—some cycles are less than a minute while others vary over hours, days or months. A circadian rhythm is a rhythm that cycles approximately every 24 h ("circa" meaning about and "dia" meaning a day). Light is the major factor which entrains this rhythm to activity during the day and rest at night, with various functions either rising or falling at various times throughout the 24-h period. For example, high body temperature, heart rate, and blood pressure are associated with increased alertness and performance and occur during the daylight hours. Sleep is associated with decreases in temperature, blood pressure, and cortisol which occur in the evening, then rise in the morning before we awaken.³⁹ The physiological tendency to sleep at night and to be awake during the day is powerful; difficulties occur when schedule changes cause personnel to work against this tendency. Altering the normal sleep/wake cycle, either through night work or time-zone changes, affects both the ability to remain alert and the ability to sleep. Shift-lag results when non-traditional work hours (night or early morning hours) are required either on a permanent night shift or a rotating schedule, because this creates a misalignment between the internal clock and the normal activity and sleep schedule. Jet-lag results when time zones are rapidly switched by at least 3 h, because this likewise causes a misalignment between the body's internal clock and the

environmental clock. In the case of time-zone changes, the newly arranged time cues (i.e., light and activity cues) lead to faster realignment of the body's rhythms. However, these changes in environmental time cues do not occur when personnel switch work schedules from day to night, so adaptation to night work and day sleep occurs very slowly if at all. Regardless of the source of the circadian rhythm disruption, until rhythm resynchronization occurs, alertness and performance difficulties will result.

Effects of sleep loss combined with circadian factors

The combination of sleep restriction and circadian factors can be especially troubling. Van Dongen and Dinges³⁹ point out that circadian rhythms influence almost every aspect of alertness and performance. In general, the speed and quality of performance follows the pattern of internal body temperature (a standard marker of the biological clock) in that low body temperature (often observed between 0300 and 0500) is associated with lower alertness, slower reaction time, and poorer accuracy than periods of higher body temperature. Thus, it is not surprising that night workers often perform more poorly than their daytime counterparts.⁴⁰ Studies from the aviation arena have shown that EEG micro-events (short episodes of brain activity associated with sleep lapses) are up to 9 times more likely during the nighttime compared to the daytime,^{41,42} and psychomotor vigilance lapses are 5 times greater.⁴³ In one flight simulation study, 9 of 14 pilots experienced outright sleep episodes during the night,⁴⁴ corroborating Moore-Ede's⁴⁵ assertion that pilots nod off at the controls significantly more frequently in the dark than during daylight.

Occupational and health risks

From a health and safety standpoint, the degree of sleep deprivation and shift work in today's 24/7 society is a significant concern. Although typical estimates of the number of shift workers range from 14.5 to 25 million, Rosekind⁴⁶ points out that if all non-standard work schedules were included, up to 83 million people in the US workforce would be considered to be on a "non-9-5 schedule." Such schedules are characterized by one or more of the following factors: early start times, extended or consecutive work periods, insufficient off-duty recovery time, night work during the circadian low, daytime sleep periods, inconsistent work

schedules, on-call status, time-zone changes, and/or unplanned duty extensions. These schedules, in comparison to standard 9-5h, pose various risks stemming from the inadequate sleep and/or circadian difficulties they impose. Unfortunately, these risks are often underestimated by physicians, employers, employees, and government officials.⁴⁶ Spurgeon⁴⁷ suggests that in addition to shift work, long work hours also exert a negative impact on safety and/or health. She concluded that working more than 48 h per week significantly increases the risk of mental health problems, and that working more than 60 h per week increases the risk of cardiovascular disease. In general, long work hours also appear to increase the incidence of physical complaints, the use of unhealthy coping behaviors such as smoking and poor diet, domestic problems, and possibly pre-term births and musculoskeletal disorders. Working shifts longer than 8-9 h is thought to increase the probability of having accidents or making errors. The consequences of shift work, and particularly night work, may include sleep disorders; mental health difficulties; and an increased risk of cardiovascular, gastrointestinal, and/or reproductive disorders. In addition, there is evidence from some studies that night work is associated with increased accidents. In fact, Folkard and Tucker⁴⁰ estimate that the relative risk of workplace incidents on the evening shift increases by about 30%.

Fatigue and real-world performance

Clearly, sleep loss and shift work can affect cognitive and physiological functions (see Table 1). But how

Table 1 Skills and functions impaired by fatigue.

Fatigue impairs a variety of skills/functions:

Accuracy and timing degrade
 Lower performance standards unconsciously become acceptable
 Multi-tasking (attention sharing) becomes difficult
 Even simple, well-practiced activities require more effort
 The ability to efficiently integrate information is lost
 Performance becomes inconsistent
 Social interactions (*critical for information exchange*) decline
 Attitude and mood deteriorate
 The ability to reason is impaired
 Situational awareness declines
 Attention wanes
 Involuntary and uncontrollable lapses into sleep begin to occur

does fatigue affect real-world safety and performance? A recent study of train operators indicates that fatigued drivers perform less consistently, utilize more fuel, and commit more speeding violations than well-rested drivers—negatively impacting both efficiency and safety.⁴⁸ Studies of highway crashes typically indicate that drowsy drivers account for approximately 100,000 accidents, 1357 fatalities, and 71,000 injury crashes in the US each year,⁴⁹ but some investigators consider this an underestimate, suggesting instead that drowsy driving could account for over 1 million accidents per year.⁴⁶ Aviation safety statistics suggest that approximately 4–7% of US commercial aviation mishaps are fatigue related.⁵⁰ A study of interns revealed that those working five or more extended shifts (those greater than or equal to 24h) were three times more likely to make fatigue-related errors resulting in a patient fatality,⁵¹ and a survey of health-care workers consisting primarily of nurses revealed that 19% believed fatigue contributed to a worsening of patients' conditions.⁴⁶ An assessment of occupational injuries to a representative sample of US adults indicated that the injury rate associated with overtime was 61% higher than the rate in jobs without overtime, working 12 h a day increased the hazard rate 37%, and working 60 h a week increased the work-related illnesses or injuries by 23%.⁵² And the list goes on.

Fatigue management

Managing fatigue in real-world contexts requires an appreciation of the nature of fatigue, an understanding of individual differences in fatigue vulnerability, and a willingness and capability to implement scientifically valid fatigue countermeasures. Understanding the principles behind recommended intervention strategies is important because some techniques are situation specific, some individuals are more fatigue tolerant than others, and some types of work are more affected by alertness status than others. For these reasons, there is no "one-size-fits-all" fatigue-management approach. Instead, individual personnel, schedulers, supervisors, and regulatory officials must consider the unique characteristics of each situation and develop a plan of action based upon those characteristics as well as up-to-date scientific data.

Understanding the nature of fatigue

As previously discussed, when work hours are in conflict with human biological programming, alertness impairments often result. The three primary

components to be considered when evaluating or predicting the fatigue levels being experienced by an individual are: (1) the *circadian mechanism* or the body's internal timing system, (2) the *homeostatic mechanism* or recent sleep history (which includes the amount of time since the last sleep period and the amount of prior sleep), and (3) sleep inertia or the temporary grogginess that occurs upon awakening from any sleep period.⁵³ Work and sleep schedules are thus of primary importance in determining the level of fatigue that exists (see Table 2).

Until fairly recently, it was believed that fatigue was a state of mind, and that the effects of self-induced sleep deprivation or overly demanding work schedules could be overcome with professionalism, training, or motivation, but it is now clear that people cannot adapt to insufficient sleep despite their beliefs to the contrary. Van Dongen et al.⁹ for instance, demonstrated that time in bed restricted to 6, or 4 h per night for 2 weeks produced cumulative decrements in cognitive performance across the entire 14 days of the study, but surprisingly, even the participants in the most sleep-restricted group were largely unaware of their progressively impaired alertness. Whether sleep is disrupted or shortened due to work demands, intentional sleep restriction, poor sleep hygiene, shift lag, jet lag, or some other factor, negative consequences of fatigue will be evident (at least from an objective viewpoint) until it becomes possible to fulfill the body's genetically predetermined sleep need. And, some individuals clearly will be more affected than others. However, there are strategies for minimizing sleep loss through better work/rest scheduling, by ensuring that available sleep opportunities are optimized,

Table 2 Factors that lead to fatigue.

Fatigue will be a factor when:

- Personnel are working long hours in a given shift
- Personnel have been working long shifts for several consecutive duty days
- Work and/or sleep schedules have been irregular and/or unpredictable
- Critical tasks are being performed during circadian low points (night or post-lunch dip)
- Insufficient sleep is obtained immediately prior to the work shift
- Insufficient sleep has occurred for several days prior to the work period (cumulative sleep debt)
- The nature of the work is boring or tedious
- The work environment is soporific (dimly lit and quiet)
- Physical and/or mental stress is present

and by speeding circadian entrainment to new work schedules or time zones. In situations where sleep loss is temporarily unavoidable, there are strategies for temporarily mitigating the negative effects of sleep deprivation until adequate recovery can occur. Applying the available techniques in a logical, systematic fashion will enhance safety and performance.

Recognition of individual differences in fatigue vulnerability

Before addressing the problem of fatigue in specific contexts, it is important to first understand that what is known about the average (group) response to sleep loss obscures the wide variations in the degree to which individuals will be affected.^{9,32,54,55} Morgan et al.⁵⁶ found that 44 h of continuous wakefulness degraded the synthetic work performance of some subjects by as much as 40% while the performance of others was essentially unaffected. Balkin et al.³² reported that chronic sleep restriction produced differential subject-specific amounts of degradations on basic vigilance tasks and driving simulations. Caldwell et al.⁵⁷ showed that 37 h of continuous wakefulness produced degradations in-flight performance ranging from 135% in one case to only 0.6% in another. Circadian rhythms also are marked by significant individual differences. These relate in part to whether an individual is a "morning" type or an "evening" type, as well as to other trait characteristics.⁵⁸

It appears that individuals who are fatigue resistant on one occasion likely will be fatigue resistant on others,^{54,56,59} but it remains to be determined whether this trait can be predicted and used for practical purposes such as to select people who are particularly well-suited for fatigue-inducing jobs. Neurotic extroverts appear to be more affected by sleep loss than non-neurotic extroverts⁶⁰; younger people seem somewhat less tolerant to sleep deprivation than their older counterparts⁶¹; and subjects who have greater sleep needs are sometimes less fatigue resistant than those with lesser sleep needs^{9,60}; but none of these characteristics serve as an accurate "litmus test" for the true degree of fatigue susceptibility. Perhaps underlying determinants of fatigue vulnerability will be found in brain imaging studies such as the Caldwell et al.⁶² fMRI evaluation suggesting a possible association between pre-sleep-deprived cortical activation and subsequent fatigue vulnerability. However, until a reliable predictor of individual fatigue susceptibility is discovered, it is important to factor inter-individual variability into

any new scheduling approach or counter-fatigue program.

Strategies for improving work/rest scheduling

Since scheduling factors often are at the heart of operator fatigue, the development and stringent implementation of more "human-centered" work routines should be a priority. Although many industrial sectors have made progress in optimizing scheduling practices, concerted efforts should continue to focus on schedules that recognize (1) sleep as being essential for optimum functioning, (2) breaks as being important for preserving sustained attention, and (3) recovery periods as being necessary to ensure full recuperation from fatiguing work conditions. Also, it must be recognized that humans simply are less alert and capable at some times of the 24-h cycle than at others due to the circadian rhythmicity of internal physiological processes. New computerized scheduling tools such as the Fatigue Avoidance Scheduling Tool (FAST)⁶³ and the System for Aircrew Fatigue Evaluation (SAFE)⁶⁴ can ease the process of developing and implementing new schedules by allowing planners to better appreciate the impact of fatigue-inducing factors and the potential benefits of appropriate counter-fatigue strategies (in addition, a space-operations oriented tool called the Astronaut Scheduling Assistant⁶⁵ may one day be available). These tools show the degree of general performance impairments that can be expected with specific work/rest schedules, and they provide an efficient way to model the impact of proposed schedule revisions. Although complete validation of computerized scheduling software has not yet been completed, these easy-to-use computerized scheduling tools already are contributing to alertness management in some transportation, military, and industrial sectors. In addition, once such tools are interfaced with sleep/wake monitoring devices such as wrist-worn activity monitors, and inputs are provided about ambient light levels and other important environmental factors, it will be possible to more precisely determine the impact of job schedules on work readiness in real time.

Techniques for optimizing sleep

Deciding how much sleep is necessary

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, adults require about

8 h of sleep per day in order to sustain optimum alertness. Although some people can function well on far less, they are small in number. Two strategies can help determine individual sleep needs.

The first strategy is to extend the nightly sleep period an extra hour over the course of the next 7 days, and after the seventh day, 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 5–7 days (excluding the first two vacation days), obtain the average sleep time and make this amount of sleep each night the goal upon returning to work.

Optimizing sleep quality with good sleep habits

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.⁶⁶ Specific strategies can help optimize each sleep opportunity, and these are presented in the practice points listed below:

Practice points

Components of good sleep hygiene:

1. Wake-up and go to bed at the same time every day to avoid circadian disruptions.
2. Use the bedroom only for sleep and sex and not for work.
3. Establish a consistent and comforting bedtime routine (i.e., reading, taking a hot shower, and then going to bed).
4. Perform aerobic exercise every day, but not within 2 h of going to bed.
5. Make sure the bedroom is quiet, totally dark, and comfortable.
6. Keep the sleep environment cool (~16–18°C if you are covered).
7. Move the alarm clock out-of-sight so you cannot be a clock watcher.
8. Avoid caffeine in drinks and other forms during the afternoons/evenings.
9. Do not use alcohol as a sleep aid (it may make you sleepy, but you will not sleep well).
10. Avoid cigarettes or other sources of nicotine right before bedtime.

11. Do not lie in bed awake if you do not fall asleep within 30 min—instead, leave the bedroom and do something relaxing and quiet until you are sleepy.

Optimizing sleep with sleep-inducing medications

Good sleep habits provide behaviorally based strategies for avoiding insomnia in many situations, but in some cases, hypnotic medications or so-called “sleeping pills” may be necessary. Clear examples are: (1) situations in which sleep is difficult because of circadian factors (as is the case of jet lag or shift lag associated with rapid time-zone changes or unconventional work schedules), and/or (2) situations in which the sleep environment is poor (as is the case when personnel must sleep in uncomfortable, hot, or noisy settings). Under such circumstances, sleep medications may be the only way to ensure adequate restful sleep prior to the next demanding work period. Although complete reliance on medications for the control of sleep cycles is not recommended, it is clear that enhancing sleep with today’s medications (which have short half-lives and minimal side effects compared to older medications) is far preferable to being sleep deprived.

Choosing the best hypnotic for each situation requires consideration of a variety of factors. From a strictly pharmacological standpoint, *temazepam* (*Restoril*®) or a similar compound with an 8–10 h half-life, is useful for maintaining sleep for relatively long periods during the night and/or for optimizing the daytime sleep of night-working personnel.^{67–69} However, some of the newer hypnotics help with sleep maintenance without the extended half-life of temazepam. For example, the *extended-release zolpidem* (*Ambien CR*®) with a half-life of 2.8 h improves sleep maintenance beyond that of original *zolpidem* (*Ambien*®),⁷⁰ which has a half-life of 2–2.5 h. In addition, *eszopiclone* (*Lunesta*®) has a half-life of 5–6 h with minimal residual drug effects after as little as 10 h post dose.⁷¹ For short sleep periods or for situations in which the primary objective is to improve sleep onset, *zolpidem* or *zaleplon* (*Sonata*®) are better than the longer-acting hypnotics since the very short half-lives (2.5 and 1 h, respectively) reduce the probability of post-sleep sedation.^{72–74} *Ramelteon* (*Rozereem*®) is a novel hypnotic that targets the melatonin receptors in the brain to regulate the sleep-wake cycle.⁷⁵ Research indicates this drug is more efficacious for sleep onset than for sleep maintenance.⁷⁵

New sleep-promoting compounds are being created by the pharmaceutical industry each year. One hypnotic slated to become available in the near future is indiplon (Neurocrine Biosciences, Inc.). This drug is similar in structure to zaleplon, and with a half-life of approximately 1.5 h, it is most effective for sleep initiation. However, it is also being formulated with a modified release which will extend its half-life to aid in sleep maintenance.⁷⁶ An apparent trend in the development of new hypnotics is the creation of compounds that not only promote sleep in general, but deep sleep in particular. For instance, although testing of the new compound gaboxadol (Merck & Co., Inc.)⁷⁷ was recently abandoned due to unexpected side effects, preliminary evidence suggested the slow-wave-sleep enhancing properties of this drug⁷⁸ might augment the restorative value of truncated sleep periods. Given that so much of society is sleep restricted, it is likely that future compounds will capitalize on this possibility.

In addition to prescription sleep medications, alternative medicines also are available. Unfortunately, most of these medications have not been studied thoroughly, and their effectiveness has not been clearly established. However, of the alternatives, valerian, kava, and melatonin have been the most frequently researched. A systematic review of valerian concluded that, while some studies have found evidence that valerian has significant effects on sleep, it does not have the clinical efficacy needed to treat insomnia.⁷⁹ There is evidence that suggests valerian is a safe herb which can be helpful with mild insomnia when taken continuously, but further clinical studies are needed to establish both its efficacy for severe insomnia and its safety profile.^{80–82} Kava has been shown to help with sleep latency and sleep quality in people with insomnia, but as is the case with valerian, more studies are needed to establish its efficacy and safety.⁸¹ Melatonin is another purported alternative treatment for insomnia, but its efficacy as a hypnotic also continues to be debated.^{83,84} Generally, as a sleep aid, it has not consistently been shown to be a clinically efficacious treatment for insomnia when taken during the biological night.⁸⁵ However, evidence is strong that melatonin has a soporific effect when taken outside the normal sleep period, particularly when taken to phase-advance the sleep period.⁸⁶ The efficacy of melatonin for circadian adjustment is discussed in a subsequent section of this paper.

In general, hypnotics can help to minimize sleep disruptions associated with circadian factors (jet lag and shift lag), and with proper planning, they can be used without undue concern about post-sleep hang-

over effects. The choice of compound depends on when the new sleep opportunity becomes available, the expected length of the sleep period, and whether there is a high probability that the sleep period will be unexpectedly truncated. An effort should be made to balance the need to improve sleep with the need to avoid residual effects, taking into account that sleep disruptions associated with the avoidance of hypnotics may be far more problematic than a hangover following a restful hypnotic-induced sleep.

Techniques for optimizing circadian adjustment

As previously noted, sleep disturbances can result from lack of knowledge or disregard of information concerning sleep requirements, poor sleep habits, uncomfortable environments, or circadian disruptions. Those stemming from the circadian desynchrony associated with rotating work schedules and/or rapid time-zone transitions are subject to partial alleviation with hypnotics; however, in the longer term, it may be better to restore the body's natural sleep/wake rhythm through other circadian re-entrainment techniques.

Behavioral recommendations

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.^{87–90} Thus, workers/travelers should pay close attention to their behaviors following schedule changes. Typical recommendations for workers attempting to adjust to new shifts are included as practice points below:

Practice points

General circadian adjustment recommendations for shift workers (consider that individual differences as well as workplace specifics will impact the efficacy of these strategies):

1. When rotating to night shift, avoid morning sunlight by wearing dark glasses and by staying indoors as much as possible prior to sleeping.
2. For daytime sleep, make sure the sleep environment is dark and cool.
3. For daytime sleep, use eye-masks and ear-plugs (or a masking noise like a box fan) to minimize light and noise interference.

4. For daytime sleep, make sure to implement the good sleep habits discussed previously.
5. When on night shift, try to take a short nap before reporting for work.
6. 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.

Individuals traveling to new time zones face problems similar to those encountered by shift workers. Specific recommendations for travelers are summarized in the practice points that follow:

Practice points

General circadian adjustment recommendations for travelers (consider that individual differences, direction of travel, types of activities, etc. will impact the efficacy of these approaches):

1. Quickly adjust meal, activity, and sleep times to the new time-zone schedule (this strategy will be most effective if the length of stay in days exceeds the number of changed time zones).
2. Maximize sunlight exposure during the first part of the day and minimize sunlight exposure during the afternoons (exposure time and amount depends on direction of travel).
3. Avoid heavy meals at night because stomach discomfort will disrupt sleep.
4. Follow good sleep habit recommendations to optimize nighttime sleep.
5. Try self-administered relaxation techniques to promote nighttime sleep.
6. Prior to bed time, take a hot bath. Cooling off afterwards may mimic the circadian-related temperature reduction that normally occurs during sleep.
7. During the first few days of adjustment, use sleep medications (if authorized) to promote sleep at night, and use caffeine to augment alertness during the day.

Note: If persons who have been working nights in the US 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!

Melatonin

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 adaptation to new time schedules.^{86,91,92} There is also evidence that melatonin possesses weak hypnotic or "soporific" properties that may facilitate out-of-phase sleep.^{93,94} Typically, exogenous melatonin should be administered at approximately the *desired bed time* since melatonin naturally peaks after sleep onset. Since melatonin is not considered a drug, it is widely available for use with few restrictions, at least in the US. 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.

Bright light

Properly timed bright light is an alternative strategy for resynchronizing circadian rhythms after schedule changes.⁹⁵⁻⁹⁷ Several researchers have published recommendations about the use of light to promote circadian adjustment, but they have pointed out difficulties associated with the correct administration of light therapy as well.⁹⁸⁻¹⁰⁰ Consensus reports summarizing issues related to the use of bright light as a treatment for jet lag and shift lag also have been published.^{101,102} Unfortunately, the difficulties associated with appropriate timing of artificial bright-light therapy (as well as melatonin therapy) often leave experts to recommend a reliance on safer self-administration techniques such as natural sunlight exposure, appropriately timed naps, and proper exposure to zeitgebers such as controlled meal, activity, and sleep times to facilitate adjustment to new work or time-zone schedules.¹⁰³⁻¹⁰⁵ However, it should be noted that these recommendation are based on the assumption that people attempting to utilize bright-light or melatonin treatments may not be able to concurrently control environmental factors, and they are probably not fully aware of their body's own circadian cycle.

Strategies for temporarily mitigating the effects of unavoidable sleep loss

Employees working in standard "9-5" office settings are usually able to avoid the scheduling difficulties that threaten to produce severe sleep

deprivation and fatigue. Their work hours are consistent, predictable, and in the daylight hours. Unfortunately, employees in other work settings often struggle with scheduling issues that stem from the misalignment of job requirements and basic physiological realities. In many medical occupations; in rescue, fire, and police work; in transportation operations; and in military settings, job pressures sometimes lead to temporarily unavoidable sleep loss and serious alertness decrements. In such cases, there are strategies that can temporarily preserve performance until restorative sleep/recovery is again possible.

Limiting time on task

A common approach to avoiding fatigue-related operational problems is to limit the amount of duty time in an effort to ensure that sleep time is adequate. This is an approach used throughout the transportation industry (i.e., in long-haul truckers, airline pilots, etc.). Controlling the amount of time at work not only avoids sleep loss, but reasonable shift durations mitigate "time-on-task" fatigue as well. The effects of extended work schedules are not fully understood at present; however, Rosa and Bonnet¹⁰⁶ found that prolonged work shifts (greater than 8 h) led to decrements in alertness and performance in an industrial setting. Akerstedt⁵³ points out that long work hours may be associated with increased sleepiness, and Morisseau and Perensky¹⁰⁷ found that overtime in the nuclear industry is related to an increase in incidents. Folkard and Tucker⁴⁰ note that the risk of an incident or accident nearly doubles when extending the shift duration from 8 to 10 h, and the risk more than doubles when extending the shift from 8 to 12 h.

Rest breaks

Rest breaks during a work shift can provide some amelioration of the degraded performance and increased fatigue associated with sleep loss (and time on task). Heslegrave and Angus¹⁰⁸ reported positive effects of 5–20-min breaks on performance and alertness in a 54-h sleep deprivation protocol. Pigeau et al.¹⁰⁹ found immediate improvements in subjective and objective performance measures after a 15-min break during a 64-h sleep deprivation protocol, but the effects dissipated rapidly following an hour of continuous cognitive work. Changes in physiological alertness have been observed in pilots flying a 6-h nighttime flight (after being awake a minimum of 18 h) in a flight simulator after receiving hourly 7-min breaks. The pilots who received the breaks showed reductions in slow eye movements, EEG theta activity, and unintended sleep episodes compared to pilots who

did not receive the breaks, but the benefits did not last longer than 15–25 min.⁴⁴ Thus, rest breaks are beneficial for promoting alertness; however, their effects are short-lived, making rest-break strategies unsuitable for maintaining long-term performance and alertness.

Napping

In situations where some sleep is possible but the amount of sleep is limited, napping is the most effective non-pharmacological technique for sustaining alertness. There is an abundance of evidence that a nap taken during long periods of otherwise continuous wakefulness is extremely beneficial.^{110–117} However, scheduling naps is not a simple matter.

One 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 that day, will result in improved performance over the night compared to performance without the nap. 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.¹¹⁸ demonstrated that when subjects received a 2–3-h nap before a night work shift (with concurrent sleep loss) they performed better than when receiving no nap. Bonnet¹¹¹ 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 Bonnet¹¹¹ 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 requirements for continuous wakefulness. This conclusion was supported in a study by Brooks and Lack¹¹⁹ 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. Smith-Coggins

et al.¹²⁰ reported superior psychomotor performance in physicians and nurses who received a 40-min nap in the middle of a 12-h night shift and noted that the improved performance lasted at least 3 h following the nap. Another study found a 40-min in-flight nap opportunity (about 26 min of actual sleep) significantly reduced the number of microsleep events experienced by pilots during the last 90 min of a long-haul flight.¹²¹ These findings are consistent with a recent meta-analysis on the efficacy of naps as a fatigue countermeasure.¹²² This meta-analysis of 12 studies in which the results of 178 tests were considered 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 versus a 4-h nap which led to 10 h of benefit). However, it was also noted that, regardless of nap length, the performance benefit decreased as post-nap 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 sleep-deprived performance).

A final consideration is the *placement of the nap with regard to the circadian phase*. Nap timing should take into account the ease of falling asleep at various times, the quality of sleep as a function of the body's internal clock, and the effects on performance both immediately after awakening and later in the work period. Sleep tendency is highest when core body temperature is in its trough (in the pre-dawn and early morning hours) and lowest when core body temperature is in its peak (in the early evening hours).¹²³ Thus, there may be significant problems initiating and/or maintaining a nap during times when core temperature is high, and for this reason, peak circadian time is sometimes termed the forbidden zone for sleep.¹²⁴ Naps placed during the circadian troughs are the easiest to maintain, and they show beneficial effects on later performance. Gillberg¹²⁵ 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 sustenance, they also are the more difficult naps from which to awaken. Generally, studies have shown that post-nap 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.¹²⁶ 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.

Posture

Several studies have suggested that a more upright postural orientation inhibits sleepiness. Nicholson and Stone¹²⁷ found that subjects experienced reductions in total sleep time, decreased sleep efficiency, and increased awakenings when they attempted to sleep in a more upright sitting position (17.5° from the vertical angle) as opposed to either lying flat or reclining 49.5° or 37°. Cole¹²⁸ found that heart rate and blood-pressure elevations were accompanied by an increase in the frequency of electroencephalographic (EEG) activity when subjects were tilted 45° upright on a tilt table. The upright tilt also inhibited sleepiness. Caldwell et al.¹²⁹ found that standing as opposed to sitting attenuated EEG theta activity as well as decrements on a sustained attention task in sleep-deprived adults. Thus, whenever possible, sleepy personnel should be advised to stand up rather than sit or lie down in order to preserve alertness.

Alertness-enhancing compounds

When, despite everyone's best intentions, sleepiness becomes a problem in safety-sensitive environments, and it is temporarily impossible to provide workers with adequate recovery sleep, stimulants may be an option. *Caffeine* can be considered a "first-line" pharmacological fatigue countermeasure (see Table 3). Numerous studies have shown that caffeine increases vigilance and improves performance in sleep-deprived individuals, especially those who normally do not consume

Table 3 Caffeine content in various products.

Coffee (100 or more mg per cup)
Coke® (31 mg) or Mountain Dew® (55 mg per 12 oz (360 ml) can)
Tea (about 40 mg per 8 oz (240 ml) cup)
Excedrin® Extra-strength (65 mg per tablet)
Certain cold remedies
NoDoz® and Vivarin® (200 mg per pill)
Various caffeinated candies and gum

Note: The recommended daily maximum is 800–1000 mg.

high doses of caffeine.¹³⁰ In many industrial and transportation sectors, caffeine (generally in the form of coffee, tea, or soft drinks) and some “dietary supplements” are the only alertness-enhancing substances allowed, whereas in some types of military applications, prescription alertness-enhancing medications are periodically authorized. This is particularly the case for lengthy missions during continuous and sustained operations. In the past, dextroamphetamine has been utilized in space operations, and it is currently the most widely used prescription stimulant within certain military aviation contexts. Dextroamphetamine, a powerful, reliable, and safe alertness-sustaining compound when properly used,¹³¹ has been shown to sustain the performance of aircraft pilots at near well-rested levels for over 50–55 h without sleep. As an alternative to amphetamine, *modafinil* has been introduced into military aviation operations. In December of 2003, modafinil was first authorized for use in extended Air Force dual-crew bomber missions, and in August 2006, it was authorized for extended fighter missions as well. Although modafinil has not been as well-tested in operational contexts as dextroamphetamine, two studies to date have shown that it is capable of significantly attenuating fatigue-related decrements in pilot performance throughout 30–40 h of continuous wakefulness.^{132,133} The attractiveness of modafinil over dextroamphetamine is that it has relatively low abuse potential, and it produces few cardiovascular side effects. However, both medications can be extremely valuable in operations devoid of sleep opportunities. A longer-acting version of modafinil (armodafinil or NuVigil®) was approved for the treatment of excessive daytime sleepiness associated with obstructive sleep apnea, narcolepsy, and shift work sleep disorder in 2007. Eventually, armodafinil may be authorized for use in military aviation or other environments, but further research will first be required. Other pharmacological alertness enhancers are no doubt being developed and tested at the time of this writing. As these become available, they will be considered for a variety of applications in which sleepiness threatens health and safety. However, for a variety of reasons, behavioral and/or administrative counter-fatigue strategies probably will continue to be preferred over drug-based remedies.

The importance of fatigue-management education

Education about the dangers of fatigue, the causes of sleepiness on the job, and the importance of

sleep and proper sleep hygiene is one of the keys to addressing fatigue in operational contexts. Ultimately, individual workers, those scheduling work periods, and supervisors/managers 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 1–2 h of sleep restriction (operationalized as time in bed) almost immediately degrade vigilance and performance in subsequent duty periods.^{9,134} Thus, educational programs for the general workforce should educate people on the central points conveyed in this review paper. Namely, they should understand that: (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. The strategies were briefly summarized here, but more detailed guidance is available elsewhere on each technique.

A promising future direction: fatigue-detection technologies

Obviously, if it were possible to objectively measure an individual's level of fatigue, an accurate assessment of the immediate impact of fatigue on performance could be made. The need for a real-time fatigue-detection device, particularly for drivers, has been realized for several years due to fatigue's persistence as a hazard and its insidious effects on alertness, judgment, and cognition.¹³⁵ Although there currently is not a valid and reliable real-time alertness monitor, there are tools (such as the Archinoetics wrist-worn Sleep Bracelet program) that can unobtrusively track the work/rest schedules and sleep quality of employees, process these data through fatigue/risk prediction models, and develop group or individual reports to warn employers or employees against impending fatigue-related performance failures. In addition, there is ongoing work to develop fatigue-detection technologies based on parameters such as the physiology and facial characteristics of drivers (EEG, eye-gaze, facial feature recognition),

driver vehicle control behavior (steering, speed, lane deviations), and physical driver characteristics (head nodding, percent eye closure, wrist inactivity). Current technologies also integrate several detection techniques such as percent eye closure (PERCLOS) and facial feature recognition,¹³⁶ steering wheel grip force, lateral position, steering wheel angle, head position, and environmental factors such as time of day and weather.¹³⁷ Once developed for driving applications, such monitors could be used in other sectors.

Research over the past 40 years has established the electroencephalogram (EEG) technique as a highly valuable neural index of cognition along with event-related brain potentials (ERPs).¹³⁸ EEG changes that occur simultaneously in the delta, theta, alpha, and beta bands have been found to correlate with various other fatigue metrics, but such correlations are typically based on post hoc analyses. EEG signals and analyses are now being incorporated into a real-time technological countermeasures device for fatigue detection.¹³⁹ The B-alert® system,¹⁴⁰ has, to a degree, been validated as an alertness-indicator for driver fatigue¹⁴¹ and has also demonstrated some sensitivity to individual fatigue vulnerability.¹⁴² The B-alert® system can also be implemented in combination with ERPs to capture a more detailed image of information processing in the brain.¹⁴⁰ Researchers (e.g., Ref. 143) 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 better real-time monitoring.

A number of other promising devices are in the validation phase for real-time, non-invasive detection of operator fatigue. These include devices that automatically assess the percentage of eye closure such as the Eye-Com (Eye-Com Corp., Reno, NV), a biosensor that measures over 20 oculomotor metrics involving monocular or binocular movement of the eyelid, eyeball and pupil to create an assessment of individual alertness. One aspect of the Eye-Com analysis, the PERCLOS metric, has been validated as an index of lapses in attention with correlations ranging from 0.8 to 0.9 with psychomotor vigilance behavior.¹⁴⁴

Off-line analyses of vehicle control parameters such as speed, speed variability, steering variability, and the lateral position of the vehicle have been found to be highly correlated with measures of driver alertness.^{145–148} However, a real-time fatigue-detection device based on vehicle control

parameters has not been developed and proven to date.¹⁴⁸ A more complex system that incorporates vehicle control parameters with physiological metrics combined through a neural network algorithm is currently under validation and appears to be promising (The SAVE Project; ¹³⁷).

Facial feature recognition technology is also currently being investigated for use in a fatigue-detection device.¹⁵⁰ 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 et al.¹³⁶ have incorporated other critical factors such as PERCLOS and circadian variations into facial feature recognition technology for the development of a real-time, non-intrusive monitoring device for driver fatigue. Additional fatigue-detection metrics that are somewhat comparable to EEG techniques 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 min¹⁵¹); and a device that assesses head position “XYZ” data analyzed over various time periods to signify micro-nods or micro-sleeps.¹⁵² For a more comprehensive review of available and developing fatigue-detection technologies, please see Hartley et al.,¹⁴⁹ Krueger¹⁵³ and Haworth et al.¹⁵⁴

Conclusion and summary

Fatigue/sleepiness in modern society is both a personal and an occupational risk factor. Insufficient sleep from self-imposed sleep restriction, intense work schedules, rotating shifts, jet lag, and other factors unfortunately are constantly challenging the ability of humans to adapt, and when adequate adaptation fails, safety, performance, and general well-being suffer. The scientific literature is replete with evidence that excessive sleepiness in the workplace and on the highways is a serious hazard. However, as discussed in this review, there are strategies that can mitigate the impact of fatigue in real-world settings. Among these are pharmacological countermeasures, attention to proper nap and sleep scheduling (with careful consideration of circadian rhythms), use of enhancing posture manipulations, introduction of appropriately timed rest breaks, employment of computerized scheduling and monitoring tools, and fatigue-detection technologies, all of which can be (or in the case of fatigue-detection technologies, soon can be) implemented in the workplace to reduce performance and safety hazards. Improving the general knowledge about

the effects of fatigue and initiating efforts to employ scientifically proven alertness-management strategies ultimately can safeguard the quality, productivity, and safety of our present and future work force.

Research agenda

The present review highlights future research areas:

1. A reliable indicator of individual fatigue susceptibility needs to be identified to allow for the development of individually tailored fatigue-management strategies.
2. The effectiveness of new slow-wave sleep-inducing medications for optimizing the benefits of shorter-duration sleep periods should be evaluated.
3. A non-intrusive, real-time fatigue-detection device that is reliable and capable of predicting fatigue-related impairment is urgently needed.

References

1. Kleitman N. Duration of sleep. In: *Sleep and wakefulness*. Chicago: University of Chicago Press; 1963. p. 114–21.
2. National Sleep Foundation. 2005 sleep in America poll. Washington: National Sleep Foundation; 2005.
3. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. *Arch Gen Psychiat* 2002;59:131–6.
4. Dinges DF, Rogers NL, Baynard MD. Chronic sleep deprivation. In: Kryger MH, Roth T, Dement WC, editors. *Principles and practice of sleep medicine*. Philadelphia: Elsevier; 2005. p. 67–76.
5. Roehrs T, Roth T. Sleep and pain: interaction of two vital functions. *Sem Neurol* 2005;25(1):106–16.
6. Leo-Chiong TL. *Sleep: a comprehensive handbook*. Hoboken: Wiley; 2006.
7. Bjerner B, Swensson A. Shiftwork and rhythm. *Acta Med Scand* 1953;278:102–7.
8. Akerstedt T. Shiftwork and disturbed sleep/wakefulness. *Occup Med* 2003;53:89–94.
- *9. 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(2):117–26.
10. Banks S, Dinges DF. Behavioral and physiological consequences of sleep restriction. *J Clin Sleep Med* 2007;3(5):519–28.
11. Bonnet MH. Sleep deprivation. In: Kryger M H, Roth T, Dement WC, editors. *Principles and practice of sleep medicine*. 2nd ed. Philadelphia: W.B. Saunders Company; 1994. p. 50–67.
12. Dinges DF. Probing the limits of functional capability: the effects of sleep loss on short-duration tasks. In: Broughton RJ, Ogilvie RD, editors. *Sleep, arousal, and performance*. Boston: Birkhauser; 1992. p. 177–88.
13. Horne JA. Sleep loss and “divergent” thinking ability. *Sleep* 1988;11:528–36.
14. Horne JA. Human sleep, sleep loss and behaviour: implications for prefrontal cortex and psychiatric disorder. *Br J Psychiatry* 1993;162:413–9.
15. Koslowsky M, Babkoff H. Meta-analysis of the relationship between total sleep deprivation and performance. *Chronobiol Int* 1992;9(2):132–6.
16. Naitoh P. Sleep deprivation in humans. In: Venables PH, Christie MJ, editors. *Research in psychophysiology*. London: Wiley; 1975.
17. Thomas M, Sing HC, Belenky G. Cerebral glucose utilization during task performance and prolonged sleep loss. *J Cerebr Blood F Met* 1993;13(1):S351.
18. Dinges DF, Pack F, Williams K, Gillen KA, Powell JW, Ott GE, et al. Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 h per night. *Sleep* 1997;20(4):267–77.
19. Blagrove M, Alexander C, Horne JA. The effects of chronic sleep reduction on the performance of cognitive tasks sensitive to sleep deprivation. *Appl Cogn Psychol* 1995;9(1):21–40.
20. Carskadon MA, Dement WC. Cumulative effects of sleep restriction on daytime sleepiness. *Psychophysiology* 1981;18:107–13.
21. Carskadon MA, Dement WC. Nocturnal determinants of daytime sleepiness. *Sleep* 1982;5:S73–81.
22. Frazier TW, Benignus VA, Every MG, Parker Jr. JF. Effects of a 72 h partial sleep deprivation on human behavioral and physiological response measures. Final report on US Army Medical Research and Development Command (contract no. DADA 17-69-C-9010). Department of the Army, Washington, DC, 1971.
23. Gillberg M, Akerstedt T. Sleep restriction and SWS suppression: effects on day time alertness and night time recovery. *J Sleep Res* 1994;3(3):144–51.
24. Hamilton P, Wilkinson RT, Edwards RS. A study of four days partial sleep deprivation. In: Colquhoun WP, editor. *Aspects of human efficiency*. London: English Universities Press; 1972.
25. Herscovitch J, Broughton R. Sensitivity of the Stanford sleepiness scale to the effects of cumulative partial sleep deprivation and recovery oversleeping. *Sleep* 1981;4:83–92.
26. Herscovitch J, Stuss D, Broughton R. Changes in cognitive processing following short term cumulative partial sleep deprivation and recovery oversleeping. *J Clin Neuropsychol* 1980;2:301–19.
27. Rosenthal L, Roehrs TA, Rosen A, Roth T. Level of sleepiness and total sleep time following various time in bed conditions. *Sleep* 1993;16:226–32.
28. Taub JM, Berger RT. Performance and mood following variations in the length and timing of sleep. *Psychophysiology* 1973;10:559–70.
29. Tilley AJ, Wilkinson RT. The effects of a restricted sleep regime on the composition of sleep and on performance. *Psychophysiology* 1984;22:406–12.

*The most important references are denoted by an asterisk.

30. Webb WB, Agnew HW. Sleep: effects of a restricted regime. *Science* 1965;150:1745–7.
31. Wilkinson RT. Sleep deprivation: performance tests for partial and selective sleep deprivation. Abt LE, Reiss BF, editors. *Progress in clinical psychology*, vol. 8. New York: Grune & Stratton; 1969.
32. Balkin T, Thorne D, Sing H, Redmond D, Wesensten N, Williams J, et al. Effects of sleep schedules on commercial motor vehicle driver performance. DOT report no. DOT-MC-00-133. Department of Transportation Federal Motor Carrier Administration, Washington, DC, 2000.
33. Carskadon MA, Roth T. Sleep restriction. In: Monk TH, editor. *Sleep, sleepiness and performance*. New York: Wiley; 1991.
34. Arnedt JT, Wilde JS, Munt PW, Maclean AW. Simulated driving performance following prolonged wakefulness and alcohol consumption: separate and combined contributions to impairment. *J Sleep Res* 2000;9:233–41.
35. Arnedt JT, Wilde JS, Munt PW, Maclean AW. How do prolonged wakefulness and alcohol compare in the decrements they produce on a simulated driving task? *Accid Anal Prev* 2001;33:337–44.
- *36. Dawson D, Reid K. Fatigue, alcohol, and performance impairment. *Nature* 1997;388:235.
37. Lamond N, Dawson D. Quantifying the performance impairment associated with fatigue. *J Sleep Res* 1999;8:255–62.
38. Falletti MG, Maruff P, Collie A, Darby DG, McStephen M. Qualitative similarities in cognitive impairment associated with 24 h of sustained wakefulness and a blood alcohol concentration of 0.05%. *J Sleep Res* 2003;12:165–274.
39. Van Dongen HPA, Dinges DF. Circadian rhythms in sleepiness, alertness, and performance. In: Kryger MH, Roth T, Dement WC, editors. *Principles and practice of sleep medicine*. Philadelphia: Elsevier; 2005. p. 435–43.
- *40. Folkard S, Tucker P. Shift work, safety and productivity. *Occup Med* 2003;53:95–101.
41. Samel A, Wegmann HM, Vejvoda M. Aircrew fatigue in long-haul operations. *Accid Anal Prev* 1997;29(4):439–52.
42. 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(1):82–106.
43. Dinges DF, Graeber RC, Connell LJ, Rosekind MR, Powell JW. Fatigue-related reaction time performance in long-haul flight crews. *Sleep Res* 1990;19:117.
44. Neri DF, Oyung RL, Colletti LM, Mallis MM, Tam PY, Dinges DF. Controlled activity as a fatigue countermeasure on the flight deck. *Aviat Space Environ Med* 2002;73(7):654–64.
45. Moore-Ede M. Aviation safety and pilot error. In: *The twenty-four-hour society: understanding human limits in a world that never stops*. Reading, MA: Addison-Wesley Publishing Company; 1993. p. 81–96.
46. Rosekind MR. Underestimating the societal costs of impaired alertness: safety, health and productivity risks. *Sleep Med* 2005;6(Suppl 1):S21–5.
47. Spurgeon A. Working time: its impact on safety and health. International Labour Office report. Geneva: International Labour Organization; 2003.
48. Dorrian J, Hussey F, Dawson D. Train driving efficiency and safety: examining the cost of fatigue. *J Sleep Res* 2007;16(1):1–11.
49. National Highway Traffic Safety Administration. NHTSA vehicle safety rulemaking and supporting research priorities 2005–2009. 2005 <<http://www.nhtsa.gov/cars/rules/rulings/PriorityPlan-2005.html>>.
50. Kirsch AD. Report on the statistical methods employed by the US federal aviation administration in its cost/benefit analysis of the proposed flight crewmember duty period limitations, flight time limitations and rest requirements. Report no.: Docket no. 28081. Washington, DC, 1996.
51. Barger LK, Ayas NT, Cade BE, Cronin JW, Rosner B, Speizer FE, et al. Impact of extended-duration shifts on medical errors, adverse events, and attentional failures. *PLoS Med* 2006;3(12):e487.
52. Dembe AE, Erickson JB, Delbos RG, Banks SM. The impact of overtime and long work hours on occupational injuries and illnesses: new evidence from the United States. *Occup Environ Med* 2005;62(9):588–97.
- *53. Akerstedt TE. Work hours, sleepiness and accidents. *J Sleep Res* 1995;4(2):15–22.
54. Van Dongen HPA, Baynard MD, Nosker GS, Dinges DF. Repeated exposure to total sleep deprivation: substantial trait differences in performance impairment among subjects. *Sleep* 2002;25:121–3.
55. Wilkinson RT. Individual differences in response to the environment. *Ergonomics* 1974;17:745–56.
56. Morgan BB, Winne PS, Dugan J. The range and consistency of individual differences in continuous work. *Hum Factors* 1980;22(3):331–40.
57. Caldwell JA, Caldwell JL, Smith JK, Alvarado LY, Heintz TR, Mylar JT, et al. The efficacy of modafinil for sustaining alertness and simulator flight performance in F-117 pilots during 37 hours continuous wakefulness. Report no. AFRL-BE-BR-TR-2004-0003. Washington, DC: United States Air Force Research Laboratory; 2004.
58. Horne JA, Ostberg A. self-assessment questionnaire to determine morningness–eveningness in human circadian rhythms. *Int J Chronobiol* 1976;4(2):97–110.
59. Mallis MM, Neri DF, Oyung R, Colletti L, Nguyen T, Dinges DF. Factors associated with behavioral alertness in pilots flying simulated night flights. *Sleep* 2001;24:A123–4.
60. Blagrove M, Akehurst L. Personality and the modulation of effects of sleep loss on mood and cognition. *Pers Individ Differ* 2001;30:819–28.
61. Belenky G, Bliese P, Wesensten N, Balkin T. Variation in sensitivity to sleep restriction as a function of age revealed by growth modeling analysis. *Sleep* 2003;26:A202.
62. Caldwell JA, Mu Q, Smith JK, Mishory A, George M, Caldwell JL, et al. Are individual differences in fatigue vulnerability related to baseline differences in cortical activation? *Behav Neurosci* 2005;119(3):694–707.
63. 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 Section II, Suppl):A44–53.
64. Belyavin A, Spencer MB. Modeling performance and alertness: the QinetiQ approach. *Aviat Space Environ Med* 2004;75(3 Section II, Suppl):A93–A103.
65. Mallis MM, Mejdal S, Lee SP, Van Dongen H, Dinges DF. Foundation for the development of an Astronaut Scheduling Assistant. In: *Space habitation research & technology proceedings*. Houston: Division of Space Life Sciences, Universities Space Research Associates; 2004.
66. Bonnet MH, Arand DL. Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Med Rev* 2003;7(4):293–5.
67. 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.

68. Rosenberg RP. Sleep maintenance insomnia: strengths and weaknesses of current pharmacologic therapies. *Ann Clin Psychiat* 2006;18:49–56.
69. Simons R, Koerhuis CL, Valk PJ, Van den Oord MH. Usefulness of temazepam and zaleplon to induce afternoon sleep. *Mil Med* 2006;171:998–1001.
70. Greenblatt DJ, Zammit G, Harmatz J, Legangneux E. Zolpidem modified-release demonstrates sustained and greater pharmacodynamic effects from 3 to 6 h postdose as compared with standard zolpidem in healthy adult subjects. *Sleep* 2005;28(Suppl):A245.
71. Leese P, Maier G, Vaikus L, Akybekova E. Esopiclone: pharmacokinetic and pharmacodynamic effects of a novel sedative hypnotic after daytime administration in healthy subjects. *Sleep* 2002;25(Suppl):A45.
72. 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.
73. Dooley M, Plosker GL. Zaleplon: a review of its use in the treatment of insomnia. *Drugs* 2000;60:413–45.
74. Whitmore JN, Fischer JR, Storm WF. Hypnotic efficacy of zaleplon for daytime sleep in rested individuals. *Sleep* 2004;27:895–8.
75. * Lieberman JA. Update on the safety considerations in the management of insomnia with hypnotics: incorporating modified-release formulations into primary care. *Prim Care Comp J Clin Psychiat* 2007;9:25–31.
76. Ebert B, Wafford KA, Deacon S. Treating insomnia: current and investigational pharmacological approaches. *Pharmacol Ther* 2006;112:612–29.
77. Lund J, Lundahl J, Nielsen GM, Mengel H. The pharmacokinetic properties of gaboxadol, a new hypnotic, in young and elderly men. *Sleep* 2005;28:A48.
78. Deacon S, Staner L, Staner C, Vorstrup S, Lundahl J. Acute administration of gaboxadol improves sleep initiation and maintenance in patients with primary insomnia. *Sleep* 2005;28:A240.
79. 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.
80. Hadley S, Petry JJ. Valerian. *Am Fam Physician* 2003;67:1755–8.
81. Monti JM. Primary and secondary insomnia: prevalence, causes and current therapeutics. *Curr Med Chem—Cent Nerv Syst Agents* 2004;4:119–37.
82. Wing YK. Herbal treatment of insomnia. *Hong Kong Med J* 2001;7:392–402.
83. Van den Heuvel CJ, Ferguson SA, Macchi MM, Dawson D. Melatonin as a hypnotic: con. *Sleep Med Rev* 2005;9:71–80.
84. Zhdanova IV. Melatonin as a hypnotic: pro. *Sleep Med Rev* 2005;9:51–65.
- *85. 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.
86. Arnedt J. Melatonin characteristics, concerns, and prospects. *J Biol Rhythms* 2005;20:291–303.
87. 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 Psychol* 2007;99(4):331–41.
88. Burgess HJ, Sharkey KM, Eastman CI. Bright light, dark and melatonin can promote circadian adaptation in night shift workers. *Sleep Med Rev* 2002;6(5):407–20.
- *89. Skene DJ, Arnedt J. Human circadian rhythms: physiological and therapeutic relevance of light and melatonin. *Ann Clin Biochem* 2006;43(5):344–53.
90. Waterhouse J, Reilly T, Atkinson G, Edwards B. Jet lag: trends and coping strategies. *Lancet* 2007;369(9567):1117–29.
91. Arnedt JT, Skene DJ. Melatonin as a chronobiotic. *Sleep Med Rev* 2005;9:25–39.
92. Touitou Y, Bogdan A. Promoting adjustment of the sleep-wake cycle by chronobiotics. *Physiol Behav* 2007;90:294–300.
93. Lewy AJ, Emens J, Jackman A, Yuhas K. Circadian uses of melatonin in humans. *Chronobiol Int* 2006;23:403–12.
94. Wirz-Justice A, Armstrong SM. Melatonin. Nature's soporific? *J Sleep Res* 1996;5:137–41.
95. Daan S, Lewy AJ. Scheduled exposure to daylight: a potential strategy to reduce “jet lag” following transmeridian flight. *Psychopharmacol Bull* 1984;20(3):566–8.
96. 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(8):733–43.
97. Samel A, Wegmann HM. Bright light: a countermeasure for jet lag? *Chronobiol Int* 1997;14(2):173–83.
98. Duffy JF, Wright KP. Entrainment of the human circadian system by light. *J Bio Rhythms* 2005;20:326–38.
99. 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 h out of phase with the PRC to light. *Chronobiol Int* 1998;15(1):71–83.
100. 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.
101. 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.
102. Eastman EI, 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.
103. Reid KJ, Burgess HJ. Circadian rhythm sleep disorders. *Prim Care* 2005;32:449–73.
104. Stone BM, Turner C. Promoting sleep in shiftworkers and intercontinental travelers. *Chronobiol Int* 1997;14(2):133–43.
105. Waterhouse J, Reilly T, Atkinson G. Jet lag. *Lancet* 1997;350:1611–6.
106. Rosa RR, Bonnett MH. Performance and alertness on 8 and 12-h rotating shifts at a natural gas utility. *Ergonomics* 1993;36:1177–93.
107. Morisseau DS, Persensky JJ. A human factors focus on work hours, sleepiness and accident risk. In: Akerstedt T, Kecklund G, editors. *Work hours, sleepiness and accidents*. Stockholm: IPM and Karolinska Institute; 1994. p. 94–7.
108. 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 Meth Instr C* 1985;17:592–603.
- *109. Pigeau R, Naitoh P, Buguet A, McCann C, Baranski J, Taylor M, et al. Modafinil, d-amphetamine, and placebo during 64 h of sustained mental work. I. Effects on mood, fatigue, cognitive performance and body temperature. *J Sleep Res* 1995;4:212–28.
110. Bonnet MH. Dealing with shift work: physical fitness, temperature, and napping. *Work Stress* 1990;4(3):261–74.

111. Bonnet MH. The effect of varying prophylactic naps on performance, alertness and mood throughout a 52-h continuous operation. *Sleep* 1991;14(4):307–15.
112. Dinges DF, Whitehouse WG, Orne EC, Orne MT. The benefits of a nap during prolonged work and wakefulness. *Work Stress* 1988;2(2):139–53.
113. Matsumoto K, Harada M. The effect of night-time naps on recovery from fatigue following night work. *Ergonomics* 1994;37(5):899–907.
114. Rogers AS, Spencer MB, Stone BM, Nicholson AN. The influence of a 1 h nap on performance overnight. *Ergonomics* 1989;32(10):1193–205.
115. Rosa RR. Napping at home and alertness on the job in rotating shift workers. *Sleep* 1993;16(8):727–35.
116. 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.
117. Webb W. The proximal effects of two and four hour naps within extended performance without sleep. *Psychophysiology* 1987;24(4):426–9.
118. 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(4):355–65.
119. Brooks A, Lack L. A brief afternoon nap following nocturnal sleep restriction: which nap duration is most recuperative? *Sleep* 2006;29:831–40.
120. Smith-Coggins R, Howard SK, Mac DT, Wang C, Kwan S, Rosekind MR, et al. Improving alertness and performance in emergency department physicians and nurses: the use of planned naps. *Ann Emerg Med* 2006;48:596–604.e1–3.
121. 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. Technical memorandum 103884. Moffett Field, CA: NASA; 1994.
- *122. Hum Factors 2005;47(2):360–77.
123. Dinges DF. Differential effects of prior wakefulness and circadian phase on nap sleep. *Electroenceph Clin Neurophysiol* 1986;64:224–7.
124. Lavie P. Ultrashort sleep-waking schedule. III. “Gates” and “forbidden zones” for sleep. *Electroenceph Clin Neurophysiol* 1986;63:414–25.
125. Gillberg M. The effects of two alternative timings of a one-hour nap on early morning performance. *Biol Psychol* 1984;19:45–54.
126. Dinges DF, Orne MT, Orne EC. Assessing performance upon abrupt awakening from naps during quasi-continuous operations. *Behav Res Meth Instr C* 1985;17(1):37–45.
127. Nicholson AN, Stone BM. Influence of back angle on the quality of sleep in seats. *Ergonomics* 1987;30(7):1033–41.
128. Cole RJ. Postural baroreflex stimuli may affect EEG arousal and sleep in humans. *J Appl Phys* 1989;67(6):2369–75.
129. Caldwell JA, Prazinko BF, Caldwell JL. Body posture affects electroencephalographic activity and psychomotor vigilance task performance in sleep-deprived subjects. *Clin Neurophysiol* 2003;114(1):23–31.
130. Committee on Military Nutrition Research. *Caffeine for the sustenance of mental task performance: formulations for military operations*. Washington, DC: National Academy Press; 2001.
131. Caldwell JA, Caldwell JL, Darlington KK. Utility of dextroamphetamine for attenuating the impact of sleep deprivation in pilots. *Aviat Space Environ Med* 2003;74(11):1125–34.
132. Caldwell JA, Caldwell JL, Smythe NK, Hall KK. A double-blind, placebo-controlled investigation of the efficacy of modafinil for sustaining the alertness and performance of aviators: a helicopter simulator study. *Psychopharmacology* 2000;150:272–82.
133. Caldwell JA, Caldwell JL, Smith JK, Brown DL. Modafinil’s effects on simulator performance and mood in pilots during 37 h without sleep. *Aviat Space Environ Med* 2004;75:777–84.
134. 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):1–12.
135. Brown ID. Prospectus for technological countermeasures against driver fatigue. *Accid Anal Prev* 1997;29(4):525–31.
136. Ji Q, Zhu Z, Lan P. Real-time nonintrusive monitoring and prediction of driver fatigue. *IEEE Trans Veh Technol* 2004;53(4):1052–68.
137. Brookhuis K, de Waard D, Peters B, Bekiaris E. SAVE-system for detection of driver impairment and emergency handling. *IATSS Res* 1998;22(2):37–42.
138. Fabiani M, Gratton G, Coles MG. Event-related brain potentials. In: Cacioppo JT, Tassinari LG, Berntson GG, editors. *Handbook of psychophysiology*. Cambridge, England: Cambridge University Press; 2000. p. 53–84.
139. Lal SKL, Craig A. Reproducibility of the spectral components of the electroencephalogram during driver fatigue. *Int J Psychophysiol* 2005;55(2):137–43.
140. 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 Int* 2004;17(2):151–70.
141. 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. Paper presented at the 29th annual meeting of the Society for Neuroscience, Miami, FL, October 1999.
142. Levendowski DJ, Olmstead RE, Konstantinovic ZR, Berka C, Westbrook PR. Detection of electroencephalographic indices of drowsiness in realtime using a multi-level discriminant function analysis. *Sleep* 2000;23(Abstr Suppl 2):A243–4.
143. Lin C, Wu R, Jung T, Liang S, Huang T. Estimating driving performance based on EEG spectrum analysis. *J Appl Signal Process* 2005;19:3165–74.
144. 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. Report no. DOT HS 808 762, National Highway Traffic Safety Administration, 1998.
145. Akerstedt T, Peters B, Anund A, Kecklund G. Impaired alertness and performance driving home from the night shift: a driving simulator study. *J Sleep Res* 2005;14:17–20.
- *146. Balkin TJ, Bliese PD, Belenky G, Sing H, Thorne DR, Thomas M, et al. Comparative utility of instruments for monitoring sleepiness-related performance decrements in the operational environment. *J Sleep Res* 2004;13:219–27.
147. O’Hanlon JF, Kelly GR. Comparison of performance and physiological changes between drivers who perform well

- and poorly during prolonged vehicular operation. In: *NATO conference series*, vol. 3, 1977. p. 87–100.
148. Thiffault P, Bergeron J. Fatigue and individual differences in monotonous simulated driving. *Pers Indiv Differ* 2003;34:159–76.
149. Hartley L, Horberry T, Mabbott N, Krueger GP. *Review of fatigue detection and prediction technologies*. National Road Transport Commission; 2000.
150. Gu H, Ji Q. An automated face reader for fatigue detection. In: *Proceedings of the sixth IEEE international conference on face recognition and gesture recognition (FGR'04)*, 2004.
151. 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.
152. Kithil PW, Jones RD, MacCuish J. Development of driver alertness detection system using overhead capacitive sensor array. White Paper, 2006. Available at <http://internet.cybermesa.com/~roger_jones/drowsy.htm>.
153. Krueger G. Technologies and methods for monitoring driver alertness and detecting driver fatigue: a review applicable to long-haul truck driving. Technical report for American Transportation Research Institute and Federal Motor Carrier Safety Administration, 2004.
154. Haworth NL, Heffernan CJ, Horne EJ. Fatigue in truck accidents. Report number 3, Monash University Accident Research Centre, 1989.

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